Sladen Library
Great Research • Great Care • Start Here

Henry Ford Health System

Henry Ford Health System Publication List – November 2020

This bibliography aims to recognize the scholarly activity and provide ease of access to journal articles, meeting abstracts, book chapters, books and other works published by Henry Ford Health System personnel. Searches were conducted in PubMed, Embase, and Web of Science during the month, and then imported into EndNote for formatting. There are **138 unique citations** listed this month, with **11 articles** and **5 conference abstracts on COVID-19**. Articles are listed first, followed by conference abstracts, books and book chapters, and a bibliography of publications on COVID-19**.** Because of various limitations, this does not represent an exhaustive list of all published works by Henry Ford Health System authors.

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 HFHS institutional repository.

Articles

Anesthesiology

Al-Darzi W, **Alalwan Y**, **Askar F**, **Sadiq O**, **Venkat D**, **Gonzalez H**, **Galusca D**, **Yoshida A**, and **Jafri SM**. Risk Factors and Outcomes of Intracardiac Thrombosis During Orthotopic Liver Transplantation. *Transplant Proc* 2020; Epub ahead of print. PMID: 33246584. Full Text

Division of Cardiology, Henry Ford Hospital, Detroit, Michigan. Electronic address: waleed.aldarzi@gmail.com.
Department of Internal Medicine, Henry Ford Hospital, Detroit, Michigan.
Department of Internal Medicine, Henry Ford Hospital, Detroit, Michigan; School of Medicine, Wayne State University, Detroit, Michigan.
Division of Gastroenterology, Henry Ford Hospital, Detroit, Michigan.
School of Medicine, Wayne State University, Detroit, Michigan; Division of Gastroenterology, Henry Ford Hospital, Detroit, Michigan.
Department of Anesthesiology, Henry Ford Hospital, Detroit, Michigan.
Transplant and Hepatobiliary Surgery, Henry Ford Hospital, Detroit, Michigan.

BACKGROUND: Intracardiac thrombosis incidence during orthotopic liver transplantation is estimated at 0.36% to 6.2% with mortality up to 68%. We aimed to evaluate risk factors and outcomes related to intracardiac thrombosis during orthotopic liver transplantation. MATERIALS AND METHODS: A comprehensive retrospective data review of 388 patients who underwent orthotopic liver transplantation at an urban transplant center from January 2013 to October 2016 was obtained. RESULTS: Six patients were found to have documented intracardiac thrombosis; 4 cases were recognized during the reperfusion stage and 1 during pre-anhepatic stage. All allografts were procured from decreased donors with a median donor age of 44 years (interquartile range, 35.25-49.75) and the cause of death was listed as cerebrovascular accident in 5 donors. Preoperative demographic, clinical, laboratory, and historical risk factors did not differ in patients with thrombosis. None had a prior history of trans-jugular intrahepatic portosystemic shunt or gastrointestinal bleeding. Three patients had renal injury, but no intraoperative hemodialysis was performed. Transesophageal echocardiographic findings included elevated pulmonary

artery pressure (1/6), right ventricular strain (1/6), and pulmonary artery thrombus (1/6). Three patients died intraoperatively. Tissue plasminogen activator alone was given to 1 patient who did not survive, intravenous heparin only to 1 patient with resolution, and a combination of both was used in 2 patients with clot resolution achieved. CONCLUSION: Cardiac thrombosis should be considered in patients having hemodynamic compromise during liver transplantation. Transesophageal echocardiography is a useful diagnostic tool. Intracardiac thrombosis treatment remains challenging; however, using both thrombolytics and heparin could achieve better results.

Anesthesiology

Chhina AK, **Loyd GE**, **Szymanski TJ**, **Nowak KA**, **Peruzzi WT**, **Yeldo NS**, **Han X**, **Kerzabi LS**, **Galusca DM**, **Cazacu S**, **Brodie C**, and **Penning DH**. Frequency and Analysis of Unplanned Extubation in Coronavirus Disease 2019 Patients. *Crit Care Explor* 2020; 2(12):e0291. PMID: 33251520. Full Text

Department of Anesthesiology, Pain Management and Perioperative Medicine, Henry Ford Hospital, Detroit, MI.
Department of Public Health Sciences, Henry Ford Hospital, Detroit, MI.
Department of Neurosurgery, Henry Ford Hospital, Detroit, MI.

OBJECTIVES: To determine if patients with coronavirus disease 2019 had a greater number of unplanned extubations resulting in reintubations than in patients without coronavirus disease 2019. DESIGN: Retrospective cohort study comparing the frequency of unplanned extubations resulting in reintubations in a group of coronavirus disease 2019 patients to a historical (noncoronavirus disease 2019) control group. SETTING: This study was conducted at Henry Ford Hospital, an academic medical center in Detroit, MI. The historical noncoronavirus disease 2019 patients were treated in the 68 bed medical ICU. The coronavirus disease 2019 patients were treated in the coronavirus disease ICU, which included the 68 medical ICU beds, 18 neuro-ICU beds, 32 surgical ICU beds, and 40 cardiovascular ICU beds, as the medical ICU was expanded to these units at the peak of the pandemic in Detroit, MI. PATIENTS: The coronavirus disease 2019 cohort included patients diagnosed with coronavirus disease 2019 who were intubated for respiratory failure from March 12, 2020, to April 13, 2020. The historic control (noncoronavirus disease 2019) group consisted of patients who were admitted to the medical ICU in the year spanning from November 1, 2018 to October 31, 2019, with a need for mechanical ventilation that was not related to surgery or a neurologic reason. INTERVENTIONS: None. MEASUREMENTS AND MAIN RESULTS: To identify how many patients in each cohort had unplanned extubations, an electronic medical records query for patients with two intubations within 30 days was performed, in addition to a review of our institutional quality and safety database of reported self-extubations. Medical charts were manually reviewed by board-certified anesthesiologists to confirm each event was an unplanned extubation followed by a reintubation within 24 hours. There was a significantly greater incidence of unplanned extubations resulting in reintubation events in the coronavirus disease 2019 cohort than in the noncoronavirus disease 2019 cohort (coronavirus disease 2019 cohort: 167 total admissions with 22 events-13.2%; noncoronavirus disease 2019 cohort: 326 total admissions with 14 events-4.3%; $p < 0.001$). When the rate of unplanned extubations was expressed per 100 intubated days, there was not a significant difference between the groups (0.88 and 0.57, respectively; $p = 0.269$). CONCLUSIONS: Coronavirus disease 2019 patients have a higher incidence of unplanned extubation that requires reintubation than noncoronavirus disease 2019 patients. Further study is necessary to evaluate the variables that contribute to this higher incidence and clinical strategies that can reduce it.

Behavioral Health Services/Psychiatry

Hoffert M, **Kerr H**, **Hegab S**, **Whitehouse S**, **Kokas M**, **MacLean L**, **Van Harn MG**, and **Baker-Genaw K**. Designing a Yoga Intervention Program to Improve Well-Being for Physician Trainees: Challenges and Lessons Learned. *Int J Yoga Therap* 2020; Epub ahead of print. PMID: 33157552. Full Text

Department of Medical Education, Henry Ford Hospital, Detroit, Mich.
Department of Dermatology, Henry Ford Hospital, Detroit, Mich.
Division of Pulmonary and Critical Care Medicine, Henry Ford Hospital, Detroit, Mich.
Behavioral Health Services, Henry Ford Hospital, Detroit, Mich.
Public Health Science Division of Biostatistics, Henry Ford Hospital, Detroit, Michigan.

Department of Medical Education and Department of Internal Medicine, Henry Ford Hospital, Detroit, Mich.

Well-being activities may help to counteract physician burnout. Yoga is known to enhance well-being, but there are few studies of yoga as an intervention for physicians in training. This prospective methodology-development study aimed to explore how to establish a yoga-based well-being intervention for physician trainees in a large urban training hospital. We aimed to identify factors that contribute to trainee participation and explore an instrument to measure changes in self-reported well-being after yoga. Cohorts included a required-attendance group, a voluntary-attendance group, and an unassigned walk-in yoga group. Weekly 1-hour yoga sessions were led by a qualified yoga instructor for 4 weeks. The seven-question Resident Physician Well-Being Index (RPWBI) was used to measure resident well-being before yoga, after 4 weeks of yoga, and 6 months post-yoga. Trainees attending each session ranged from 17 for required yoga to 0-2 for voluntary yoga, 2-9 for lunchtime walk-in yoga, and 1-7 for evening walk-in yoga. In the required-yoga group (n = 17), overall RPWBI mean scores did not change significantly across the three query times, and participation in the survey declined over time. The mean baseline RPWBI score for the required group before yoga was in the non-distressed range and answers to the seven individual questions varied. Requiring a yoga activity for medical trainees may be a good strategy for promoting participation in yoga. The RPWBI may have limited utility for measuring changes in overall group well-being after a yoga intervention.

Behavioral Health Services/Psychiatry

Miller-Matero LR, **Hamann A**, **LaLonde L**, **Martens KM**, Son J, **Clark-Sienkiewicz S**, **Sata M**, **Coleman JP**, **Hecht LM**, **Braciszewski JM**, and **Carlin AM**. Predictors of Alcohol Use after Bariatric Surgery. *J Clin Psychol Med Settings* 2020; Epub ahead of print. PMID: 33205321. Full Text

Behavioral Health, Henry Ford Health System, 1 Ford Place, 3A, Detroit, MI, 48202, USA. Lmatero1@hfhs.org.
Center for Health Policy and Health Services Research, Henry Ford Health System, Detroit, MI, USA. Lmatero1@hfhs.org.
Behavioral Health, Henry Ford Health System, 1 Ford Place, 3A, Detroit, MI, 48202, USA.
Department of Surgery, Henry Ford Health System, Detroit, MI, USA.
Wayne State University School of Medicine, Henry Ford Health System, Detroit, MI, USA.
Center for Health Policy and Health Services Research, Henry Ford Health System, Detroit, MI, USA.

Patients undergoing bariatric surgery are at risk for devloping an alcohol use disorder (AUD). The purpose of this study was to investigate pre-surgical psychosocial risk factors for post-surgical alcohol consumption and hazardous drinking. Participants (N = 567) who underwent bariatric surgery between 2014 and 2017 reported their post-surgical alcohol use. Information was collected from the pre-surgical evaluation including history of alcohol use, psychiatric symptoms, and maladaptive eating behaviors (i.e., binge eating, purging, and emotional eating). Younger age and pre-surgical alcohol use predicted post-surgical alcohol use and hazardous drinking. In addition, higher levels of depressive symptoms and maladaptive eating patterns predicted post-surgical binge drinking. Clinicians conducting pre-surgical psychosocial evaluations should be aware of the multiple risk factors related to post-surgical problematic alcohol use. Future research should evaluate whether preventive interventions for high-risk patients decrease risk for post-surgical alcohol misuse.

Behavioral Health Services/Psychiatry

Prabhakar D, **Peterson EL**, **Hu Y**, **Chawa S**, Rossom RC, Lynch FL, Lu CY, Waitzfelder BE, Owen-Smith AA, **Williams LK**, Beck A, Simon GE, and Ahmedani BK. Serious Suicide Attempts and Risk of Suicide Death. *Crisis* 2020;1-8. Epub ahead of print. PMID: 33151092. Request Article

Sheppard Pratt, Baltimore, MD, USA.
Department of Public Health Sciences, Henry Ford Health System, Detroit, MI, USA.
Center for Health Policy and Health Services Research (CHSR), Henry Ford Health System, Detroit, MI, USA.
Behavioral Health Sciences, Henry Ford Health System, Detroit, MI, USA.

Health Partners Institute, University of Minnesota, Minneapolis, MN, USA.
Center for Health Research, Kaiser Permanente Northwest, Portland, OR, USA.
Department of Population Medicine, Harvard Medical School, Boston, MA, USA.
Center for Health Research, Kaiser Permanente, Honolulu, HI, USA.
Center for Research and Evaluation, Kaiser Permanente Georgia, Atlanta, GA, USA.
Center of Individualized and Genomic Medicine Research (CIGMA), Department of Internal Medicine, Henry Ford Health System, Detroit, MI, USA.
Institute for Health Research, Kaiser Permanente Colorado, Denver, CO, USA.
Health Research Institute, Kaiser Permanente, Seattle, WA, USA.

Background: In the US, more than one million people attempt suicide each year. History of suicide attempt is a significant risk factor for death by suicide; however, there is a paucity of data from the US general population on this relationship. Aim: The objective of this study was to examine suicide attempts needing medical attention as a risk for suicide death. Method: We conducted a case-control study involving eight US healthcare systems. A total of 2,674 individuals who died by suicide from 2000 to 2013 were matched to 267,400 individuals by year and location. Results: Prior suicide attempt associated with a medical visit increases risk for suicide death by 39.1 times, particularly for women (OR = 79.2). However, only 11.3% of suicide deaths were associated with an attempt that required medical attention. The association was the strongest for children 10-14 years old (OR = 98.0). Most suicide attempts were recorded during the 20-week period prior to death. Limitations: Our study is limited to suicide attempts for which individuals sought medical care. Conclusion: In the US, prior suicide attempt is associated with an increased risk of suicide death; the risk is high especially during the period immediately following a nonlethal attempt.

Behavioral Health Services/Psychiatry

Sablaban IM, and **Sivananthan M**. Letter to the Editor: Treating Autism-Associated Sexual Compulsions with Naltrexone. *J Child Adolesc Psychopharmacol* 2020; Epub ahead of print. PMID: 33146546. Request Article

Department of Psychiatry, Wayne State University, Henry Ford Hospital, Detroit, Michigan, USA.

Cardiology and Cardiovascular Research

Al-Darzi W, **Alalwan Y**, **Askar F**, **Sadiq O**, **Venkat D**, **Gonzalez H**, **Galusca D**, **Yoshida A**, and **Jafri SM**. Risk Factors and Outcomes of Intracardiac Thrombosis During Orthotopic Liver Transplantation. *Transplant Proc* 2020; Epub ahead of print. PMID: 33246584. Full Text

Division of Cardiology, Henry Ford Hospital, Detroit, Michigan. Electronic address: waleed.aldarzi@gmail.com.
Department of Internal Medicine, Henry Ford Hospital, Detroit, Michigan.
Department of Internal Medicine, Henry Ford Hospital, Detroit, Michigan; School of Medicine, Wayne State University, Detroit, Michigan.
Division of Gastroenterology, Henry Ford Hospital, Detroit, Michigan.
School of Medicine, Wayne State University, Detroit, Michigan; Division of Gastroenterology, Henry Ford Hospital, Detroit, Michigan.
Department of Anesthesiology, Henry Ford Hospital, Detroit, Michigan.
Transplant and Hepatobiliary Surgery, Henry Ford Hospital, Detroit, Michigan.

BACKGROUND: Intracardiac thrombosis incidence during orthotopic liver transplantation is estimated at 0.36% to 6.2% with mortality up to 68%. We aimed to evaluate risk factors and outcomes related to intracardiac thrombosis during orthotopic liver transplantation. MATERIALS AND METHODS: A comprehensive retrospective data review of 388 patients who underwent orthotopic liver transplantation at an urban transplant center from January 2013 to October 2016 was obtained. RESULTS: Six patients were found to have documented intracardiac thrombosis; 4 cases were recognized during the reperfusion stage and 1 during pre-anhepatic stage. All allografts were procured from decreased donors with a median donor age of 44 years (interquartile range, 35.25-49.75) and the cause of death was listed as cerebrovascular accident in 5 donors. Preoperative demographic, clinical, laboratory, and historical risk

factors did not differ in patients with thrombosis. None had a prior history of trans-jugular intrahepatic portosystemic shunt or gastrointestinal bleeding. Three patients had renal injury, but no intraoperative hemodialysis was performed. Transesophageal echocardiographic findings included elevated pulmonary artery pressure (1/6), right ventricular strain (1/6), and pulmonary artery thrombus (1/6). Three patients died intraoperatively. Tissue plasminogen activator alone was given to 1 patient who did not survive, intravenous heparin only to 1 patient with resolution, and a combination of both was used in 2 patients with clot resolution achieved. CONCLUSION: Cardiac thrombosis should be considered in patients having hemodynamic compromise during liver transplantation. Transesophageal echocardiography is a useful diagnostic tool. Intracardiac thrombosis treatment remains challenging; however, using both thrombolytics and heparin could achieve better results.

Cardiology and Cardiovascular Research
Aurora L, **Nona P**, and **Ananthasubramaniam K**. A Pregnant Patient with Elevated Heart Rate. *Am J Med* 2020; Epub ahead of print. PMID: 33181101. Full Text

Heart and Vascular Institute, Henry Ford West Bloomfield Hospital, West Bloomfield Michigan. Electronic address: laurora1@hfhs.org.
Heart and Vascular Institute, Henry Ford West Bloomfield Hospital, West Bloomfield Michigan.

Cardiology and Cardiovascular Research
Chehab O, Morsi RZ, Kanj A, Rachwan RJ, Pahuja M, Mansour S, Tabaja H, Ahmad U, Zein SE, **Raad M**, Saker A, Alvarez P, and Briasoulis A. Incidence and clinical outcomes of nosocomial infections in patients presenting with STEMI complicated by cardiogenic shock in the United States. *Heart Lung* 2020; 49(6):716-723. PMID: 32866743. Full Text

Department of Medicine, Detroit Medical Center/Wayne State University School of Medicine, Detroit, Michigan, USA. Electronic address: omar.chehab@wayne.edu.
Department of Neurology, University of Chicago, Chicago, Illinois, USA.
Division of Pulmonary and Critical Care Medicine, Department of Medicine, Mayo Clinic, Rochester, Minnesota, USA.
Department of Cardiovascular Medicine, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin, USA.
Department of Medicine, Detroit Medical Center/Wayne State University School of Medicine, Detroit, Michigan, USA.
Division of Cardiovascular Medicine, Department of Medicine, University of Iowa Hospitals and Clinics, Iowa City, Iowa, USA.
Division of Cardiology, Department of Medicine, Henry Ford Hospital, Detroit, Michigan, USA.
Division of Cardiovascular Medicine, Department of Medicine, University of Iowa Hospitals and Clinics, Iowa City, Iowa, USA. Electronic address: alexandros-briasoulis@uiowa.edu.

OBJECTIVES: This study addresses the incidence, trends, and impact of nosocomial infections (NI) on the outcomes of patients admitted with ST-segment elevation myocardial infarction (STEMI) and cardiogenic shock (STEMI-CS) using the United States National Inpatient Sample (NIS) database. METHODS: We analyzed data from 105,184 STEMI-CS patients using the NIS database from the years 2005-2014. NI was defined as infections of more than or equal to three days, comprising of central line-associated bloodstream infection (CLABSI), urinary tract infection (UTI), hospital-acquired pneumonia (HAP), Clostridium difficile infection (CDI), bacteremia, and skin related infections. Outcomes of the impact of NI on STEMI-CS included in-hospital mortality, length of hospital stay (LOS) and costs. Significant associations of NI in patients admitted with STEMI-CS were also identified. RESULTS: Overall, 19.1% (20,137) of patients admitted with STEMI-CS developed NI. Trends of NI have decreased from 2005-2014. The most common NI were UTI (9.2%), followed by HAP (6.8%), CLABSI (1.5%), bacteremia (1.5%), skin related infections (1.5%), and CDI (1.3%). The strongest association of developing a NI was increasing LOS (7-9 days; OR: 1.99; 95% CI: 1.75-2.26; >9 days; OR: 4.51; 95% CI: 4.04-5.04 compared to 4-6 days as reference). Increased mortality risk among patients with NI was significant, especially those with sepsis-associated NI compared to those without sepsis (OR: 2.95; 95% CI: 2.72-3.20). Patients with NI were found to be associated with significantly longer LOS and higher

costs, irrespective of percutaneous mechanical circulatory support placement. CONCLUSIONS: NI were common among patients with STEMI-CS. Those who developed NI were at a greater risk of in-hospital mortality, increased LOS and costs.

Cardiology and Cardiovascular Research
Choi AD, Thomas DM, **Lee J**, Abbara S, Cury RC, Leipsic JA, Maroules C, Nagpal P, Steigner ML, **Wang DD**, Williams MC, Zeb I, Villines TC, and Blankstein R. 2020 SCCT Guideline for Training Cardiology and Radiology Trainees as Independent Practitioners (Level II) and Advanced Practitioners (Level III) in Cardiovascular Computed Tomography: A Statement from the Society of Cardiovascular Computed Tomography. *JACC Cardiovasc Imaging* 2020; Epub ahead of print. PMID: 33168479. Full Text

Division of Cardiology & Department of Radiology, The George Washington University School of Medicine, Washington, DC. Electronic address: adchoi@gwu.edu.
Heart Institute, Parkview Health, Fort Wayne, Indiana.
Department of Medicine, Division of Cardiology, Henry Ford Health System, Center for Structural Heart Disease, Detroit, Michigan.
Division of Cardiothoracic Imaging, Department of Radiology, University of Texas Southwestern Medical Center, Dallas, Texas.
Miami Cardiac and Vascular Institute, Baptist Health of South Florida, Miami, Florida and Department of Radiology, Herbert Wertheim College of Medicine, Florida International University, Miami, Florida;
Department of Radiology, Herbert Wertheim College of Medicine, Florida International University, Miami, Florida.
Department of Radiology, St. Paul's Hospital, Vancouver, British Columbia, Canada.
Department of Radiology, Naval Medical Center, Portsmouth, Virginia.
Department of Radiology, University of Iowa Hospitals and Clinics, Iowa City, Iowa.
Cardiovascular Imaging Program, Department of Radiology, Brigham and Women's Hospital, Boston, Massachusetts.
University of Edinburgh/British Heart Foundation Centre for Cardiovascular Science, Edinburgh, United Kingdom.
Division of Cardiology, West Virginia University School of Medicine, Morgantown, West Virginia.
Division of Cardiology, University of Virginia Health System, Charlottesville, Virginia.
Cardiovascular Imaging Program, Departments of Medicine (Cardiovascular Division) and Radiology, Brigham and Women's Hospital, Boston, Massachusetts.

Cardiovascular computed tomography (CCT) is a well-validated non-invasive imaging tool with an ever-expanding array of applications beyond the assessment of coronary artery disease. These include the evaluation of structural heart diseases, congenital heart diseases, peri-procedural electrophysiology applications, and the functional evaluation of ischemia. This breadth requires a robust and diverse training curriculum to ensure graduates of CCT training programs meet minimum competency standards for independent CCT interpretation. This statement from the Society of Cardiovascular Computed Tomography aims to supplement existing societal training guidelines by providing a curriculum and competency framework to inform the development of a comprehensive, integrated training experience for cardiology and radiology trainees in CCT.

Cardiology and Cardiovascular Research
Eng MH. Foreword. *Interv Cardiol Clin* 2021; 10(1):xiii. PMID: 33223112. Full Text

Center of Structural Heart Disease, Henry Ford Hospital, Clara Ford Pavilion RM 434, 2799 West Grand Boulevard, Detroit, MI 48202, USA. Electronic address: meng1@hfhs.org.

Cardiology and Cardiovascular Research
Garan AR, Kanwar M, Thayer KL, Whitehead E, Zweck E, Hernandez-Montfort J, Mahr C, Haywood JL, Harwani NM, Wencker D, Sinha SS, Vorovich E, Abraham J, **O'Neill W**, Burkhoff D, and Kapur NK. Complete Hemodynamic Profiling With Pulmonary Artery Catheters in Cardiogenic Shock Is Associated With Lower In-Hospital Mortality. *JACC Heart Fail* 2020; 8(11):903-913. PMID: 33121702. Full Text

Department of Medicine, Division of Cardiology, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, Massachusetts.
Cardiovascular Institute at Allegheny Health Network, Pittsburgh, Pennsylvania.
Department of Medicine, Division of Cardiology, The Cardiovascular Center, Tufts Medical Center, Boston, Massachusetts.
Department of Medicine, Massachusetts General Hospital, Boston, Massachusetts.
Department of Medicine, Division of Cardiology, The Cardiovascular Center, Tufts Medical Center, Boston, Massachusetts; Department of Medicine, Heinrich Heine University, Düsseldorf, Germany.
Department of Medicine, Division of Cardiology, Cleveland Clinic Florida, Weston, Florida.
Department of Medicine, Division of Cardiology, University of Washington, Seattle, Washington.
Department of Medicine, Division of Cardiology, Baylor Scott & White Advanced Heart Failure Clinic, Dallas, Texas.
Department of Medicine, Division of Cardiology, Inova Heart and Vascular Institute, Inova Fairfax Medical Center, Falls Church, Virginia.
Department of Medicine, Division of Cardiology, Northwestern Memorial Hospital, Chicago, Illinois.
Department of Medicine, Division of Cardiology, Providence Heart Institute, Portland, Oregon.
Department of Medicine, Division of Cardiology, Henry Ford Hospital, Detroit, Michigan.
Cardiovascular Research Foundation, New York, New York.
Department of Medicine, Division of Cardiology, The Cardiovascular Center, Tufts Medical Center, Boston, Massachusetts. Electronic address: Nkapur@tuftsmedicalcenter.org.

OBJECTIVES: The purpose of this study was to investigate the association between obtaining hemodynamic data from early pulmonary artery catheter (PAC) placement and outcomes in cardiogenic shock (CS). BACKGROUND: Although PACs are used to guide CS management decisions, evidence supporting their optimal use in CS is lacking. METHODS: The Cardiogenic Shock Working Group (CSWG) collected retrospective data in CS patients from 8 tertiary care institutions from 2016 to 2019. Patients were divided by Society for Cardiovascular Angiography and Interventions (SCAI) stages and outcomes analyzed by the PAC-use group (no PAC data, incomplete PAC data, complete PAC data) prior to initiating mechanical circulatory support (MCS). RESULTS: Of 1,414 patients with CS analyzed, 1,025 (72.5%) were male, and 494 (34.9%) presented with myocardial infarction; 758 (53.6%) were in SCAI Stage D shock, and 263 (18.6%) were in Stage C shock. Temporary MCS devices were used in 1,190 (84%) of those in advanced CS stages. PAC data were not obtained in 216 patients (18%) prior to MCS, whereas 598 patients (42%) had complete hemodynamic data. Mortality differed significantly between PAC-use groups within the overall cohort ($p < 0.001$), and each SCAI Stage subcohort (Stage C: $p = 0.03$; Stage D: $p = 0.05$; Stage E: $p = 0.02$). The complete PAC assessment group had the lowest in-hospital mortality than the other groups across all SCAI stages. Having no PAC assessment was associated with higher in-hospital mortality than complete PAC assessment in the overall cohort (adjusted odds ratio: 1.57; 95% confidence interval: 1.06 to 2.33). CONCLUSIONS: The CSWG is a large multicenter registry representing real-world patients with CS in the contemporary MCS era. Use of complete PAC-derived hemodynamic data prior to MCS initiation is associated with improved survival from CS.

Cardiology and Cardiovascular Research

Kang G, **So CY**, **Villablanca PA**, **Frisoli TM**, **Wang DD**, **O'Neill BP**, and **O'Neill WW**. Balloon-Assisted Valve Tracking: Atraumatic Retrieval of a Ventricularized Transcatheter Aortic Valve Prosthesis. *JACC Cardiovasc Interv* 2020; 13(21):2576-2578. PMID: 32861635. Full Text

Center for Structural Heart Disease, Henry Ford Health System, Detroit, Michigan. Electronic address: guson.kang@gmail.com.
Center for Structural Heart Disease, Henry Ford Health System, Detroit, Michigan.
Center for Structural Heart Disease, Henry Ford Health System, Detroit, Michigan. Electronic address: https://twitter.com/BillONeillMD.

Cardiology and Cardiovascular Research

Lemor A, Hernandez GA, **Basir MB**, **Patel S**, **Villablanca PA**, **Alaswad K**, and **O'Neill W**. Impact of Prior Coronary Artery Bypass Grafting in Patients ≥75 Years Old Presenting With Acute Myocardial Infarction (From the National Readmission Database). *Am J Cardiol* 2020; 135:9-16. PMID: 32866445. Full Text

Department of Cardiology, Henry Ford Hospital, Detroit, Michigan. Electronic address: alejandrolemor@outlook.com.
Department of Cardiology, University of Mississippi Medical Center, Jackson, Mississippi.
Department of Cardiology, Henry Ford Hospital, Detroit, Michigan.

Patients ≥75 years old presenting with acute myocardial infarction (AMI) have complex coronary anatomy in part due to prior coronary artery bypass grafting (CABG), percutaneous coronary interventions (PCI), calcific and valvular disease. Using the National Readmission Database from January 2016 to November 2017, we identified hospital admissions for acute myocardial infarction in patients ≥75 years old and divided them based on a history of CABG. We evaluated in-hospital outcomes, 30-day mortality, 30-day readmission and predictors of PCI in cohorts. Out of a total of 296,062 patients ≥75 years old presenting with an AMI, 42,147 (14%) had history of previous CABG. Most presented with a non-ST segment elevation myocardial infarction, and those with previous CABG had higher burden of co-morbidities and were more commonly man. The in-hospital mortality was significantly lower in those with previous CABG (6.7% vs 8.8%, adjusted odds ratio, 0.88, 95% confidence interval, 0.82 to 0.94). Medical therapy was more common in those with previous CABG and 30-day readmission rates were seen more frequently in those with prior CABG. Predictors of not undergoing PCI included previous PCI, female, older ager groups, heart failure, dementia, malignancy, and higher number of co-morbidities. In conclusion, in patients ≥75 years old with AMI the presence of prior CABG was associated with lower odds of in-hospital and 30-day mortality, as well as lower complications rates, and a decreased use of invasive strategies (PCI, CABG, and MCS). However, 30-day MACE readmission was higher in those with previous CABG.

Cardiology and Cardiovascular Research

Lemor A, **Michaels A**, **Al-Darzi W**, Hernandez GA, **Nasr Y**, **Villablanca P**, Blumer V, **Tita C**, **Williams CT**, **Selektor Y**, **Lanfear DE**, Lindenfeld J, and **Cowger J**. National Landscape of Hospitalizations in Patients with Left Ventricular Assist Device. Insights from the National Readmission Database 2010-2015. *Asaio j* 2020; 66(10):1087-1094. PMID: 33136594. Full Text

From the Division of Cardiology, Department of Medicine, Henry Ford Hospital, Detroit, Michigan.
Centro de Investigacion de Epidemiologia Clinica y Medicina Basada en Evidencias, Facultad de Medicina Humana, Universidad de San Martin de Porres, Lima, Peru.
Division of Cardiology, University of Mississippi Medical Center, Jackson, Mississippi.
Division of Cardiology, Duke University Medical Center, Durham, North Carolina.
Division of Advanced Heart Failure and Transplant Cardiology, Vanderbilt University Medical Center, Nashville, Tennessee.

The number of patients with left ventricular assist devices (LVAD) has increased over the years and it is important to identify the etiologies for hospital admission, as well as the costs, length of stay and in-hospital complications in this patient group. Using the National Readmission Database from 2010 to 2015, we identified patients with a history of LVAD placement using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) code V43.21. We aimed to identify the etiologies for hospital admission, patient characteristics, and in-hospital outcomes. We identified a total of 15,996 patients with an LVAD, the mean age was 58 years and 76% were males. The most common cause of hospital readmission after LVAD was heart failure (HF, 13%), followed by gastrointestinal (GI) bleed (11.8%), device complication (11.5%), and ventricular tachycardia/fibrillation (4.2%). The median length of stay was 6 days (3-11 days) and the median hospital costs was $12,723 USD. The in-hospital mortality was 3.9%, blood transfusion was required in 26.8% of patients, 20.5% had acute kidney injury, 2.8% required hemodialysis, and 6.2% of patients underwent heart transplantation. Interestingly, the most common cause of readmission was the same as the diagnosis for the preceding admission. One in every four LVAD patients experiences a readmission within 30 days of a prior admission, most commonly due

to HF and GI bleeding. Interventions to reduce HF readmissions, such as speed optimization, may be one means of improving LVAD outcomes and resource utilization.

Cardiology and Cardiovascular Research

Loungani RS, Teerlink JR, Metra M, Allen LA, Butler J, Carson PE, Chen CW, Cotter G, Davison BA, Eapen ZJ, Filippatos GS, Gimpelewicz C, Greenberg B, Holbro T, Januzzi JL, Jr., **Lanfear DE**, Pang PS, Piña IL, Ponikowski P, Miller AB, Voors AA, and Felker GM. Cause of Death in Patients With Acute Heart Failure: Insights From RELAX-AHF-2. *JACC Heart Fail* 2020; Epub ahead of print. PMID: 33189635. Full Text

Division of Cardiology and Duke Clinical Research Institute, Duke University School of Medicine, Durham, North Carolina.
Section of Cardiology, San Francisco Veterans Affairs Medical Center and School of Medicine, University of California, San Francisco, California.
Cardiology, ASST Civil Hospitals, and Department of Medical and Surgical Specialties, Radiological Sciences and Public Health, University of Brescia, Brescia, Italy.
Division of Cardiology, Department of Medicine, University of Colorado School of Medicine, Aurora, Colorado.
Department of Medicine, University of Mississippi, Jackson, Mississippi.
Department of Cardiology, Washington VA Medical Center, Washington, DC.
Novartis Pharmaceuticals Corporation, East Hanover, New Jersey.
Momentum Research, Durham, North Carolina.
Anthem Incorporated, Indianapolis, Indiana.
School of Medicine, University of Cyprus, Nicosia, Cyprus, and Attikon University Hospital, School of Medicine, and National and Kapodistrian University of Athens, Athens, Greece.
Novartis Pharma AG, Basel, Switzerland.
University of California San Diego Health, Cardiovascular Institute, La Jolla, California.
Division of Cardiology, Department of Medicine, Harvard Medical School, and Cardiometabolic Trials, Baim Institute for Clinical Research, Boston, Massachusetts.
Division of Cardiovascular Medicine, Henry Ford Hospital, Detroit, Michigan.
Department of Emergency Medicine, Indiana University School of Medicine, Indianapolis, Indiana.
Division of Cardiology, Wayne State University, Detroit, Michigan.
Department of Cardiology, Wroclaw Medical University, Wroclaw, Poland.
Department of Cardiology, University of Florida, Jacksonville, Florida.
University of Groningen, Department of Cardiology, University Medical Center Groningen, Groningen, the Netherlands.
Division of Cardiology and Duke Clinical Research Institute, Duke University School of Medicine, Durham, North Carolina. Electronic address: Michael.felker@duke.edu.

OBJECTIVES: This study sought to better understand the discrepant results of 2 trials of serelaxin on acute heart failure (AHF) and short-term mortality after AHF by analyzing causes of death of patients in the RELAX-AHF-2 (Efficacy, Safety and Tolerability of Serelaxin When Added to Standard Therapy in AHF-2) trial. BACKGROUND: Patients with AHF continue to suffer significant short-term mortality, but limited systematic analyses of causes of death in this patient population are available. METHODS: Adjudicated cause of death of patients in RELAX-AHF-2, a randomized, double-blind, placebo-controlled trial of serelaxin in patients with AHF across the spectrum of ejection fraction (EF), was analyzed. RESULTS: By 180 days of follow-up, 11.5% of patients in RELAX-AHF-2 died, primarily due to heart failure (HF) (38% of all deaths). Unlike RELAX-AHF, there was no apparent effect of treatment with serelaxin on any category of cause of death. Older patients (≥75 years) had higher rates of mortality (14.2% vs. 8.8%) and non-cardiovascular (CV) death (27% vs. 19%) compared to younger patients. Patients with preserved EF (≥50%) had lower rates of HF-related mortality (30% vs. 40%) but higher non-CV mortality (36% vs. 20%) compared to patients with reduced EF. CONCLUSIONS: Despite previous data suggesting benefit of serelaxin in AHF, treatment with serelaxin was not found to improve overall mortality or have an effect on any category of cause of death in RELAX-AHF-2. Careful adjudication of events in the serelaxin trials showed that older patients and those with preserved EF had fewer deaths from HF or sudden death and more deaths from other CV causes and from noncardiac causes. (Efficacy,

Safety and Tolerability of Serelaxin When Added to Standard Therapy in AHF [RELAX-AHF-2]; NCT01870778).

Cardiology and Cardiovascular Research

Reid A, Ben Zekry S, Turaga M, Tarazi S, Bax JJ, **Wang DD**, Piazza N, Bapat VN, Ihdayhid AR, Cavalcante JL, Blanke P, and Leipsic J. Neo-LVOT and Transcatheter Mitral Valve Replacement: Expert Recommendations. *JACC Cardiovasc Imaging* 2020; Epub ahead of print. PMID: 33248959. Full Text

Center for Heart Lung Innovation, St. Paul's Hospital, University of British Columbia, Vancouver, British Columbia, Canada.
Department of Cardiology, Leiden University Medical Center, Leiden, the Netherlands.
Center for Structural Heart Disease, Henry Ford Health System, Detroit, Michigan.
Department of Medicine, Division of Cardiology, McGill University Health Centre, Montreal, Quebec, Canada.
Department of Medicine, Division of Cardiology, NewYork-Presbyterian/Columbia University Irving Medical Center, New York, New York.
Minneapolis Heart Institute, Abbott Northwestern Hospital, Minneapolis, Minnesota.
Center for Heart Lung Innovation, St. Paul's Hospital, University of British Columbia, Vancouver, British Columbia, Canada. Electronic address: jleipsic@providencehealth.bc.ca.

With the advent of transcatheter mitral valve replacement (TMVR), the concept of the neo-left ventricular outflow tract (LVOT) was introduced and remains an essential component of treatment planning. This paper describes the LVOT anatomy and provides a step-by-step computed tomography methodology to segment and measure the neo-LVOT while discussing the current evidence and outstanding challenges. It also discusses the technical and hemodynamic factors that play a major role in assessing the neo-LVOT. A summary of expert-based recommendations about the overall risk of LVOT obstruction in different scenarios is presented along with the currently available methods to reduce the risk of LVOT obstruction and other post-procedural complications.

Cardiology and Cardiovascular Research

Schuger C, Daubert JP, Zareba W, Rosero S, Yong P, McNitt S, and Kutyifa V. Reassessing the role of Antitachycardia Pacing in Fast Ventricular Arrhythmias in Primary Prevention Implantable Cardioverter Defibrillator Recipients: Results from MADIT-RIT. *Heart Rhythm* 2020; Epub ahead of print. PMID: 33232811. Full Text

Henry Ford Heart & Vascular Institute. Electronic address: cschuge1@hfhs.org.
Duke University Medical Center.
University of Rochester Medical Center.
Boston Scientific Corporation.

BACKGROUND: In MADIT-RIT high rate cut-off (Arm B) and delayed therapy (Arm C) reduced the risk of inappropriate ICD interventions, when compared to conventional programming (Arm A), however appropriate but unnecessary therapies were not evaluated. OBJECTIVE: To assess the value of ATP for fast ventricular arrhythmias (VA)≥200 bpm in primary prevention (PP) ICD patients. METHODS: We compared ATP only, ATP and shock, and shock only rates in MADIT-RIT patients treated for VA≥200 bpm. The only difference between these randomized groups was the time delay between VT detection and therapy (3.4 sec vs. 4.9 sec vs. 14.4 sec). RESULTS: Arm A, 11.5% had events, initial therapy in 10.5% was ATP, in 1% was shock. Final therapy was ATP in 8% and shock in 3.5%. Arm B, 6.6% had events, 4.2% were initially treated with ATP, 2.4% with shock. Final therapy was ATP in 2.8% and shock in 3.8%. Arm C, 4.7% patients had events, 2.5% were initially treated with ATP, 2.3% with shock. Final therapy was ATP in 1.4%, and shock in 3.3%. The final shock rate was similar, Arms A vs. B (3.5% vs. 3.8%, p=0.800) and in Arms A vs. C (3.5% vs. 3.3%, p=0.855) despite the marked discrepancy in initial ATP therapy utilization. CONCLUSION: In MADIT-RIT, there was a significant reduction in ATP interventions with therapy delays due to spontaneous termination, with no difference in shock therapies, suggesting that earlier interventions for VA≥200 bpm are likely unnecessary leading to an overestimation of the value of ATP in PP ICD recipients.

Cardiology and Cardiovascular Research

Teerlink JR, Diaz R, Felker GM, McMurray JJV, Metra M, Solomon SD, Adams KF, Anand I, Arias-Mendoza A, Biering-Sørensen T, Böhm M, Bonderman D, Cleland JGF, Corbalan R, Crespo-Leiro MG, Dahlström U, Echeverria LE, Fang JC, Filippatos G, Fonseca C, Goncalvesova E, Goudev AR, Howlett JG, **Lanfear DE**, Li J, Lund M, Macdonald P, Mareev V, Momomura SI, O'Meara E, Parkhomenko A, Ponikowski P, Ramires FJA, Serpytis P, Sliwa K, Spinar J, Suter TM, Tomcsanyi J, Vandekerckhove H, Vinereanu D, Voors AA, Yilmaz MB, Zannad F, Sharpsten L, Legg JC, Varin C, Honarpour N, Abbasi SA, Malik FI, and Kurtz CE. Cardiac Myosin Activation with Omecamtiv Mecarbil in Systolic Heart Failure. *N Engl J Med* 2020; Epub ahead of print. PMID: 33185990. Full Text

BACKGROUND: The selective cardiac myosin activator omecamtiv mecarbil has been shown to improve cardiac function in patients with heart failure with a reduced ejection fraction. Its effect on cardiovascular outcomes is unknown. METHODS: We randomly assigned 8256 patients (inpatients and outpatients) with symptomatic chronic heart failure and an ejection fraction of 35% or less to receive omecamtiv mecarbil (using pharmacokinetic-guided doses of 25 mg, 37.5 mg, or 50 mg twice daily) or placebo, in addition to standard heart-failure therapy. The primary outcome was a composite of a first heart-failure event (hospitalization or urgent visit for heart failure) or death from cardiovascular causes. RESULTS: During a median of 21.8 months, a primary-outcome event occurred in 1523 of 4120 patients (37.0%) in the omecamtiv mecarbil group and in 1607 of 4112 patients (39.1%) in the placebo group (hazard ratio, 0.92; 95% confidence interval [CI], 0.86 to 0.99; P = 0.03). A total of 808 patients (19.6%) and 798 patients (19.4%), respectively, died from cardiovascular causes (hazard ratio, 1.01; 95% CI, 0.92 to 1.11). There was no significant difference between groups in the change from baseline on the Kansas City Cardiomyopathy Questionnaire total symptom score. At week 24, the change from baseline for the median N-terminal pro-B-type natriuretic peptide level was 10% lower in the omecamtiv mecarbil group than in the placebo group; the median cardiac troponin I level was 4 ng per liter higher. The frequency of cardiac ischemic and ventricular arrhythmia events was similar in the two groups. CONCLUSIONS: Among patients with heart failure and a reduced ejection, those who received omecamtiv mecarbil had a lower incidence of a composite of a heart-failure event or death from cardiovascular causes than those who received placebo. (Funded by Amgen and others; GALACTIC-HF ClinicalTrials.gov number, NCT02929329; EudraCT number, 2016-002299-28.).

Cardiology and Cardiovascular Research

Xenogiannis I, **Alaswad K**, Krestyaninov O, Khelimskii D, Khatri JJ, Choi JW, Jaffer FA, Patel M, Mahmud E, Doing AH, Dattilo P, Koutouzis M, Tsiafoutis I, Uretsky B, Jefferson BK, Patel T, Jaber W, Samady H, Sheikh AM, Yeh RW, Tamez H, Elbaruny B, Love MP, Abi Rafeh N, Maalouf A, Fadi AJ, Toma C, Shah AR, Chandwaney RH, Omer M, Megaly MS, Vemmou E, Nikolakopoulos I, Rangan BV, Garcia S, Abdullah S, Banerjee S, Burke MN, Karmpaliotis D, and Brilakis ES. Impact of adherence to the hybrid algorithm for initial crossing strategy selection in chronic total occlusion percutaneous coronary intervention. *Rev Esp Cardiol (Engl Ed)* 2020; Epub ahead of print. PMID: 33189636. Full Text

Coronary Artery Disease Science Center, Minneapolis Heart Institute, Minneapolis Heart Institute Foundation, Abbott Northwestern Hospital, Minneapolis, Minnesota, United States.
Department of Cardiology, Henry Ford Hospital, Detroit, Michigan, United States.
Meshalkin Novosibrisk Research Institute, Novosibirsk, Russia.
Department of Cardiology, Cleveland Clinic, Cleveland, Ohio, United States.
Department of Cardiology, Baylor Heart and Vascular Hospital, Dallas, Texas, United States.
Department of Cardiology, Massachusetts General Hospital, Boston, Massachussetts, United States.
VA San Diego Healthcare System, La Jolla, California, United States.
Department of Cardiology, Medical Center of the Rockies, Loveland, Colorado, United States.
Department of Cardiology, Red Cross Hospital of Athens, Athens, Greece.
Department of Cardiology, VA Central Arkansas Healthcare System, Little Rock, Arkansas, United States.
Department of Cardiology, Tristar Centennial Medical Center, Nashville, Tennessee, United States.
Department of Cardiology, Emory University Hospital Midtown, Atlanta, Georgia, United States.
Wellstar Health System, Marietta, Georgia, United States.
Department of Cardiology, Beth Israel Deaconess Medical Center, Boston, Massachusetts, United States.
Department of Cardiology, St. Boniface General Hospital, Winnipeg, Manitoba, Canada.

Department of Cardiology, St. George Hospital University Medical Center, Beirut, Lebanon.
University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania, United States.
Department of Cardiology, Houston Methodist Hospital, Houston, Texas, United States.
Oklahoma Heart Institute, Tulsa, Oklahoma, United States.
Department of Cardiology, VA North Texas Health Care System, Dallas, Texas, United States.
Columbia University, New York, United States.
Coronary Artery Disease Science Center, Minneapolis Heart Institute, Minneapolis Heart Institute Foundation, Abbott Northwestern Hospital, Minneapolis, Minnesota, United States. Electronic address: esbrilakis@gmail.com.

INTRODUCTION AND OBJECTIVES: The hybrid algorithm was designed to assist with initial and subsequent crossing strategy selection in chronic total occlusion (CTO) percutaneous coronary interventions (PCIs). However, the success of the initially selected strategy has received limited study. METHODS: We examined the impact of adherence to the hybrid algorithm recommendation for initial CTO crossing technique selection in 4178 CTO PCIs from a large multicenter registry. RESULTS: The initial crossing strategy was concordant with the hybrid algorithm recommendation in 1833 interventions (44%). Patients in the concordant group had a similar age to those in the discordant group but a lower mean J-CTO score (2.0 ± 1.4 vs 2.8 ± 1.1; P < .01). The concordant group showed higher technical success with the first crossing strategy (68% vs 48%; P < .01) and higher overall technical success (88% vs 83%; P < .01) with no difference in the incidence of in-hospital major adverse events (1.8% vs 2.3%; P = .26). In multivariable analysis, after adjustment for age, prior myocardial infarction, prior PCI, prior coronary artery bypass grafting, J-CTO score, and scheduled CTO PCI, nonadherence to the hybrid algorithm was independently associated with lower technical success of the initial crossing strategy (odds ratio, 0.55; 95% confidence interval, 0.48-0.64; P < .01). CONCLUSIONS: Adherence to the hybrid algorithm for initial crossing strategy selection is associated with higher CTO PCI success but similar in-hospital major adverse cardiac events.

Center for Health Policy and Health Services Research
Lu M, Bowlus CL, Lindor K, Rodriguez-Watson CV, Romanelli RJ, Haller IV, Anderson H, VanWormer JJ, Boscarino JA, Schmidt MA, Daida YG, Sahota A, Vincent J, **Li J**, Trudeau S, **Rupp LB**, and **Gordon SC**. Validity of an Automated Algorithm to Identify Cirrhosis Using Electronic Health Records in Patients with Primary Biliary Cholangitis. *Clin Epidemiol* 2020; 12:1261-1267. PMID: 33204167. Full Text

Department of Public Health Sciences, Henry Ford Health System, Detroit, MI, USA.
University of California Davis School of Medicine, Sacramento, CA, USA.
College of Health Solutions, Arizona State University, Phoenix, AZ, USA.
Center for Health Research Kaiser Permanente Mid-Atlantic Research Institute, Rockville, MD; Reagan-Udall Foundation for the FDA, Washington, DC, USA.
Palo Alto Medical Foundation Research Institute, Palo Alto, CA, USA.
Essentia Institute of Rural Health, Essentia Health, Duluth, MN, USA.
Skaggs School of Pharmacy and Pharmaceutical Sciences, University of Colorado Anschutz Medical Campus, Aurora, CO, USA.
Marshfield Clinic Research Foundation, Marshfield, WI, USA.
Department of Population Health Sciences, Geisinger Clinic, Danville, PA, USA.
Center for Health Research, Kaiser Permanente Northwest, Portland, OR, USA.
Center for Integrated Health Care Research, Kaiser Permanente Hawai'i, Honolulu, HI, USA.
Department of Research and Evaluation, Kaiser Permanente Southern California, Los Angeles, CA, USA.
Baylor, Scott & White Research Institute, Temple, TX, USA.
Center for Health Policy and Health Services Research, Henry Ford Health System, Detroit, MI, USA.
Division of Gastroenterology and Hepatology, Henry Ford Health System; and Wayne State University School of Medicine, Detroit, MI, USA.

BACKGROUND: Biopsy remains the gold standard for determining fibrosis stage in patients with primary biliary cholangitis (PBC), but it is unavailable for most patients. We used data from the 11 US health systems in the FibrOtic Liver Disease Consortium to explore a combination of biochemical markers and electronic health record (EHR)-based diagnosis/procedure codes (DPCs) to identify the presence of

cirrhosis in PBC patients. METHODS: Histological fibrosis staging data were obtained from liver biopsies. Variables considered for the model included demographics (age, gender, race, ethnicity), total bilirubin, alkaline phosphatase, albumin, aspartate aminotransferase (AST) to platelet ratio index (APRI), Fibrosis 4 (FIB4) index, AST to alanine aminotransferase (ALT) ratio, and >100 DPCs associated with cirrhosis/decompensated cirrhosis, categorized into ten clusters. Using least absolute shrinkage and selection operator regression (LASSO), we derived and validated cutoffs for identifying cirrhosis. RESULTS: Among 4328 PBC patients, 1350 (32%) had biopsy data; 121 (9%) were staged F4 (cirrhosis). DPC clusters (including codes related to cirrhosis and hepatocellular carcinoma diagnoses/procedures), Hispanic ethnicity, ALP, AST/ALT ratio, and total bilirubin were retained in the final model (AUROC=0.86 and 0.83 on learning and testing data, respectively); this model with two cutoffs divided patients into three categories (no cirrhosis, indeterminate, and cirrhosis) with specificities of 81.8% (for no cirrhosis) and 80.3% (for cirrhosis). A model excluding DPCs retained ALP, AST/ALT ratio, total bilirubin, Hispanic ethnicity, and gender (AUROC=0.81 and 0.78 on learning and testing data, respectively). CONCLUSION: An algorithm using laboratory results and DPCs can categorize a majority of PBC patients as cirrhotic or noncirrhotic with high accuracy (with a small remaining group of patients' cirrhosis status indeterminate). In the absence of biopsy data, this EHR-based model can be used to identify cirrhosis in cohorts of PBC patients for research and/or clinical follow-up.

Center for Health Policy and Health Services Research
Miller-Matero LR, **Hamann A**, **LaLonde L**, **Martens KM**, Son J, **Clark-Sienkiewicz S**, **Sata M**, **Coleman JP**, **Hecht LM**, **Braciszewski JM**, and **Carlin AM**. Predictors of Alcohol Use after Bariatric Surgery. *J Clin Psychol Med Settings* 2020; Epub ahead of print. PMID: 33205321. Full Text

Behavioral Health, Henry Ford Health System, 1 Ford Place, 3A, Detroit, MI, 48202, USA. Lmatero1@hfhs.org.
Center for Health Policy and Health Services Research, Henry Ford Health System, Detroit, MI, USA. Lmatero1@hfhs.org.
Behavioral Health, Henry Ford Health System, 1 Ford Place, 3A, Detroit, MI, 48202, USA.
Department of Surgery, Henry Ford Health System, Detroit, MI, USA.
Wayne State University School of Medicine, Henry Ford Health System, Detroit, MI, USA.
Center for Health Policy and Health Services Research, Henry Ford Health System, Detroit, MI, USA.

Patients undergoing bariatric surgery are at risk for devloping an alcohol use disorder (AUD). The purpose of this study was to investigate pre-surgical psychosocial risk factors for post-surgical alcohol consumption and hazardous drinking. Participants (N = 567) who underwent bariatric surgery between 2014 and 2017 reported their post-surgical alcohol use. Information was collected from the pre-surgical evaluation including history of alcohol use, psychiatric symptoms, and maladaptive eating behaviors (i.e., binge eating, purging, and emotional eating). Younger age and pre-surgical alcohol use predicted post-surgical alcohol use and hazardous drinking. In addition, higher levels of depressive symptoms and maladaptive eating patterns predicted post-surgical binge drinking. Clinicians conducting pre-surgical psychosocial evaluations should be aware of the multiple risk factors related to post-surgical problematic alcohol use. Future research should evaluate whether preventive interventions for high-risk patients decrease risk for post-surgical alcohol misuse.

Center for Health Policy and Health Services Research
Parghi N, Chennapragada L, Barzilay S, Newkirk S, **Ahmedani B**, Lok B, and Galynker I. Assessing the predictive ability of the Suicide Crisis Inventory for near-term suicidal behavior using machine learning approaches. *Int J Methods Psychiatr Res* 2020; Epub ahead of print. PMID: 33166430. Full Text

Courant Institute of Mathematical Sciences, New York University, New York City, New York, USA.
Department of Psychiatry and Behavioral Health, Mount Sinai Beth Israel Medical Center, New York City, New York, USA.
Psychiatry Department, Schneider Children's Medical Centre, Tel Aviv University, Tel Aviv, Israel.
Center for Health Policy and Health Services Research, Henry Ford Health System, Detroit, Michigan, USA.
College of Engineering, University of Florida, Gainesville, Florida, USA.

Department of Psychiatry, Icahn School of Medicine at Mount Sinai, New York City, New York, USA.

OBJECTIVE: This study explores the prediction of near-term suicidal behavior using machine learning (ML) analyses of the Suicide Crisis Inventory (SCI), which measures the Suicide Crisis Syndrome, a presuicidal mental state. METHODS: SCI data were collected from high-risk psychiatric inpatients (N = 591) grouped based on their short-term suicidal behavior, that is, those who attempted suicide between intake and 1-month follow-up dates (N = 20) and those who did not (N = 571). Data were analyzed using three predictive algorithms (logistic regression, random forest, and gradient boosting) and three sampling approaches (split sample, Synthetic minority oversampling technique, and enhanced bootstrap). RESULTS: The enhanced bootstrap approach considerably outperformed the other sampling approaches, with random forest (98.0% precision; 33.9% recall; 71.0% Area under the precision-recall curve [AUPRC]; and 87.8% Area under the receiver operating characteristic [AUROC]) and gradient boosting (94.0% precision; 48.9% recall; 70.5% AUPRC; and 89.4% AUROC) algorithms performing best in predicting positive cases of near-term suicidal behavior using this dataset. CONCLUSIONS: ML can be useful in analyzing data from psychometric scales, such as the SCI, and for predicting near-term suicidal behavior. However, in cases such as the current analysis where the data are highly imbalanced, the optimal method of measuring performance must be carefully considered and selected.

Center for Health Policy and Health Services Research
Prabhakar D, **Peterson EL**, **Hu Y**, **Chawa S**, Rossom RC, Lynch FL, Lu CY, Waitzfelder BE, Owen-Smith AA, **Williams LK**, Beck A, Simon GE, and Ahmedani BK. Serious Suicide Attempts and Risk of Suicide Death. *Crisis* 2020;1-8. Epub ahead of print. PMID: 33151092. Request Article

Sheppard Pratt, Baltimore, MD, USA.
Department of Public Health Sciences, Henry Ford Health System, Detroit, MI, USA.
Center for Health Policy and Health Services Research (CHSR), Henry Ford Health System, Detroit, MI, USA.
Behavioral Health Sciences, Henry Ford Health System, Detroit, MI, USA.
Health Partners Institute, University of Minnesota, Minneapolis, MN, USA.
Center for Health Research, Kaiser Permanente Northwest, Portland, OR, USA.
Department of Population Medicine, Harvard Medical School, Boston, MA, USA.
Center for Health Research, Kaiser Permanente, Honolulu, HI, USA.
Center for Research and Evaluation, Kaiser Permanente Georgia, Atlanta, GA, USA.
Center of Individualized and Genomic Medicine Research (CIGMA), Department of Internal Medicine, Henry Ford Health System, Detroit, MI, USA.
Institute for Health Research, Kaiser Permanente Colorado, Denver, CO, USA.
Health Research Institute, Kaiser Permanente, Seattle, WA, USA.

Background: In the US, more than one million people attempt suicide each year. History of suicide attempt is a significant risk factor for death by suicide; however, there is a paucity of data from the US general population on this relationship. Aim: The objective of this study was to examine suicide attempts needing medical attention as a risk for suicide death. Method: We conducted a case-control study involving eight US healthcare systems. A total of 2,674 individuals who died by suicide from 2000 to 2013 were matched to 267,400 individuals by year and location. Results: Prior suicide attempt associated with a medical visit increases risk for suicide death by 39.1 times, particularly for women (OR = 79.2). However, only 11.3% of suicide deaths were associated with an attempt that required medical attention. The association was the strongest for children 10-14 years old (OR = 98.0). Most suicide attempts were recorded during the 20-week period prior to death. Limitations: Our study is limited to suicide attempts for which individuals sought medical care. Conclusion: In the US, prior suicide attempt is associated with an increased risk of suicide death; the risk is high especially during the period immediately following a nonlethal attempt.

Center for Individualized and Genomic Medicine Research
Cocco MP, **White E**, **Xiao S**, Hu D, Mak A, Sleiman P, **Yang M**, **Bobbitt KR**, **Gui H**, **Levin AM**, **Hochstadt S**, **Whitehouse K**, **Rynkowski D**, Barczak AJ, Abecasis G, Blackwell TW, Kang HM, Nickerson DA, Germer S, Ding J, **Lanfear DE**, Gilliland F, Gauderman WJ, Kumar R, Erle DJ, Martinez F,

Hakonarson H, Burchard EG, and **Williams LK**. Asthma and its relationship to mitochondrial copy number: Results from the Asthma Translational Genomics Collaborative (ATGC) of the Trans-Omics for Precision Medicine (TOPMed) program. *PLoS One* 2020; 15(11):e0242364. PMID: 33237978. Full Text

Center for Individualized and Genomic Medicine Research (CIGMA), Department of Internal Medicine, Henry Ford Health System, Detroit, Michigan, United States of America.
Department of Medicine, University of California San Francisco, San Francisco, California, United States of America.
Center for Applied Genomics, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, United States of America.
Department of Pediatrics, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, United States of America.
Department of Public Health Sciences, Henry Ford Health System, Detroit, Michigan, United States of America.
Lung Biology Center and UCSF CoLabs, University of California San Francisco, San Francisco, California, United States of America.
Center for Statistical Genetics, University of Michigan, Ann Arbor, Michigan, United States of America.
Regeneron Pharmaceuticals, Inc., Tarrytown, New York, United States of America.
Department of Genome Sciences, University of Washington, Seattle, Washington, United States of America.
Northwest Genomics Center, Seattle, Washington, United States of America.
Brotman Baty Institute, Seattle, Washington, United States of America.
New York Genome Center, New York, New York, United States of America.
Human Statistical Genetics Unit, Laboratory of Genetics and Genomics, National Institute on Aging, National Institutes of Health, Bethesda, Maryland, United States of America.
Department of Preventive Medicine, Keck School of Medicine, University of Southern California, Los Angeles, California, United States of America.
Department of Pediatrics, Northwestern University Feinberg School of Medicine, Chicago, Illinois, United States of America.
Arizona Respiratory Center and Department of Pediatrics, University of Arizona, Tucson, Arizona, United States of America.
Department of Bioengineering & Therapeutic Sciences, University of California San Francisco, San Francisco, California, United States of America.

BACKGROUND: Mitochondria support critical cellular functions, such as energy production through oxidative phosphorylation, regulation of reactive oxygen species, apoptosis, and calcium homeostasis. OBJECTIVE: Given the heightened level of cellular activity in patients with asthma, we sought to determine whether mitochondrial DNA (mtDNA) copy number measured in peripheral blood differed between individuals with and without asthma. METHODS: Whole genome sequence data was generated as part of the Trans-Omics for Precision Medicine (TOPMed) Program on participants from the Study of Asthma Phenotypes and Pharmacogenomic Interactions by Race-ethnicity (SAPPHIRE) and the Study of African Americans, Asthma, Genes, & Environment II (SAGE II). We restricted our analysis to individuals who self-identified as African American (3,651 asthma cases and 1,344 controls). Mitochondrial copy number was estimated using the sequencing read depth ratio for the mitochondrial and nuclear genomes. Respiratory complex expression was assessed using RNA-sequencing. RESULTS: Average mitochondrial copy number was significantly higher among individuals with asthma when compared with controls (SAPPHIRE: 218.60 vs. 200.47, P<0.001; SAGE II: 235.99 vs. 223.07, P<0.001). Asthma status was significantly associated with mitochondrial copy number after accounting for potential explanatory variables, such as participant age, sex, leukocyte counts, and mitochondrial haplogroup. Despite the consistent relationship between asthma status and mitochondrial copy number, the latter was not associated with time-to-exacerbation or patient-reported asthma control. Mitochondrial respiratory complex gene expression was disproportionately lower in individuals with asthma when compared with individuals without asthma and other protein-encoding genes. CONCLUSIONS: We observed a robust association between asthma and higher mitochondrial copy number. Asthma having an effect on mitochondria function was also supported by lower respiratory complex gene expression in this group.

Center for Individualized and Genomic Medicine Research

Prabhakar D, **Peterson EL**, **Hu Y**, **Chawa S**, Rossom RC, Lynch FL, Lu CY, Waitzfelder BE, Owen-Smith AA, **Williams LK**, Beck A, Simon GE, and Ahmedani BK. Serious Suicide Attempts and Risk of Suicide Death. *Crisis* 2020; Epub ahead of print.:1-8. PMID: 33151092. Request Article

Sheppard Pratt, Baltimore, MD, USA.
Department of Public Health Sciences, Henry Ford Health System, Detroit, MI, USA.
Center for Health Policy and Health Services Research (CHSR), Henry Ford Health System, Detroit, MI, USA.
Behavioral Health Sciences, Henry Ford Health System, Detroit, MI, USA.
Health Partners Institute, University of Minnesota, Minneapolis, MN, USA.
Center for Health Research, Kaiser Permanente Northwest, Portland, OR, USA.
Department of Population Medicine, Harvard Medical School, Boston, MA, USA.
Center for Health Research, Kaiser Permanente, Honolulu, HI, USA.
Center for Research and Evaluation, Kaiser Permanente Georgia, Atlanta, GA, USA.
Center of Individualized and Genomic Medicine Research (CIGMA), Department of Internal Medicine, Henry Ford Health System, Detroit, MI, USA.
Institute for Health Research, Kaiser Permanente Colorado, Denver, CO, USA.
Health Research Institute, Kaiser Permanente, Seattle, WA, USA.

Background: In the US, more than one million people attempt suicide each year. History of suicide attempt is a significant risk factor for death by suicide; however, there is a paucity of data from the US general population on this relationship. Aim: The objective of this study was to examine suicide attempts needing medical attention as a risk for suicide death. Method: We conducted a case-control study involving eight US healthcare systems. A total of 2,674 individuals who died by suicide from 2000 to 2013 were matched to 267,400 individuals by year and location. Results: Prior suicide attempt associated with a medical visit increases risk for suicide death by 39.1 times, particularly for women (OR = 79.2). However, only 11.3% of suicide deaths were associated with an attempt that required medical attention. The association was the strongest for children 10-14 years old (OR = 98.0). Most suicide attempts were recorded during the 20-week period prior to death. Limitations: Our study is limited to suicide attempts for which individuals sought medical care. Conclusion: In the US, prior suicide attempt is associated with an increased risk of suicide death; the risk is high especially during the period immediately following a nonlethal attempt.

Dermatology

Alam M, Harikumar V, Ibrahim SA, Kang BY, Maher IA, Cartee TV, Sobanko JF, Kibbi N, Owen JL, Reynolds KA, Bolotin D, Waldman AH, Minkis K, Petersen B, Council ML, Nehal KS, Xu YG, Jiang SB, Somani AK, Bichakjian CK, Huang CC, Eisen DB, **Ozog DM**, Lee EH, Samie FH, Neuhaus IM, Bordeaux JS, Wang JV, Leitenberger JJ, Mann MW, Lawrence N, Zeitouni NC, Golda N, Behshad R, Ibrahim SF, Yu SS, Shin TM, Stebbins WG, and Worley B. Principles for developing and adapting clinical practice guidelines and guidance for pandemics, wars, shortages, and other crises and emergencies: the PAGE criteria. *Arch Dermatol Res* 2020; Epub ahead of print. PMID: 33206210. Full Text

Department of Dermatology, Feinberg School of Medicine, Northwestern University, 676 N St Clair St, Suite 1600, Chicago, IL, 60611, USA. m-alam@northwestern.edu.
Department of Dermatology, Feinberg School of Medicine, Northwestern University, 676 N St Clair St, Suite 1600, Chicago, IL, 60611, USA.
Department of Dermatology, University of Minnesota, Minneapolis, MN, USA.
Department of Dermatology, Penn State College of Medicine, Hershey, PA, USA.
Department of Dermatology, Hospital of the University of Pennsylvania, Philadelphia, PA, USA.
Department of Dermatology, Stanford University School of Medicine, Redwood City, CA, USA.
South Texas Skin Cancer Center, San Antonio, TX, USA.
Section of Dermatology, The University of Chicago, Chicago, IL, USA.
Brigham and Women's Hospital Department of Dermatology, Harvard Medical School, Boston, MA, USA.
Department of Dermatology, Weill-Cornell Medical College, New York, NY, USA.
Department of Dermatology, Colorado Permanente Medical Group, Denver, CO, USA.

Division of Dermatology, Center for Dermatologic and Cosmetic Surgery, Washington University in Saint Louis, Saint Louis, MO, USA.
Dermatology Service, Memorial Sloan Kettering Cancer Center, New York, NY, USA.
Department of Dermatology, University of Wisconsin-Madison, Madison, WI, USA.
Department of Dermatology, University of California San Diego, San Diego, CA, USA.
Department of Dermatology, Indiana University School of Medicine, Indianapolis, IN, USA.
Department of Dermatology, University of Michigan, Ann Arbor, MI, USA.
Department of Dermatology, University of Alabama, Birmingham, AL, USA.
Department of Dermatology, University of California Davis, Sacramento, CA, USA.
Department of Dermatology, Henry Ford Hospital, Detroit, MI, USA.
Department of Dermatology, Columbia University Irving Medical Center, New York, NY, USA.
Department of Dermatology, University of California at San Francisco, San Francisco, CA, USA.
Department of Dermatology, Case Western Reserve University School of Medicine, Cleveland, OH, USA.
Department of Dermatology, University Hospitals Cleveland Medical Center, Cleveland, OH, USA.
Laser and Skin Surgery Center of New York, New York, NY, USA.
Department of Dermatology, Oregon Health and Science University, Portland, OR, USA.
Division of Dermatology, Section of Procedural Dermatology, Cooper Hospital, Rowan University, Camden, NJ, USA.
Department of Dermatology, University of Arizona, Phoenix, AZ, USA.
Department of Dermatology, University of Missouri School of Medicine, Columbia, MO, USA.
Department of Dermatology, Saint Louis University School of Medicine, Saint Louis, MO, USA.
Department of Dermatology, University of Rochester, Rochester, NY, USA.
Department of Dermatology, Vanderbilt University Medical Center, Nashville, TN, USA.

Dermatology

Alam M, Harikumar V, Kang BY, Ibrahim SA, Kibbi N, Owen JL, Maher IA, Cartee TV, Sobanko JF, Reynolds KA, Bolotin D, Waldman AH, Minkis K, Petersen B, Council ML, Nehal KS, Xu YG, Jiang SB, Somani AK, Bichakjian CK, Huang CC, Eisen DB, **Ozog DM**, Lee EH, Samie FH, Neuhaus IM, Bordeaux JS, Wang JV, Leitenberger JJ, Mann MW, Lawrence N, Zeitouni NC, Golda N, Behshad R, Ibrahim SF, Yu SS, Shin TM, Stebbins WG, and Worley B. Development of international clinical practice guidelines: benefits, limitations, and alternative forms of international collaboration. *Arch Dermatol Res* 2020; Epub ahead of print. PMID: 33216212. Full Text

Department of Dermatology, Feinberg School of Medicine, Northwestern University, 676 N St Clair St, Suite 1600, Chicago, IL, 60611, USA. m-alam@northwestern.edu.
Department of Dermatology, Feinberg School of Medicine, Northwestern University, 676 N St Clair St, Suite 1600, Chicago, IL, 60611, USA.
Department of Dermatology, Stanford University School of Medicine, Redwood, CA, USA.
South Texas Skin Cancer Center, San Antonio, TX, USA.
Department of Dermatology, University of Minnesota, Minneapolis, MN, USA.
Department of Dermatology, Penn State College of Medicine, Hershey, PA, USA.
Department of Dermatology, Hospital of the University of Pennsylvania, Philadelphia, PA, USA.
Section of Dermatology, The University of Chicago, Chicago, IL, USA.
Brigham and Women's Hospital Department of Dermatology, Harvard Medical School, Boston, MA, USA.
Department of Dermatology, Weill-Cornell Medical College, New York, NY, USA.
Department of Dermatology, Colorado Permanente Medical Group, Denver, CO, USA.
Division of Dermatology, Center for Dermatologic and Cosmetic Surgery, Washington University in Saint Louis, Saint Louis, MO, USA.
Dermatology Service, Memorial Sloan Kettering Cancer Center, New York, NY, USA.
Department of Dermatology, University of Wisconsin-Madison, Madison, WI, USA.
Department of Dermatology, University of California San Diego, San Diego, CA, USA.
Department of Dermatology, Indiana University School of Medicine, Indianapolis, IN, USA.
Department of Dermatology, University of Michigan, Ann Arbor, MI, USA.
Department of Dermatology, University of Alabama, Birmingham, AL, USA.
Department of Dermatology, University of California Davis, Sacramento, CA, USA.
Department of Dermatology, Henry Ford Hospital, Detroit, MI, USA.

Department of Dermatology, Columbia University Irving Medical Center, New York, NY, USA.
Department of Dermatology, University of California At San Francisco, San Francisco, CA, USA.
Department of Dermatology, Case Western Reserve University School of Medicine, Cleveland, OH, USA.
Department of Dermatology, University Hospitals Cleveland Medical Center, Cleveland, OH, USA.
Laser and Skin Surgery Center of New York, New York, NY, USA.
Department of Dermatology, Oregon Health and Science University, Portland, OR, USA.
Innova Dermatology, Hendersonville, TN, USA.
Division of Dermatology, Section of Procedural Dermatology, Cooper Hospital, Rowan University, Camden, NJ, USA.
Department of Dermatology, University of Arizona, Phoenix, AZ, USA.
Department of Dermatology, University of Missouri School of Medicine, Columbia, MO, USA.
Department of Dermatology, Saint Louis University School of Medicine, Saint Louis, MO, USA.
Department of Dermatology, University of Rochester, Rochester, NY, USA.
Department of Dermatology, Vanderbilt University Medical Center, Nashville, TN, USA.

Dermatology

Bissonnette R, **Gold LS**, Rubenstein DS, Tallman AM, and Armstrong A. Tapinarof in the treatment of psoriasis: A review of the unique mechanism of action of a novel therapeutic AhR modulating agent (TAMA). *J Am Acad Dermatol* 2020; Epub ahead of print. PMID: 33157177. Full Text

Innovaderm Research Inc., Montreal, QC, Canada. Electronic address: rbissonnette@innovaderm.com.
Henry Ford Health System, Detroit, MI, USA.
Dermavant Sciences, Inc., Durham, NC, USA.
Dermavant Sciences, Inc., Long Beach, CA, USA.
Keck School of Medicine of the University of Southern California, Los Angeles, CA, USA.

Tapinarof, a novel, first-in-class small-molecule topical therapeutic aryl hydrocarbon receptor (AhR) modulating agent (TAMA), is in clinical development for the treatment of psoriasis and atopic dermatitis. The efficacy of tapinarof in psoriasis is attributed to its specific binding and activation of AhR, a ligand-dependent transcription factor, leading to the downregulation of pro-inflammatory cytokines, including interleukin-17, and regulation of skin barrier protein expression to promote skin barrier normalization. AhR signaling regulates gene expression in immune cells and skin cells, and has critical roles in the regulation of skin homeostasis. Tapinarof-mediated AhR signaling underlies the mechanistic basis for the significant efficacy and acceptable tolerability observed in early phase clinical trials of tapinarof cream in the treatment of psoriasis.

Dermatology

Harikumar V, Worley B, Ibrahim SA, Kang BY, Maher IA, Cartee TV, Sobanko JF, Kibbi N, Owen JL, Reynolds KA, Bolotin D, Waldman AH, Minkis K, Petersen B, Council ML, Nehal KS, Xu YG, Jiang SB, Somani AK, Huang CC, Eisen DB, **Ozog DM**, Lee EH, Samie FH, Neuhaus IM, Leitenberger JJ, Mann MW, Lawrence N, Zeitouni NC, Golda N, Behshad R, Ibrahim SF, Yu SS, Shin TM, Stebbins WG, and Alam M. Broad versus narrow clinical practice guidelines: avoiding rules for the high risk 1. *Arch Dermatol Res* 2020; Epub ahead of print. PMID: 33175206. Full Text

Department of Dermatology, Feinberg School of Medicine, Northwestern University, 676 N St Clair St, Suite 1600, Chicago, IL, 60611, USA.
Department of Dermatology, University of Minnesota, Minneapolis, MN, USA.
Department of Dermatology, Penn State College of Medicine, Hershey, PA, USA.
Department of Dermatology, Hospital of the University of Pennsylvania, Philadelphia, PA, USA.
Department of Dermatology, Stanford University School of Medicine, Redwood City, CA, USA.
South Texas Skin Cancer Center, San Antonio, TX, USA.
Section of Dermatology, The University of Chicago, Chicago, IL, USA.
Brigham and Women's Hospital Department of Dermatology, Harvard Medical School, Boston, MA, USA.
Department of Dermatology, Weill-Cornell Medical College, New York, NY, USA.
Department of Dermatology, Colorado Permanente Medical Group, Denver, CO, USA.

Division of Dermatology, Center for Dermatologic and Cosmetic Surgery, Washington University in Saint Louis, Saint Louis, MO, USA.
Dermatology Service, Memorial Sloan Kettering Cancer Center, New York, NY, USA.
Department of Dermatology, University of Wisconsin-Madison, Madison, WI, USA.
Department of Dermatology, University of California San Diego, San Diego, CA, USA.
Department of Dermatology, Indiana University School of Medicine, Indianapolis, IN, USA.
Department of Dermatology, University of Alabama, Birmingham, AL, USA.
Department of Dermatology, University of California Davis, Sacramento, CA, USA.
Department of Dermatology, Henry Ford Hospital, Detroit, MI, USA.
Department of Dermatology, Columbia University Irving Medical Center, New York, NY, USA.
Department of Dermatology, University of California at San Francisco, San Francisco, CA, USA.
Department of Dermatology, Oregon Health and Science University, Portland, OR, USA.
Department of Dermatology, Case Western Reserve University School of Medicine, Cleveland, OH, USA.
Department of Dermatology, University Hospitals Cleveland Medical Center, Cleveland, OH, USA.
Division of Dermatology, Section of Procedural Dermatology, Cooper Hospital, Rowan University, Camden, NJ, USA.
Department of Dermatology, University of Arizona, Phoenix, AZ, USA.
Department of Dermatology, University of Missouri School of Medicine, Columbia, MO, USA.
Department of Dermatology, Saint Louis University School of Medicine, Saint Louis, MO, USA.
Department of Dermatology, University of Rochester, Rochester, NY, USA.
Department of Dermatology, Vanderbilt University Medical Center, Nashville, TN, USA.
Department of Dermatology, Feinberg School of Medicine, Northwestern University, 676 N St Clair St, Suite 1600, Chicago, IL, 60611, USA. m-alam@northwestern.edu.

Dermatology
Hoffert M, **Kerr H**, **Hegab S**, **Whitehouse S**, **Kokas M**, **MacLean L**, **Van Harn MG**, and **Baker-Genaw K**. Designing a Yoga Intervention Program to Improve Well-Being for Physician Trainees: Challenges and Lessons Learned. *Int J Yoga Therap* 2020; Epub ahead of print. PMID: 33157552. Full Text

Department of Medical Education, Henry Ford Hospital, Detroit, Mich.
Department of Dermatology, Henry Ford Hospital, Detroit, Mich.
Division of Pulmonary and Critical Care Medicine, Henry Ford Hospital, Detroit, Mich.
Behavioral Health Services, Henry Ford Hospital, Detroit, Mich.
Public Health Science Division of Biostatistics, Henry Ford Hospital, Detroit, Michigan.
Department of Medical Education and Department of Internal Medicine, Henry Ford Hospital, Detroit, Mich.

Well-being activities may help to counteract physician burnout. Yoga is known to enhance well-being, but there are few studies of yoga as an intervention for physicians in training. This prospective methodology-development study aimed to explore how to establish a yoga-based well-being intervention for physician trainees in a large urban training hospital. We aimed to identify factors that contribute to trainee participation and explore an instrument to measure changes in self-reported well-being after yoga. Cohorts included a required-attendance group, a voluntary-attendance group, and an unassigned walk-in yoga group. Weekly 1-hour yoga sessions were led by a qualified yoga instructor for 4 weeks. The seven-question Resident Physician Well-Being Index (RPWBI) was used to measure resident well-being before yoga, after 4 weeks of yoga, and 6 months post-yoga. Trainees attending each session ranged from 17 for required yoga to 0-2 for voluntary yoga, 2-9 for lunchtime walk-in yoga, and 1-7 for evening walk-in yoga. In the required-yoga group (n = 17), overall RPWBI mean scores did not change significantly across the three query times, and participation in the survey declined over time. The mean baseline RPWBI score for the required group before yoga was in the non-distressed range and answers to the seven individual questions varied. Requiring a yoga activity for medical trainees may be a good strategy for promoting participation in yoga. The RPWBI may have limited utility for measuring changes in overall group well-being after a yoga intervention.

Dermatology
Kashlan R, **Lyons AB**, Hivnor C, and **Ozog DM**. N95 Respirators for Dermatologic Surgery and Laser Procedures During COVID-19 and Beyond. *Dermatol Surg* 2020; 46(11):1441-1442. PMID: 33105244. Full Text

Wayne State University School of Medicine, Detroit, Michigan.
Department of Dermatology, Henry Ford Health System, Detroit, Michigan.
Dermatology Associates of San Antonio, San Antonio, Texas.

Dermatology
Luke J, Cornelius L, and **Lim HW**. Dermatology Resident Selection: Shifting Toward Holistic Review? *J Am Acad Dermatol* 2020; Epub ahead of print. PMID: 33245933. Full Text

Department of Dermatology, Loma Linda University Loma Linda, CA. Electronic address: jdluke@llu.edu.
Division of Dermatology, Department of Medicine, Washington University School of Medicine, St. Louis, MO.
Department of Dermatology, Henry Ford Health System, Detroit, Michigan, USA.

Dermatology
Madan E, Peixoto ML, **Dimitrion P**, Eubank TD, Yekelchyk M, Talukdar S, Fisher PB, **Mi QS**, Moreno E, and Gogna R. Cell Competition Boosts Clonal Evolution and Hypoxic Selection in Cancer. *Trends Cell Biol* 2020; 30(12):967-978. PMID: 33160818. Full Text

Champalimaud Centre for the Unknown, 1400-038 Lisbon, Portugal.
Center for Cutaneous Biology and Immunology, Department of Dermatology, Henry Ford Health System, Detroit, MI, USA; Immunology Research Program, Henry Ford Cancer Institute, Henry Ford Health System, Detroit, MI, USA; Department of Biochemistry, Microbiology and Immunology, Wayne State University Medical School, Detroit, MI, USA.
In Vivo Multifunctional Magnetic Resonance Center, Robert C. Byrd Health Sciences Center, West Virginia University, Morgantown, WV, USA; Department of Microbiology, Immunology, and Cell Biology, West Virginia University School of Medicine, Morgantown, WV, USA.
Department of Cardiac Development and Remodeling, Max Planck Institute for Heart and Lung Research, 61231 Bad Nauheim, Germany.
Department of Human and Molecular Genetics, Virginia Commonwealth University, School of Medicine, Richmond, VA, USA; VCU Massey Cancer Center, Virginia Commonwealth University, School of Medicine, Richmond, VA, USA.
Champalimaud Centre for the Unknown, 1400-038 Lisbon, Portugal. Electronic address: eduardo.moreno@research.fchampalimaud.org.
Champalimaud Centre for the Unknown, 1400-038 Lisbon, Portugal. Electronic address: rajan.gogna@research.fchampalimaud.org.

The comparison of fitness between cells leads to the elimination of less competent cells in the presence of more competent neighbors via cell competition (CC). This phenomenon has been linked with several cancer-related genes and thus may play an important role in cancer. Various processes are involved in the regulation of tumor initiation and growth, including tumor hypoxia, clonal stem cell selection, and immune cell response, all of which have been recently shown to have a potential connection with the mechanisms involved in CC. This review aims to unravel the relation between these processes and competitive cell interactions and how this affects disease progression.

Dermatology
Zarbo A, **Inamdar K**, and **Friedman BJ**. Tender Nodules on the Extremities: Answer. *Am J Dermatopathol* 2020; 42(11):889. PMID: 33086227. Full Text

Department of Dermatology, Henry Ford Health System, Detroit, MI.

Diagnostic Radiology

Gandhi D, Boregowda U, Sharma P, Ahuja K, Jain N, **Khanna K**, and Gupta N. A review of commonly performed bariatric surgeries: Imaging features and its complications. *Clin Imaging* 2020; 72:122-135. PMID: 33232899. Full Text

Department of Radiology, Northwestern Memorial Hospital, Northwestern University Feinberg School of Medicine, 676 N St. Clair St, Suite 800, Chicago, IL 60611, USA. Electronic address: darshangandhi7@gmail.com.
Department of Internal Medicine, Bassett Medical Center, Cooperstown, NY 13326, USA.
Department of Diagnostic Radiology, Vascular and Interventional Radiology University of Minnesota Medical Center, Minneapolis, MN 55455, USA.
Department of Internal Medicine, John H Stroger Jr. Hospital of Cook County, 1969 Ogden Ave, Chicago, IL 60612, USA.
Department of Diagnostic Radiology, Ascension St. John Macomb and Oakland Hospitals, Warren & Madison Heights Campuses, Troy, MI 48098, USA.
Department of Radiology, Henry Ford Hospital, Detroit, MI 48202, USA.
Department of Radiology, Bassett Healthcare, 1 Atwell Road, Cooperstown, NY 13326, USA.

Obesity is a disease that has achieved the level that can be considered an epidemic. According to the National Center for Health Statistics data, the prevalence of obesity has increased from 30.5% in 1999-2000 to 42.4% in 2017-2018. During the same period, severe obesity has increased from 4.7% to 9.2%. With the growing prevalence of obesity, related conditions such as coronary artery disease, diabetes, and strokes have also become more prevalent. In the past few years, the need for bariatric surgeries such as laparoscopic Roux-en-Y gastric bypass, sleeve gastrectomy, and laparoscopic adjustable gastric banding has increased considerably. With an increasing number of bariatric surgeries, multiple postoperative complications have become common. In this review, we have attempted to describe normal postsurgical anatomical findings after bariatric surgeries and pictorial review of a few common postoperative complications.

Diagnostic Radiology

Khanna K, Mofakham FA, Gandhi D, and Jain N. Desmoid fibromatosis of the pancreas--A case report with radiologic-pathologic correlation. *Radiol Case Rep* 2020; 15(11):2324-2328. PMID: 32994833. Full Text

Wayne State University School of Medicine, Department of Radiology, Abdominal Imaging, Henry Ford Hospital, Detroit, MI, USA.
Department of Diagnostic Radiology, UC Davis Medical Center, Sacramento, CA, USA.
Department of Radiology, Northwestern Memorial Hospital, Northwestern University Feinberg School of Medicine, 676 N St. Clair St, Suite 800, Chicago, IL 60611, USA.
Department of Diagnostic Radiology, Ascension St. John Macomb and Oakland Hospitals, Warren and Madison Heights Campuses, Troy, MI, USA.

Pancreas is an exceptionally rare location for desmoid tumors. There are very few case reports of pancreatic fibromatosis in the English radiology literature. We present a case of a 45-year-old male with a mixed solid and cystic desmoid tumor of the pancreas which was surgically resected and was followed by recurrence in the mesentery. This will be the first case report of pancreatic desmoid with documented recurrence of fibromatosis in the mesentery which was also surgically resected and confirmed on pathology. In this case report, we discuss this entity's radiological findings with pathology correlation, clinical findings and management along with literature review.

Diagnostic Radiology

Reaume M, Duong T, **Song T**, and **Diaz-Mendoza J**. The pulmonary nodule following lung transplantation. *Clin Imaging* 2020; 72:37-41. PMID: 33202293. Full Text

Department of Pulmonary and Critical Care Medicine, Henry Ford Hospital, Detroit, MI, United States of America.

Department of Medicine, Weiss Memorial Hospital, Chicago, IL, United States of America.
Department of Radiology, Henry Ford Hospital, Detroit, MI, United States of America.
Department of Pulmonary and Critical Care Medicine, Henry Ford Hospital, Detroit, MI, United States of America; Department of Medicine, Wayne State University, Detroit, MI, United States of America.
Electronic address: Jdiaz1@hfhs.org.

The clinical scenario of a pulmonary nodule following lung transplantation is one with limited experience and no supporting guidelines for the approach to diagnosis and management. Given the broad differential diagnosis for pulmonary nodules in this setting, most of which are life-threatening without appropriate treatment, aggressive evaluation is required. Here we present a case of a 70-year-old female with the development of a large pulmonary nodule in the native lung four years following a single lung transplant. She underwent bronchoscopy with endobronchial ultrasound to achieve a tissue diagnosis which showed small cell lung carcinoma. The patient was started on chemotherapy and has shown clinical and radiographic improvement at most recent follow up seven months after the initial diagnosis. In this report we discuss the differential diagnosis and corresponding imaging findings for the pulmonary nodule following lung transplantation to aid in guiding clinicians navigate this challenging clinical situation.

Diagnostic Radiology
Tran G, **Khalil LS**, **Wrubel A**, **Klochko CL**, **Davis JJ**, and **Soliman SB**. Incidental findings detected on preoperative CT imaging obtained for robotic-assisted joint replacements: clinical importance and the effect on the scheduled arthroplasty. *Skeletal Radiol* 2020; Epub ahead of print. PMID: 33140168. Full Text

Division of Musculoskeletal Radiology, Department of Radiology, Henry Ford Hospital, Detroit, MI, USA.
Division of Orthopedic Surgery, Department of Orthopedics, Henry Ford Hospital, Detroit, MI, USA.
Division of Musculoskeletal Radiology, Department of Radiology, Henry Ford Hospital, Detroit, MI, USA.
stevens@rad.hfh.edu.

OBJECTIVE: To determine the type and frequency of incidental findings detected on preoperative computed tomography (CT) imaging obtained for robotic-assisted joint replacements and their effect on the planned arthroplasty. MATERIALS AND METHODS: All preoperative CT examinations performed for a robotic-assisted knee or total hip arthroplasty were obtained. This resulted in 1432 examinations performed between September 2016 and February 2020 at our institution. These examinations were initially interpreted by 1 of 9 fellowship-trained musculoskeletal radiologists. Using a diagnosis search, the examination reports were then reviewed to catalog all incidental findings and further classify as significant or non-significant findings. Demographic information was obtained. In those with significant findings, a chart review was performed to record the relevant workup, outcomes, and if the planned arthroplasty was affected. RESULTS: Incidental findings were diagnosed in 740 (51.7%) patients. Of those with incidental findings, 41 (5.5%) were considered significant. A significant finding was more likely to be detected in males (P = 0.007) and on the hip protocol CT (P = 0.014). In 8 patients, these diagnoses resulted in either delay or cancelation of the arthroplasty. A planned total hip arthroplasty was more likely to be altered as compared to a knee arthroplasty (P = 0.018). CONCLUSION: Incidental findings are commonly detected by radiologists on preoperative CT imaging obtained for robotic-assisted joint replacement. Several were valuable findings and resulted in a delay or even cancelation of the planned arthroplasty after the detection of critical diagnoses, which if not identified may have resulted in devastating outcomes.

Diagnostic Radiology
Tran G, Parrinello D, and **Dalal I**. Laparoscopic Port-Site Metastasis From Prostate Cancer on 18F-Fluciclovine PET/CT. *Clin Nucl Med* 2020; Epub ahead of print. PMID: 33208626. Full Text

From the Henry Ford Hospital, Detroit, MI.
New York Institute of Technology College of Osteopathic Medicine at Arkansas State University, Jonesboro, AR.

Laparoscopic port-site metastasis from prostate cancer is a rare complication after radical prostatectomy and pelvic lymph node dissection. We report a case of port-site metastasis from prostate cancer identified

on F-fluciclovine PET/CT for a patient with evidence of biochemical recurrence. Final pathology after targeted ultrasound and biopsy of the mass in the right abdominal wall revealed prostatic adenocarcinoma.

Emergency Medicine
Berger DA, Chen NW, **Miller JB**, Welch RD, Reynolds JC, Pribble JM, and Swor DR. Substantial Variation Exists in Post-Cardiac Arrest Outcomes Across Michigan Hospitals. *Resuscitation* 2020; Epub ahead of print. PMID: 33221364. Full Text

Oakland University William Beaumont School of Medicine, Rochester, MI, United States; Beaumont Hospital-Royal Oak, Royal Oak, MI, United States. Electronic address: David.berger@beaumont.edu.
Beaumont Hospital-Royal Oak, Royal Oak, MI, United States.
Henry Ford Health System, Detroit, MI, United States.
Wayne State University, Detroit, MI, United States.
Spectrum Health System, Grand Rapids, MI, United States.
University of Michigan Health System, Ann Arbor, MI, United States.
Oakland University William Beaumont School of Medicine, Rochester, MI, United States; Beaumont Hospital-Royal Oak, Royal Oak, MI, United States.
Oakland University William Beaumont School of Medicine, Rochester, MI, United States; Beaumont Hospital-Royal Oak, Royal Oak, MI, United States; Henry Ford Health System, Detroit, MI, United States; Wayne State University, Detroit, MI, United States; University of Michigan Health System, Ann Arbor, MI, United States.

AIM: Resuscitation from out of hospital cardiac arrest (OHCA) requires success across the entire chain of survival. Using a large state-wide registry, we characterized variation in clinical outcomes at hospital discharge in Michigan hospitals. METHODS: We utilized the Michigan Cardiac Arrest Registry to Enhance Survival (CARES) and included adult OHCA subjects with return of spontaneous circulation (ROSC) from 2014 - 2017 that survived to hospital admission. 39 Michigan hospitals were included which managed >30 cases during the study period. Multilevel logistic regression, controlling for both subject characteristics and clustering of subjects within hospitals, assessed variation across hospitals in survival to hospital discharge and survival with cerebral performance category (CPC 1-2). RESULTS: There were 5,486 CARES subjects that survived to hospital admission, and 4,690 met inclusion for analysis. Of 39 included hospitals, median survival to discharge was 31.3% (range 12.5%-46.7%) and median survival to discharge with CPC 1-2 was 25.0% (range 5.2%-42.2%). We identified 12-fold variation in the utilization of TTM by hospital (median 47.9%, range 6.7%-80.0%) for all admitted subjects. Similarly, there was nearly an eight-fold variation in LHC for all post-arrest subjects (median 22.1%, range 5.4%-42.2%). In multivariable analyses, median adjusted survival to discharge was 26.9% (range 18.1%-42.1%) and median adjusted survival to discharge with CPC 1-2 was 21.3% (range 9.6%-32.1%). CONCLUSION: We observed substantial variation in clinical outcomes at discharge between Michigan hospitals, including a four-fold range of survival and eight-fold range of survival with CPC 1-2. This variation was ameliorated but still persisted in adjusted modeling. Variation in post arrest survival by hospital was not fully explained by available covariates, which suggests the possibility of improving post-arrest clinical outcomes at some hospitals via quality improvement activities.

Emergency Medicine
Hamam MS, **Kunjummen E**, **Hussain MS**, Nasereldin M, **Bennett S**, and **Miller J**. Anxiety, Depression, and Pain: Considerations in the Treatment of Patients with Uncontrolled Hypertension. *Curr Hypertens Rep* 2020; 22(12):106. PMID: 33170388. Full Text

Henry Ford Hospital, Emergency Medicine, Detroit, MI, 48202, USA.
Wayne State University, Detroit, MI, 48202, USA.
Henry Ford Hospital, Emergency Medicine, Detroit, MI, 48202, USA. JMILLER6@hfhs.org.
Wayne State University, Detroit, MI, 48202, USA. JMILLER6@hfhs.org.

PURPOSE OF REVIEW: The association between mental health, pain, and treatment-resistant hypertension is an important consideration for treating physicians. We review and discuss the connection

between conditions of anxiety, depression, and chronic pain and their effect on uncontrolled hypertension. RECENT FINDINGS: There is significant co-occurrence of hypertension with anxiety, depression, and chronic pain which may lead to undertreatment of hypertension and undertreatment of the underlying mental health disorder. The association between mental health and hypertension is complex and is modulated by physiologic and environmental factors. Physicians treating patients with hypertension should be cognizant of the role anxiety, depression, and chronic pain play in treatment efficacy and compliance. Patients undergoing treatment should be screened for mental health disorders at treatment initiation and frequently thereafter to ensure optimal overall health and compliance.

Emergency Medicine

Nowak RM, Peacock WF, and deFilippi CR. In reply. *Ann Emerg Med* 2020; 76(5):692-693. PMID: 33097134. Full Text

Department of Emergency Medicine, Henry Ford Health System, Detroit, MI.
Department of Emergency Medicine, Baylor College of Medicine, Houston, TX.
Inova Heart and Vascular Institute, Falls Church, VA.

Endocrinology and Metabolism

Hilliard ME, Marrero DG, Minard CG, Cao VT, de Wit M, DuBose SN, Verdejo A, Jaser SS, **Kruger D**, Monzavi R, Shah VN, Paul Wadwa R, Weinstock RS, Thompson D, and Anderson BJ. Design and Psychometrics for New Measures of Health-Related Quality of Life in Adults with Type 1 Diabetes: Type 1 Diabetes and Life (T1DAL). *Diabetes Res Clin Pract* 2020; Epub ahead of print. PMID: 33189791. Full Text

Department of Pediatrics, Baylor College of Medicine and Texas Children's Hospital, Houston TX. Electronic address: marisa.hilliard@bcm.edu.
University of Arizona Health Sciences, Tucson AZ.
Institute for Clinical and Translational Research, Baylor College of Medicine, Houston TX.
Department of Pediatrics, Baylor College of Medicine and Texas Children's Hospital, Houston TX.
Department of Medical Psychology, Amsterdam UMC, Vrije Universiteit Amsterdam, Amsterdam NL.
Jaeb Center for Health Research, Tampa FL.
Department of Pediatrics, Vanderbilt University Medical Center, Nashville TN.
Division of Endocrinology, Diabetes, Bone and Mineral Disorders, Henry Ford Medical Center, Detroit MI.
Center for Endocrinology, Diabetes and Metabolism, Children's Hospital Los Angeles and Keck School of Medicine of University of Southern California, Los Angeles CA.
Barbara Davis Center for Diabetes, University of Colorado Anschutz Medical Campus, Aurora CO.
Department of Medicine, SUNY Upstate Medical University, Syracuse NY.
USDA/ARS Children's Nutrition Research Center, Department of Pediatrics, Baylor College of Medicine, Houston TX.

AIMS: To use a three-phase process to develop and validate new self-report measures of diabetes-specific health-related quality of life (HRQOL) for adults with type 1 diabetes. We report on four versions of the Type 1 Diabetes and Life (T1DAL) measure for people age 18-25, 26-45, 46-60, and over 60 years. METHODS: We first conducted qualitative interviews to guide measure creation, then piloted the draft measures. We evaluated psychometric properties at six T1D Exchange Clinic Network sites via completion of T1DAL and validated measures of related constructs. Participants completed the T1DAL again in 4-6 weeks. We used psychometric data to reduce each measure to 23-27 items in length. Finally, we obtained participant feedback on the final measures. RESULTS: The T1DAL-Adult measures demonstrated good internal consistency (α=0.85-0.88) and test-retest reliability (r=0.77-0.87). Significant correlations with measures of general quality of life, generic and diabetes-specific HRQOL, diabetes burden, self-management, and glycemic control demonstrated validity. Factor analyses yielded 4-5 subscales per measure. Participants were satisfied with the final measures and reported they took 5-10 minutes to complete. CONCLUSIONS: The strong psychometric properties of the newly developed self-report T1DAL measures for adults with type 1 diabetes make them appropriate for use in clinical research and care.

Gastroenterology

Al-Darzi W, **Alalwan Y**, **Askar F**, **Sadiq O**, **Venkat D**, **Gonzalez H**, **Galusca D**, **Yoshida A**, and **Jafri SM**. Risk Factors and Outcomes of Intracardiac Thrombosis During Orthotopic Liver Transplantation. *Transplant Proc* 2020; Epub ahead of print. PMID: 33246584. Full Text

Division of Cardiology, Henry Ford Hospital, Detroit, Michigan. Electronic address: waleed.aldarzi@gmail.com.
Department of Internal Medicine, Henry Ford Hospital, Detroit, Michigan.
Department of Internal Medicine, Henry Ford Hospital, Detroit, Michigan; School of Medicine, Wayne State University, Detroit, Michigan.
Division of Gastroenterology, Henry Ford Hospital, Detroit, Michigan.
School of Medicine, Wayne State University, Detroit, Michigan; Division of Gastroenterology, Henry Ford Hospital, Detroit, Michigan.
Department of Anesthesiology, Henry Ford Hospital, Detroit, Michigan.
Transplant and Hepatobiliary Surgery, Henry Ford Hospital, Detroit, Michigan.

BACKGROUND: Intracardiac thrombosis incidence during orthotopic liver transplantation is estimated at 0.36% to 6.2% with mortality up to 68%. We aimed to evaluate risk factors and outcomes related to intracardiac thrombosis during orthotopic liver transplantation. MATERIALS AND METHODS: A comprehensive retrospective data review of 388 patients who underwent orthotopic liver transplantation at an urban transplant center from January 2013 to October 2016 was obtained. RESULTS: Six patients were found to have documented intracardiac thrombosis; 4 cases were recognized during the reperfusion stage and 1 during pre-anhepatic stage. All allografts were procured from decreased donors with a median donor age of 44 years (interquartile range, 35.25-49.75) and the cause of death was listed as cerebrovascular accident in 5 donors. Preoperative demographic, clinical, laboratory, and historical risk factors did not differ in patients with thrombosis. None had a prior history of trans-jugular intrahepatic portosystemic shunt or gastrointestinal bleeding. Three patients had renal injury, but no intraoperative hemodialysis was performed. Transesophageal echocardiographic findings included elevated pulmonary artery pressure (1/6), right ventricular strain (1/6), and pulmonary artery thrombus (1/6). Three patients died intraoperatively. Tissue plasminogen activator alone was given to 1 patient who did not survive, intravenous heparin only to 1 patient with resolution, and a combination of both was used in 2 patients with clot resolution achieved. CONCLUSION: Cardiac thrombosis should be considered in patients having hemodynamic compromise during liver transplantation. Transesophageal echocardiography is a useful diagnostic tool. Intracardiac thrombosis treatment remains challenging; however, using both thrombolytics and heparin could achieve better results.

Gastroenterology

Brown KA, and Collaborators PO. The case for simplifying and using absolute targets for viral hepatitis elimination goals. *J Viral Hepat* 2020; Epub ahead of print. PMID: 32979881. Full Text

The 69th World Health Assembly endorsed the Global Health Sector Strategy for Viral Hepatitis, embracing a goal to eliminate hepatitis infection as a public health threat by 2030. This was followed by the World Health Organization's (WHO) global targets for the care and management of hepatitis B virus (HBV) and hepatitis C virus (HCV) infections. These announcements and targets were important in raising awareness and calling for action; however, tracking countries' progress towards these elimination goals has provided insights to the limitations of these targets. The existing targets compare a country's progress relative to its 2015 values, penalizing countries who started their programmes prior to 2015, countries with a young population, or countries with a low prevalence. We recommend that (1) WHO simplify the hepatitis elimination targets, (2) change to absolute targets and (3) allow countries to achieve these disease targets with their own service coverage initiatives that will have the maximum impact. The recommended targets are as follows: reduce HCV new chronic cases to ≤5 per 100 000, reduce HBV prevalence among 1-year-olds to ≤0.1%, reduce HBV and HCV mortality to ≤5 per 100 000, and demonstrate HBV and HCV year-to-year decrease in new HCV- and HBV-related HCC cases. The objective of our recommendations is not to lower expectations or diminish the hepatitis elimination standards, but to provide clearer targets that recognize the past and current elimination efforts by countries, help measure progress towards true elimination, and motivate other countries to follow suit.

Gastroenterology
Lu M, Bowlus CL, Lindor K, Rodriguez-Watson CV, Romanelli RJ, Haller IV, Anderson H, VanWormer JJ, Boscarino JA, Schmidt MA, Daida YG, Sahota A, Vincent J, **Li J**, Trudeau S, **Rupp LB**, and **Gordon SC**. Validity of an Automated Algorithm to Identify Cirrhosis Using Electronic Health Records in Patients with Primary Biliary Cholangitis. *Clin Epidemiol* 2020; 12:1261-1267. PMID: 33204167. Full Text

Department of Public Health Sciences, Henry Ford Health System, Detroit, MI, USA.
University of California Davis School of Medicine, Sacramento, CA, USA.
College of Health Solutions, Arizona State University, Phoenix, AZ, USA.
Center for Health Research Kaiser Permanente Mid-Atlantic Research Institute, Rockville, MD; Reagan-Udall Foundation for the FDA, Washington, DC, USA.
Palo Alto Medical Foundation Research Institute, Palo Alto, CA, USA.
Essentia Institute of Rural Health, Essentia Health, Duluth, MN, USA.
Skaggs School of Pharmacy and Pharmaceutical Sciences, University of Colorado Anschutz Medical Campus, Aurora, CO, USA.
Marshfield Clinic Research Foundation, Marshfield, WI, USA.
Department of Population Health Sciences, Geisinger Clinic, Danville, PA, USA.
Center for Health Research, Kaiser Permanente Northwest, Portland, OR, USA.
Center for Integrated Health Care Research, Kaiser Permanente Hawai'i, Honolulu, HI, USA.
Department of Research and Evaluation, Kaiser Permanente Southern California, Los Angeles, CA, USA.
Baylor, Scott & White Research Institute, Temple, TX, USA.
Center for Health Policy and Health Services Research, Henry Ford Health System, Detroit, MI, USA.
Division of Gastroenterology and Hepatology, Henry Ford Health System; and Wayne State University School of Medicine, Detroit, MI, USA.

BACKGROUND: Biopsy remains the gold standard for determining fibrosis stage in patients with primary biliary cholangitis (PBC), but it is unavailable for most patients. We used data from the 11 US health systems in the FibrOtic Liver Disease Consortium to explore a combination of biochemical markers and electronic health record (EHR)-based diagnosis/procedure codes (DPCs) to identify the presence of cirrhosis in PBC patients. METHODS: Histological fibrosis staging data were obtained from liver biopsies. Variables considered for the model included demographics (age, gender, race, ethnicity), total bilirubin, alkaline phosphatase, albumin, aspartate aminotransferase (AST) to platelet ratio index (APRI), Fibrosis 4 (FIB4) index, AST to alanine aminotransferase (ALT) ratio, and >100 DPCs associated with cirrhosis/decompensated cirrhosis, categorized into ten clusters. Using least absolute shrinkage and selection operator regression (LASSO), we derived and validated cutoffs for identifying cirrhosis. RESULTS: Among 4328 PBC patients, 1350 (32%) had biopsy data; 121 (9%) were staged F4 (cirrhosis). DPC clusters (including codes related to cirrhosis and hepatocellular carcinoma diagnoses/procedures), Hispanic ethnicity, ALP, AST/ALT ratio, and total bilirubin were retained in the final model (AUROC=0.86 and 0.83 on learning and testing data, respectively); this model with two cutoffs divided patients into three categories (no cirrhosis, indeterminate, and cirrhosis) with specificities of 81.8% (for no cirrhosis) and 80.3% (for cirrhosis). A model excluding DPCs retained ALP, AST/ALT ratio, total bilirubin, Hispanic ethnicity, and gender (AUROC=0.81 and 0.78 on learning and testing data, respectively). CONCLUSION: An algorithm using laboratory results and DPCs can categorize a majority of PBC patients as cirrhotic or noncirrhotic with high accuracy (with a small remaining group of patients' cirrhosis status indeterminate). In the absence of biopsy data, this EHR-based model can be used to identify cirrhosis in cohorts of PBC patients for research and/or clinical follow-up.

Gastroenterology
Varma A, **Trudeau S**, **Zhou Y**, **Jafri SM**, **Krajenta R**, **Lamerato L**, **Brown K**, Luzzi V, **Lu M**, and **Gordon SC**. African Americans Demonstrate Significantly Lower Serum Alanine Aminotransferase Compared to Non-African Americans. *J Racial Ethn Health Disparities* 2020; Epub ahead of print. PMID: 33230736. Request Article

Department of Gastroenterology and Hepatology, Henry Ford Health System, 3E One Ford Place, Detroit, MI, 48202, USA.

Department of Public Health Sciences, Henry Ford Health System, Detroit, MI, USA.
Providence Health and Services Regional Laboratory, Portland, OR, USA.
Department of Gastroenterology and Hepatology, Henry Ford Health System, 3E One Ford Place, Detroit, MI, 48202, USA. sgordon3@hfhs.org.

BACKGROUND AND AIMS: Normal ranges of serum alanine aminotransferase (ALT) may vary by race. However, results from research studies are contradictory, and many of these studies have included only small numbers of African Americans. We investigated ALT values in patients without evidence of liver disease to determine whether normal ranges differ across race groups. We also evaluated whether a race- and sex-dependent upper limit of normal (ULN) would improve the ability of ALT to predict liver disease compared to the sex-dependent ULN currently in use. METHODS: We identified ICD9 codes for liver conditions and diabetes in medical records from a sample of 6719 patients. Analysis of variance (ANOVA) was used to assess differences in ALT log-transformed distributions by race. Logistic regression was used to evaluate whether the addition of race to the current sex-dependent ULN improves the ability of ALT to predict liver disease (assessed by area under the receiver operating characteristic curve (AUROC)). RESULTS: Among 1200 patients with BMI 18.5 < 25 and no evidence of liver disease or type 2 diabetes in their medical record, African Americans demonstrated significantly lower ALT (23.47 IU/L; 95% CL 22.87-24.10) than a combined group of Asian American/White/Other patients (25.71 IU/L; 95% CL 24.69-26.77). This difference remained across BMI categories. The race- and sex-dependent model demonstrated significantly better predictive ability than the sex-dependent model (AUROC = 66.6% versus 59.6%, respectively; p < 0.0001). CONCLUSIONS: In a large, racially diverse sample, African Americans demonstrated significantly lower ALT compared to non-African Americans; this difference remained as BMI increased. The establishment of race-specific normal ranges for ALT could contribute to better screening and care for African American patients.

Graduate Medical Education

Hoffert M, **Kerr H**, **Hegab S**, **Whitehouse S**, **Kokas M**, **MacLean L**, **Van Harn MG**, and **Baker-Genaw K**. Designing a Yoga Intervention Program to Improve Well-Being for Physician Trainees: Challenges and Lessons Learned. *Int J Yoga Therap* 2020; Epub ahead of print. PMID: 33157552. Full Text

Department of Medical Education, Henry Ford Hospital, Detroit, Mich.
Department of Dermatology, Henry Ford Hospital, Detroit, Mich.
Division of Pulmonary and Critical Care Medicine, Henry Ford Hospital, Detroit, Mich.
Behavioral Health Services, Henry Ford Hospital, Detroit, Mich.
Public Health Science Division of Biostatistics, Henry Ford Hospital, Detroit, Michigan.
Department of Medical Education and Department of Internal Medicine, Henry Ford Hospital, Detroit, Mich.

Well-being activities may help to counteract physician burnout. Yoga is known to enhance well-being, but there are few studies of yoga as an intervention for physicians in training. This prospective methodology-development study aimed to explore how to establish a yoga-based well-being intervention for physician trainees in a large urban training hospital. We aimed to identify factors that contribute to trainee participation and explore an instrument to measure changes in self-reported well-being after yoga. Cohorts included a required-attendance group, a voluntary-attendance group, and an unassigned walk-in yoga group. Weekly 1-hour yoga sessions were led by a qualified yoga instructor for 4 weeks. The seven-question Resident Physician Well-Being Index (RPWBI) was used to measure resident well-being before yoga, after 4 weeks of yoga, and 6 months post-yoga. Trainees attending each session ranged from 17 for required yoga to 0-2 for voluntary yoga, 2-9 for lunchtime walk-in yoga, and 1-7 for evening walk-in yoga. In the required-yoga group (n = 17), overall RPWBI mean scores did not change significantly across the three query times, and participation in the survey declined over time. The mean baseline RPWBI score for the required group before yoga was in the non-distressed range and answers to the seven individual questions varied. Requiring a yoga activity for medical trainees may be a good strategy for promoting participation in yoga. The RPWBI may have limited utility for measuring changes in overall group well-being after a yoga intervention.

Hematology-Oncology

Chun SG, Simone CB, 2nd, Amini A, **Chetty IJ**, Donington J, Edelman MJ, Higgins KA, Kestin LL, **Movsas B**, Rodrigues GB, Rosenzweig KE, Slotman BJ, **Rykbin, II**, Wolf A, and Chang JY. American Radium Society Appropriate Use Criteria: Radiation Therapy for Limited-Stage SCLC 2020. *J Thorac Oncol* 2020; Epub ahead of print. PMID: 33166720. Full Text

Department of Radiation Oncology, The University of Texas, MD Anderson Cancer Center, Houston, Texas. Electronic address: sgchun@mdanderson.org.
New York Proton Center, New York, New York.
Department of Radiation Oncology, City of Hope Comprehensive Cancer Center, Duarte, California.
Department of Radiation Oncology, Henry Ford Cancer Institute, Detroit, Michigan.
Department of Surgery, The University of Chicago, Chicago, Illinois.
Department of Hematology and Oncology, Fox Chase Comprehensive Cancer Center, Philadelphia, Pennsylvania.
Department of Radiation Oncology, Emory University Winship Cancer Institute, Atlanta, Georgia.
MHP Radiation Oncology Institute/GenesisCare USA, Farmington Hills, Michigan.
Department of Radiation Oncology, London Health Sciences Centre, London, Ontario, Canada.
Department of Radiation Oncology, Mount Sinai School of Medicine, New York, New York.
Department of Radiation Oncology, Amsterdam University Medical Center, Amsterdam, The Netherlands.
Department of Hematology and Oncology, Henry Ford Cancer Institute, Detroit, Michigan.
Department of Thoracic Surgery, Mount Sinai School of Medicine, New York, New York.
Department of Radiation Oncology, The University of Texas, MD Anderson Cancer Center, Houston, Texas.

INTRODUCTION: Combined modality therapy with concurrent chemotherapy and radiation has long been the standard of care for limited-stage SCLC (LS-SCLC). However, there is controversy over best combined modality practices for LS-SCLC. To address these controversies, the American Radium Society (ARS) Thoracic Appropriate Use Criteria (AUC) Committee have developed updated consensus guidelines for the treatment of LS-SCLC. METHODS: The ARS AUC are evidence-based guidelines for specific clinical conditions that are reviewed by a multidisciplinary expert panel. The guidelines include a review and analysis of current evidence with application of consensus methodology (modified Delphi) to rate the appropriateness of treatments recommended by the panel for LS-SCLC. Agreement or consensus was defined as less than or equal to 3 rating points from the panel median. The consensus ratings and recommendations were then vetted by the ARS Executive Committee and subject to public comment before finalization. RESULTS: The ARS Thoracic AUC committee developed multiple consensus recommendations for LS-SCLC. There was strong consensus that patients with unresectable LS-SCLC should receive concurrent chemotherapy with radiation delivered either once or twice daily. For medically inoperable T1-T2N0 LS-SCLC, either concurrent chemoradiation or stereotactic body radiation followed by adjuvant chemotherapy is a reasonable treatment option. The panel continues to recommend whole-brain prophylactic cranial irradiation after response to chemoradiation for LS-SCLC. There was panel agreement that prophylactic cranial irradiation with hippocampal avoidance and programmed cell death protein-1/programmed death-ligand 1-directed immune therapy should not be routinely administered outside the context of clinical trials at this time. CONCLUSIONS: The ARS Thoracic AUC Committee provide consensus recommendations for LS-SCLC that aim to provide a groundwork for multidisciplinary care and clinical trials.

Hematology-Oncology

Jacobs SA, Lee JJ, George TJ, Wade JL, Stella PJ, **Wang D**, Sama A, Piette F, Pogue-Geile KL, Kim RS, Gavin PG, Lipchik C, Feng H, Wang Y, Finnigan M, Kiesel B, Beumer JH, Wolmark N, Lucas PC, Allegra CJ, and Srinivasan A. Neratinib plus Cetuximab in Quadruple WT (KRAS, NRAS, BRAF, PIK3CA) Metastatic Colorectal Cancer Resistant to Cetuximab or Panitumumab: NSABP FC-7, A Phase Ib Study. *Clin Cancer Res* 2020; Epub ahead of print. PMID: 33203645. Full Text

Medicine, NSABP Foundation Samuel.jacobs@nsabp.org.
UPMC Hillman Cancer Center, UPMC.
Department of Medicine, University of Florida.

Medical Oncology, Cancer Care Specialists of Illinois.
Medical Oncology, St. Joseph Mercy Health System.
Henry Ford Cancer Institute/Henry Ford Health System, Clinical Trial Office.
Thomas Jefferson University.
Clinical Research, IDDI.
Pathology, NSABP Foundation, Inc.
NSABP Foundation, Inc.
Pathology, NSABP.
Department of Pharmaceutical Sciences, UPMC Hillman Cancer Center.
Cancer Therapeutics Program, UPMC Hillman Cancer Center.
Surg, NSABP Foundation, Inc, and The University of Pittsburgh.
Pathology, University of Pittsburgh School of Medicine.
Medicine, University of Florida.

PURPOSE: In metastatic colorectal cancer (mCRC), HER2 (ERBB2) gene amplification is implicated in anti-EGFR therapy resistance. We sought to determine the recommended phase II dose (RP2D) and efficacy of neratinib, a pan-ERBB kinase inhibitor, combined with cetuximab, in patients with progressive disease (PD) on anti-EGFR treatment. EXPERIMENTAL DESIGN: Twenty-one patients with quadruple-wild-type, refractory mCRC enrolled in this 3+3 phase-Ib study. Standard dosage cetuximab was administered with neratinib at 120mg, 160mg, 200mg, and 240mg/day orally in 28-day cycles. Samples were collected for molecular and pharmacokinetic studies. RESULTS: Sixteen patients were evaluable for dose-limiting toxicity (DLT). 240mg was determined to be the RP2D wherein a single DLT occurred (1/7 patients). Treatment-related DLTs were not seen at lower doses. Best response was stable disease (SD) in 7/16 (44%). HER2 amplification (CISH) was detected in 2/21 (9.5%) treatment-naïve tumors and 4/16 (25%) biopsies upon trial enrollment (post-anti-EGFR treatment and progression). Compared to matched enrollment biopsies, 6/8 (75%) blood samples showed concordance for HER2 CNV in cfDNA. Five SD patients had HER2 amplification in either treatment-naïve or enrollment biopsies. Examination of gene-expression, total protein, and protein phosphorylation levels showed relative upregulation of ≥2 members of the HER-family receptors or ligands upon enrollment versus matched treatment-naïve samples. CONCLUSIONS: The RP2D of neratinib in this combination was 240mg/day, which was well tolerated with low incidence of G3 AEs. There were no objective responses; SD was seen at all neratinib doses. HER2 amplification, detectable in both tissue and blood, was more frequent post-anti-EGFR therapy.

Hematology-Oncology

Mazieres J, Rittmeyer A, **Gadgeel S**, Hida T, Gandara DR, Cortinovis DL, Barlesi F, Yu W, Matheny C, Ballinger M, and Park K. Atezolizumab vs Docetaxel in Pretreated Patients with Non-Small Cell Lung Cancer: Final Results From the Randomized Phase II POPLAR and Phase III OAK Clinical Trials. *J Thorac Oncol* 2020; Epub ahead of print. PMID: 33166718. Full Text

Toulouse University Hospital, Institut Universitaire du Cancer de Toulouse, Université Paul Sabatier, Toulouse, France; Address: Toulouse University Hospital, Larrey Hospital, Chemin de Pouvourville, 314àà Toulouse, France. Electronic address: mazieres.j@chu-toulouse.fr.
Lungenfachklinik Immenhausen, Immenhausen, Germany; Address: Lungenfachklinik, Immenhausen, Robert-Koch-Straße 3, 34376 Immenhausen, Germany.
Henry Ford Cancer Institute/Henry Ford Hospital, Detroit, MI, USA; Address: Henry Ford Cancer Institute/Henry Ford Hospital, Hematology/Oncology-CFP-5, 2799 West Grand Boulevard, Detroit, MI 48202.
Aichi Cancer Center Hospital, Nagoya, Japan; Address: Aichi Cancer Center Hospital, 1-1 Kanokoden, Chikusa-ku, Nagoya, 464-8681, Japan.
UC Davis Comprehensive Cancer Center, Sacramento, CA, USA; Address: UC Davis Comprehensive Cancer Center, 4501 X St, Sacramento, CA 95817.
SC Oncologia Medica, SS Lung Unit Asst Ospedale San Gerardo, Monza, Italy; Address: SC Oncologia Medica, VIa Pergolesi 33 Monza, Italy.
Aix-Marseille University, CNRS, INSERM, CRCM, APHM, Marseille, France; Address: Hôpital Nord - Chemin des Bourrelly - 13915 Marseille Cedex 20.

Genentech, Inc., South San Francisco, CA, USA; Address: Genentech, Inc., 1 DNA Way, South San Francisco, CA 94080.
Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea; Address: Samsung Medical Center, 81 Irwon-ro, Gananam-gu, Seoul, 06351, Korea.

INTRODUCTION: The phase II POPLAR and phase III OAK studies of the anti-PD-L1 immunotherapy atezolizumab in patients with previously treated advanced non-small cell lung cancer (NSCLC) showed significant improvements in survival vs docetaxel. Longer follow-up permits evaluation of continued benefit of atezolizumab. This study reports final overall survival (OS) and safety findings from both trials. METHODS: POPLAR randomized 287 (atezolizumab,144; docetaxel,143) and OAK randomized 1225 (atezolizumab, 613; docetaxel, 612) patients. Patients received atezolizumab (1200-mg fixed dose) or docetaxel (75 mg/m(2)) every 3 weeks. Efficacy and safety outcomes were evaluated. RESULTS: A longer OS was observed in patients receiving atezolizumab vs docetaxel in POPLAR (median OS: 12.6 months vs 9.7 months; HR: 0.76 [95% CI: 0.58-1.00]) and OAK (median OS: 13.3 vs 9.8 months; HR: 0.78 [95% CI: 0.68-0.89]. Four-year OS rates in POPLAR were 14.8% (8.7-20.8) and 8.1% (3.2-13.0) for atezolizumab and docetaxel, respectively, and 15.5% (12.4-18.7) and 8.7% (6.2-11.3) in OAK. Atezolizumab had improved OS benefit compared with docetaxel across all PD-L1 expression and histology groups. Most 4-year survivors in the docetaxel arms received subsequent immunotherapy (POPLAR, 50%; OAK, 65%). Of 4-year survivors, most had ECOG PS 0 and nonsquamous histology; approximately half were responders (POPLAR: atezolizumab, 7/15; docetaxel, 3/4; OAK: atezolizumab, 24/43; docetaxel, 11/26). Treatment-related Grade 3/4 adverse events occurred in 27% and 16% of atezolizumab 4-year survivors in POPLAR and OAK, respectively. CONCLUSIONS: Long-term follow-up suggests a consistent survival benefit with atezolizumab vs docetaxel in patients with previously treated NSCLC regardless of PD-L1 expression, histology, or subsequent immunotherapy. Atezolizumab had no new safety signals, and the safety profile was similar to previous studies. STUDY IDENTIFIERS: NCT01903993, NCT02008227.

Hematology-Oncology
Spigel D, Jotte R, Nemunaitis J, Shum M, Schneider J, Goldschmidt J, Eisenstein J, Berz D, Seneviratne L, Socoteanu M, Bhanderi V, Konduri K, Xia M, Wang H, Hozak RR, Gueorguieva I, Ferry D, Gandhi L, Chao BH, and **Rybkin I**. Brief Report: Randomized Phase 2 Studies of Checkpoint Inhibitors Alone or in Combination with Pegilodecakin in Patients with Metastatic Non-Small-Cell Lung Cancer (CYPRESS-1 and CYPRESS-2). *J Thorac Oncol* 2020; Epub ahead of print. PMID: 33166722. Request Article

Sarah Cannon Research Institute and Tennessee Oncology, Nashville, TN, USA. Electronic address: david.spigel@sarahcannon.com.
US Oncology Research Houston Texas, and Rocky Mountain Cancer Centers, Denver, CO, USA.
University of Toledo, Toledo, OH, USA.
The Oncology Institute of Hope and Innovation, Whittier, CA, USA.
NYU Winthrop Hospital, Mineola, NY, USA.
Oncology and Hematology Association of SW Virginia, Blacksburg, VA, USA.
Colorado Permanente Medical Group/Kaiser Lafayette, CO, USA.
Beverly Hills Cancer Center, Beverly Hills, CA, USA.
Los Angeles Hematology Oncology Medical Group, Los Angeles, CA, USA.
Texas Oncology-Longview Cancer Center, Longview, TX, USA.
Florida Cancer Specialist, Tallahassee, FL, USA.
Baylor Charles A. Sammons Cancer Center, Texas Oncology PA, Dallas, TX, USA.
Eli Lilly and Company, Indianapolis, IN, USA.
Eli Lilly and Company, New York, NY, USA.
Henry Ford Cancer Institute, Detroit, MI, USA.

INTRODUCTION: Checkpoint inhibitors (CPI) have been approved to treat metastatic NSCLC. Pegilodecakin+CPI suggested promising efficacy in phase 1 IVY, providing rationale for randomized phase 2 trials CYPRESS-1 and CYPRESS-2. METHODS: CYPRESS-1 (N=101) and CYPRESS-2 (N=52) included ECOG 0-1, 1L/2L metastatic NSCLC, respectively, without known EGFR/ALK mutations. Patients were randomized 1:1; control arms received pembrolizumab (CYPRESS-1) or nivolumab

(CYPRESS-2); experimental arms received pegilodecakin+CPI. Patients had PD-L1 tumor proportion score (TPS) ≥50% (CYPRESS-1) or 0-49% (CYPRESS-2). Primary endpoint was ORR per investigator. Secondary endpoints included PFS, OS, and safety. Exploratory endpoints included immune activation biomarkers. RESULTS: Median follow-up for CYPRESS-1 and CYPRESS-2 was 10.0 and 11.6 months, respectively. Results for pegilodecakin+pembrolizumab versus pembrolizumab were: ORR per investigator 47%vs.44% (Odds ratio:1.1;95%CI[0.5,2.5]); mPFS 6.3vs.6.1 months (HR:0.937;95%CI[0.541,1.625]); and mOS 16.3 months vs.not reached (HR:1.507;95%CI[0.708,3.209]). Results per blinded independent central review (BICR) were consistent. Treatment discontinuation rate due to AEs doubled in the experimental arm (32%vs.15%). Gr≥3 treatment related adverse events (TRAEs)(62%vs.19%) included anemia(20%vs.0%) and thrombocytopenia(12%vs.2%). Results for pegilodecakin+nivolumab versus nivolumab were:ORR per investigator 15%vs.12% (Odds ratio:1.2;95%CI[0.3,5.9]); mPFS 1.9vs.1.9 months (HR:1.006;95%CI[0.519,1.951]); and mOS 6.7vs.10.7 months (HR:1.871;95%CI[0.772,4.532]). Gr≥3 TRAEs (70.4%vs.16.7%) included anemia(40.7%vs.0%), fatigue(18%vs.0%), and thrombocytopenia(14.8%vs.0%). Biomarker data suggested activation of immunostimulatory signals of IL-10R pathway in pegilodecakin-containing arms. CONCLUSION: Despite evidence of biological effect in peripheral blood, adding pegilodecakin to CPI did not improve ORR, PFS, or OS, in 1L/2L NSCLC. Pegilodecakin+CPI demonstrated overall higher toxicity compared to CPI alone, leading to doubling of treatment discontinuation rate due to AEs.

Hematology-Oncology

Tam S, **Wu VF**, **Williams AM**, **Girgis M**, **Sheqwara JZ**, **Siddiqui F**, and **Chang SS**. Disparities in the Uptake of Telemedicine During the COVID-19 Surge in a Multidisciplinary Head and Neck Cancer Population by Patient Demographic Characteristics and Socioeconomic Status. *JAMA Otolaryngol Head Neck Surg* 2020; Epub ahead of print. PMID: 33151289. Full Text

Department of Otolaryngology-Head and Neck Surgery, Henry Ford Health System and Henry Ford Cancer Institute, Detroit, Michigan.
Department of Hematology/Medical Oncology, Henry Ford Health System and Henry Ford Cancer Institute, Detroit, Michigan.
Department of Radiation Oncology, Henry Ford Health System and Henry Ford Cancer Institute, Detroit, Michigan.

This cohort study examines the association between patient demographic characteristics and socioeconomic status and engagement in telemedicine during the COVID-19 pandemic.

Hospital Medicine

Dawson T, DeCamillo D, Kong X, Shensky B, **Kaatz S**, **Krol GD**, Ali M, Haymart B, Froehlich JB, and Barnes GD. Correcting Inappropriate Prescribing of Direct Oral Anticoagulants: A Population Health Approach. *J Am Heart Assoc* 2020; 9(22):e016949. PMID: 33150804. Full Text

Division of Cardiovascular Medicine Department of Internal Medicine Michigan Medicine Ann Arbor MI.
Michigan Clinical Outcomes Research and Reporting Program Michigan Medicine Ann Arbor MI.
Division of Hospital Medicine Henry Ford Hospital Detroit MI.
Department of General Internal Medicine Henry Ford Hospital Detroit MI.
Department of Pharmacy Beaumont Hospital, Royal Oak MI.

Hospital Medicine

Gunasekaran K, Ahmad M, Rehman S, **Thilagar B**, Gopalratnam K, Ramalingam S, Paramasivam V, Arora A, and Chandran A. Impact of a Positive Viral Polymerase Chain Reaction on Outcomes of Chronic Obstructive Pulmonary Disease (COPD) Exacerbations. *Int J Environ Res Public Health* 2020; 17(21). PMID: 33147795. Full Text

Division of Pulmonary Diseases and Critical Care, Yale-New Haven Health Bridgeport Hospital, 267 Grant Street, Bridgeport, CT 06610, USA.
Division of Pulmonary Diseases and Critical Care, St. Peter's University Hospital, New Brunswick, NJ 08901, USA.

Department of Medicine, Shaikh Khalifa Bin Zayed Al-Nahyan Medical and Dental College, Lahore 53720, Pakistan.
Division of Hospital Medicine, Henry Ford Hospital, 2799 W Grand Blvd, Detroit, MI 48202, USA.
Division of Hospital Medicine, Lovelace Medical Center, 601 Dr. Martin Luther King Jr. Ave NE, Albuquerque, NM 87102, USA.
Division of Nephrology, Baystate Medical Center, 759 Chestnut St, Springfield, MA 01199, USA.
Division of Pulmonary Diseases and Critical Care, Saint Mary's Hospital, 56 Franklin St, Waterbury, CT 06610, USA.
Division of Pulmonary Diseases and Critical Care, Hurley Medical Center, G-3252 Beecher Road, Flint, MI 48532, USA.

INTRODUCTION: More than 15 million adults in the USA have chronic obstructive pulmonary disease. Chronic obstructive pulmonary disease (COPD) places a high burden on the healthcare system. Many hospital admissions are due to an exacerbation, which is suspected to be from a viral cause. The purpose of this analysis was to compare the outcomes of patients with a positive and negative respiratory virus panel who were admitted to the hospital with COPD exacerbations. METHODS: This retrospective cohort study was conducted in the Geisinger Healthcare System. The dataset included 2729 patient encounters between 1 January 2006 and 30 November 2017. Hospital length of stay was calculated as the discrete number of calendar days a patient was in the hospital. Patient encounters with a positive and negative respiratory virus panel were compared using Pearson's chi-square or Fisher's exact test for categorical variables and Student's t-test or Wilcoxon rank-sum tests for continuous variables. RESULTS: There were 1626 patients with a total of 2729 chronic obstructive pulmonary disease exacerbation encounters. Nineteen percent of those encounters (n = 524) had a respiratory virus panel performed during their admission. Among these encounters, 161 (30.7%) had positive results, and 363 (69.3%) had negative results. For encounters with the respiratory virus panel, the mean age was 64.5, 59.5% were female, 98.9% were white, and the mean body mass index was 26.6. Those with a negative respiratory virus panel had a higher median white blood cell count (11.1 vs. 9.9, p = 0.0076). There were no other statistically significant differences in characteristics between the two groups. Respiratory virus panel positive patients had a statistically significant longer hospital length of stay. There were no significant differences with respect to being on mechanical ventilation or ventilation-free days. CONCLUSION: This study shows that a positive respiratory virus panel is associated with increased length of hospital stay. Early diagnosis of chronic obstructive pulmonary disease exacerbation patients with positive viral panel would help identify patients with a longer length of stay.

Hypertension and Vascular Research

Manis AD, Palygin O, Isaeva E, Levchenko V, LaViolette PS, **Pavlov TS**, Hodges MR, and Staruschenko A. Kcnj16 knockout produces audiogenic seizures in the Dahl salt-sensitive rat. *JCI Insight* 2020; Epub ahead of print. PMID: 33232300. Full Text

Department of Physiology, Medical College of Wisconsin, Milwaukee, United States of America.
Department of Radiology, Medical College of Wisconsin, Milwaukee, United States of America.
Division of Hypertension and Vascular Research, Henry Ford Health System, Detroit, United States of America.

Kir5.1 is an inwardly rectifying potassium (Kir) channel subunit abundantly expressed in the kidney and brain. We previously established the physiologic consequences of a Kcnj16 (gene encoding Kir5.1) knockout in the Dahl SS rat (SSKcnj16-/-), which caused electrolyte/pH dysregulation and high salt diet-induced mortality. Since Kir channel gene mutations may alter neuronal excitability and are linked to human seizure disorders, we hypothesized that SSKcnj16-/- rats would exhibit neurological phenotypes, including increased susceptibility to seizures. SSKcnj16-/- rats exhibited increased light sensitivity (fMRI) and reproducible sound-induced tonic-clonic audiogenic seizures confirmed by electroencephalography. Repeated seizure induction altered behavior, exacerbated hypokalemia, and led to approximately 38% mortality in male SSKcnj16-/- rats. Dietary potassium supplementation did not prevent audiogenic seizures but mitigated hypokalemia and prevented mortality induced by repeated seizures. These results reveal a distinct, non-redundant role for Kir5.1 channels in the brain, introduce a novel rat model of

audiogenic seizures, and suggest yet to be identified mutations in Kcnj16 may cause or contribute to seizure disorders.

Infectious Diseases
Alangaden GJ, and **Mayur RS**. Response to "Is the outcome of SARS-CoV-2 infection in solid organ transplant recipients really similar to that of the general population?". *Am J Transplant* 2020; Epub ahead of print. PMID: 33249750. Full Text

Department of Medicine, Division of Infectious Diseases, Henry Ford Hospital, Detroit, MI, USA.

We thank the authors Maria Mendoza et al. (1) for their comments related to our publication on the clinical characteristics and outcomes of COVID-19 in solid organ transplant (SOT) recipients (2). Our study included a cohort of 47 consecutive SOT recipients with COVID-19. As noted in our study the 12 patients with mild to moderate COVID-19 that were treated as outpatients were excluded from the analysis to avoid potential selection bias. The study therefore compares 35 hospitalized SOT and 100 hospitalized non-transplant patients with COVID-19.

Infectious Diseases
Hutton MA, Sundaram A, **Perri MB**, **Zervos MJ**, and **Herc ES**. Assessment of invitrosynergy of daptomycin or vancomycin plus ceftaroline for daptomycin non-susceptible Staphylococcus aureus. *Diagn Microbiol Infect Dis* 2020; 98(3):115126. PMID: 32861155. Full Text

Department of Pharmacy, Henry Ford Health System, 2799 West Grand Boulevard, Detroit, MI 48202. Electronic address: mary.hutton@imail.org.
Wayne State University, 540 E Canfield St, Detroit, MI 48201.
Division of Infectious Diseases, Henry Ford Hospital, 2799 West Grand Boulevard, Detroit, MI 48202.
Wayne State University, 540 E Canfield St, Detroit, MI 48201; Division of Infectious Diseases, Henry Ford Hospital, 2799 West Grand Boulevard, Detroit, MI 48202.
Wayne State University, 540 E Canfield St, Detroit, MI 48201; Division of Infectious Diseases, Henry Ford Hospital, 2799 West Grand Boulevard, Detroit, MI 48202. Electronic address: eherc1@hfhs.org.

The combination of vancomycin or daptomycin plus ceftaroline has showed synergistic results in vitro. This study aimed to investigate in vitro synergy of vancomycin or daptomycin plus ceftaroline for seven patients with daptomycin non-susceptible Staphylococcus aureus (SA) bacteremia Thirteen isolates from seven patients were evaluated: two methicillin-susceptible and five methicillin-resistant SA infections. All patients were treated with daptomycin and became non-susceptible (minimum inhibitory concentration (MIC) >1 μg/mL) with therapy or had resistant strains initially. Time kill experiments were completed with 0.25 × MIC, 0.5 × MIC, and 0.75 × MIC concentrations. No synergy was seen at 0.25 × MIC. Synergy was observed for 4 isolates with vancomycin plus ceftaroline and with daptomycin plus ceftaroline for 2 isolates at 0.5 × MIC. These results are in accordance with literature that supports synergistic combinations of daptomycin or vancomycin with ceftaroline for SA bacteremia. Daptomycin non-susceptible SA bacteremia presents a treatment challenge.

Internal Medicine
Al-Darzi W, **Alalwan Y**, **Askar F**, **Sadiq O**, **Venkat D**, **Gonzalez H**, **Galusca D**, **Yoshida A**, and **Jafri SM**. Risk Factors and Outcomes of Intracardiac Thrombosis During Orthotopic Liver Transplantation. *Transplant Proc* 2020; Epub ahead of print. PMID: 33246584. Full Text

Division of Cardiology, Henry Ford Hospital, Detroit, Michigan. Electronic address: waleed.aldarzi@gmail.com.
Department of Internal Medicine, Henry Ford Hospital, Detroit, Michigan.
Department of Internal Medicine, Henry Ford Hospital, Detroit, Michigan; School of Medicine, Wayne State University, Detroit, Michigan.
Division of Gastroenterology, Henry Ford Hospital, Detroit, Michigan.
School of Medicine, Wayne State University, Detroit, Michigan; Division of Gastroenterology, Henry Ford Hospital, Detroit, Michigan.

Department of Anesthesiology, Henry Ford Hospital, Detroit, Michigan.
Transplant and Hepatobiliary Surgery, Henry Ford Hospital, Detroit, Michigan.

BACKGROUND: Intracardiac thrombosis incidence during orthotopic liver transplantation is estimated at 0.36% to 6.2% with mortality up to 68%. We aimed to evaluate risk factors and outcomes related to intracardiac thrombosis during orthotopic liver transplantation. MATERIALS AND METHODS: A comprehensive retrospective data review of 388 patients who underwent orthotopic liver transplantation at an urban transplant center from January 2013 to October 2016 was obtained. RESULTS: Six patients were found to have documented intracardiac thrombosis; 4 cases were recognized during the reperfusion stage and 1 during pre-anhepatic stage. All allografts were procured from decreased donors with a median donor age of 44 years (interquartile range, 35.25-49.75) and the cause of death was listed as cerebrovascular accident in 5 donors. Preoperative demographic, clinical, laboratory, and historical risk factors did not differ in patients with thrombosis. None had a prior history of trans-jugular intrahepatic portosystemic shunt or gastrointestinal bleeding. Three patients had renal injury, but no intraoperative hemodialysis was performed. Transesophageal echocardiographic findings included elevated pulmonary artery pressure (1/6), right ventricular strain (1/6), and pulmonary artery thrombus (1/6). Three patients died intraoperatively. Tissue plasminogen activator alone was given to 1 patient who did not survive, intravenous heparin only to 1 patient with resolution, and a combination of both was used in 2 patients with clot resolution achieved. CONCLUSION: Cardiac thrombosis should be considered in patients having hemodynamic compromise during liver transplantation. Transesophageal echocardiography is a useful diagnostic tool. Intracardiac thrombosis treatment remains challenging; however, using both thrombolytics and heparin could achieve better results.

Internal Medicine
Dawson T, DeCamillo D, Kong X, Shensky B, **Kaatz S**, **Krol GD**, Ali M, Haymart B, Froehlich JB, and Barnes GD. Correcting Inappropriate Prescribing of Direct Oral Anticoagulants: A Population Health Approach. *J Am Heart Assoc* 2020; 9(22):e016949. PMID: 33150804. Full Text

Division of Cardiovascular Medicine Department of Internal Medicine Michigan Medicine Ann Arbor MI.
Michigan Clinical Outcomes Research and Reporting Program Michigan Medicine Ann Arbor MI.
Division of Hospital Medicine Henry Ford Hospital Detroit MI.
Department of General Internal Medicine Henry Ford Hospital Detroit MI.
Department of Pharmacy Beaumont Hospital, Royal Oak MI.

Internal Medicine
Hoffert M, **Kerr H**, **Hegab S**, **Whitehouse S**, **Kokas M**, **MacLean L**, **Van Harn MG**, and **Baker-Genaw K**. Designing a Yoga Intervention Program to Improve Well-Being for Physician Trainees: Challenges and Lessons Learned. *Int J Yoga Therap* 2020; Epub ahead of print. PMID: 33157552. Full Text

Department of Medical Education, Henry Ford Hospital, Detroit, Mich.
Department of Dermatology, Henry Ford Hospital, Detroit, Mich.
Division of Pulmonary and Critical Care Medicine, Henry Ford Hospital, Detroit, Mich.
Behavioral Health Services, Henry Ford Hospital, Detroit, Mich.
Public Health Science Division of Biostatistics, Henry Ford Hospital, Detroit, Michigan.
Department of Medical Education and Department of Internal Medicine, Henry Ford Hospital, Detroit, Mich.

Well-being activities may help to counteract physician burnout. Yoga is known to enhance well-being, but there are few studies of yoga as an intervention for physicians in training. This prospective methodology-development study aimed to explore how to establish a yoga-based well-being intervention for physician trainees in a large urban training hospital. We aimed to identify factors that contribute to trainee participation and explore an instrument to measure changes in self-reported well-being after yoga. Cohorts included a required-attendance group, a voluntary-attendance group, and an unassigned walk-in yoga group. Weekly 1-hour yoga sessions were led by a qualified yoga instructor for 4 weeks. The seven-question Resident Physician Well-Being Index (RPWBI) was used to measure resident well-being before yoga, after 4 weeks of yoga, and 6 months post-yoga. Trainees attending each session ranged from 17

for required yoga to 0-2 for voluntary yoga, 2-9 for lunchtime walk-in yoga, and 1-7 for evening walk-in yoga. In the required-yoga group (n = 17), overall RPWBI mean scores did not change significantly across the three query times, and participation in the survey declined over time. The mean baseline RPWBI score for the required group before yoga was in the non-distressed range and answers to the seven individual questions varied. Requiring a yoga activity for medical trainees may be a good strategy for promoting participation in yoga. The RPWBI may have limited utility for measuring changes in overall group well-being after a yoga intervention.

Nephrology

Weinreb JC, Rodby RA, **Yee J**, Wang CL, Fine D, McDonald RJ, Perazella MA, Dillman JR, and Davenport MS. Use of Intravenous Gadolinium-based Contrast Media in Patients with Kidney Disease: Consensus Statements from the American College of Radiology and the National Kidney Foundation. *Radiology* 2020; Epub ahead of print. PMID: 33170103. Full Text

From the American College of Radiology, Reston, Va (J.C.W., C.L.W., R.J.M., J.R.D., M.S.D.); National Kidney Foundation, New York, NY (R.A.R., J.Y., D.F., M.A.P.); Department of Radiology and Biomedical Imaging (J.C.W.) and Department of Internal Medicine, Section of Nephrology (M.A.P.), Yale University School of Medicine, New Haven, Conn; Department of Nephrology, Rush University Medical Center, Chicago, Ill (R.A.R.); Department of Nephrology, Henry Ford Health System, Detroit, Mich (J.Y.); Department of Radiology, University of Washington, Seattle, Wash (C.L.W.); Department of Nephrology, Johns Hopkins University School of Medicine, Baltimore, Md (D.F.); Department of Radiology, Mayo Clinic, Rochester, Minn (R.J.M.); Department of Radiology, Cincinnati Children's Hospital Medical Center at University of Cincinnati College of Medicine, Cincinnati, Ohio (J.R.D.); Departments of Radiology (M.S.D.) and Urology (M.S.D.), Michigan Medicine, 1500 E Medical Center Dr, Room B2 A209P, Ann Arbor, MI 48109-5030; and Michigan Radiology Quality Collaborative, Ann Arbor, Mich (M.S.D.).

Inaugural consensus statements were developed and endorsed by the American College of Radiology (ACR) and the National Kidney Foundation to improve and standardize the care of patients with kidney disease who have indication(s) to receive ACR-designated group II or group III intravenous gadolinium-based contrast media (GBCM). The risk of nephrogenic systemic fibrosis (NSF) from group II GBCM in patients with advanced kidney disease is thought to be very low (zero events following 4931 administrations to patients with estimated glomerular filtration rate [eGFR] <30 mL/min per 1.73 m(2); upper bounds of the 95% confidence intervals: 0.07% overall, 0.2% for stage 5D chronic kidney disease [CKD], 0.5% for stage 5 CKD and no dialysis). No unconfounded cases of NSF have been reported for the only available group III GBCM (gadoxetate disodium). Depending on the clinical indication, the potential harms of delaying or withholding group II or group III GBCM for an MRI in a patient with acute kidney injury or eGFR less than 30 mL/min per 1.73 m(2) should be balanced against and may outweigh the risk of NSF. Dialysis initiation or alteration is likely unnecessary based on group II or group III GBCM administration. This article is a simultaneous joint publication in Radiology and Kidney Medicine. The articles are identical except for stylistic changes in keeping with each journal's style. Either version may be used in citing this article.

Neurology

Anand SK, **Macki M**, Culver LG, **Wasade VS**, Hendren S, and **Schwalb JM**. Patient navigation in epilepsy care. *Epilepsy Behav* 2020; 113:107530. PMID: 33232897. Full Text

Wayne State University School of Medicine, 540 E Canfield St., Detroit, MI, USA. Electronic address: asharath@med.wayne.edu.
Department of Neurosurgery, Henry Ford Hospital, 2799 W Grand Blvd, Detroit, MI, USA.
Wayne State University School of Medicine, 540 E Canfield St., Detroit, MI, USA.
Department of Neurology, Henry Ford Hospital, 2799 W Grand Blvd, Detroit, MI, USA; Department of Neurology, Wayne State University School of Medicine, 540 E Canfield St., Detroit, MI, USA.
Division of Colorectal Surgery, Department of Surgery, University of Michigan, 1500 E Medical Center Dr., Ann Arbor, MI, USA.

Department of Neurosurgery, Henry Ford Hospital, 2799 W Grand Blvd, Detroit, MI, USA; Center for Health Policy and Health Services Research, Henry Ford Health System, 2799 W Grand Blvd, Detroit MI 48202, USA.

The concept of patient navigation was first introduced in 1989 by the American Cancer Society and was first implemented in 1990 by Dr. Harold Freeman in Harlem, NY. The role of a patient navigator (PN) is to coordinate care between the care team, the patient, and their family while also providing social support. In the last 30 years, patient navigation in oncological care has expanded internationally and has been shown to significantly improve patient care experience, especially in the United States cancer care system. Like oncology care, patients who require epilepsy care face socioeconomic and healthcare system barriers and are at significant risk of morbidity and mortality if their care needs are not met. Although shortcomings in epilepsy care are longstanding, the COVID-19 pandemic has exacerbated these issues as both patients and providers have reported significant delays in care secondary to the pandemic. Prior to the pandemic, preliminary studies had shown the potential efficacy of patient navigation in improving epilepsy care. Considering the evidence that such programs are helpful for severely disadvantaged cancer patients and in enhancing epilepsy care, we believe that professional societies should support and encourage PN programs for coordinated and comprehensive care for patients with epilepsy.

Neurology

Bowyer SM, **Zillgitt A**, Greenwald M, and Lajiness-O'Neill R. Language Mapping With Magnetoencephalography: An Update on the Current State of Clinical Research and Practice With Considerations for Clinical Practice Guidelines. *J Clin Neurophysiol* 2020; 37(6):554-563. PMID: 33165228. Full Text

Department of Neurology, Henry Ford Health System, Detroit, Michigan, U.S.A.
Department of Neurology, Wayne State University, Detroit, Michigan, U.S.A.
Department of Physics, Oakland University, Rochester, Michigan, U.S.A.
Department of Communication Sciences and Disorders, Wayne State University, Detroit, Michigan, U.S.A.
Department of Psychology, Eastern Michigan University, Ypsilanti, Michigan, U.S.A.

Numerous studies have shown that language processing is not limited to a few brain areas. Visual or auditory stimuli activate corresponding cortical areas, then memory identifies the word or image, Wernicke's and Broca's areas support the processing for either reading/listening or speaking and many areas of the brain are recruited. Determining how a normal person processes language helps clinicians and scientist to understand how brain pathologies such as tumor or stroke can affect changes in language processing. Patients with epilepsy may develop atypical language organization. Over time, the chronic nature of epileptic activity, or changes from a tumor or stroke, can result in a shift of language processing area from the left to the right hemisphere, or re-routing of language pathways from traditional to non-traditional areas within the dominant left hemisphere. It is important to determine where these language areas are prior to brain surgery. MEG evoked responses reflecting cerebral activation of receptive and expressive language processing can be localized using several different techniques: Single equivalent current dipole, current distribution techniques or beamformer techniques. Over the past 20 years there have been at least 25 validated MEG studies that indicate MEG can be used to determine the dominant hemisphere for language processing. The use of MEG neuroimaging techniques is needed to reliably predict altered language networks in patients and to provide identification of language eloquent cortices for localization and lateralization necessary for clinical care.

Neurology

Carneiro T, Dashkoff J, Leung LY, Nobleza COS, Marulanda-Londono E, Hathidara M, Koch S, Sur N, Boske A, Voetsch B, **Aboul Nour H**, **Miller DJ**, Daneshmand A, Shulman J, Curiale G, Greer DM, Romero JR, Anand P, and Cervantes-Arslanian AM. Intravenous tPA for Acute Ischemic Stroke in Patients with COVID-19. *J Stroke Cerebrovasc Dis* 2020; 29(11):105201. PMID: 33066885. Full Text

Department of Neurology, Boston University School of Medicine, 72 East Concord Street, Collamore C3 Neurology, Boston, MA 02118, United States.

Department of Neurology, Stroke and Cerebrovascular Diseases Division, Tufts Medical Center, Boston, MA, United States.
Department of Neurology, Neuroscience Critical Care Division, University of Mississippi Medical Center, Jackson, MS, United States.
Department of Neurology, University of Miami Miller School of Medicine, Miami, FL, United States.
Department of Neurology, Saint David's Round Rock Medical Center, Round Rock, TX, United States.
Department of Neurology, Lahey Hospital and Medical Center, Burlington, MA, United States.
Department of Neurology, Henry Ford Hospital, Wayne State University, Detroit, MI, United States.
Department of Neurology, Boston University School of Medicine, 72 East Concord Street, Collamore C3 Neurology, Boston, MA 02118, United States; NHLBI's Framingham Heart Study, Framingham, MA, United States.
Department of Neurology, Boston University School of Medicine, 72 East Concord Street, Collamore C3 Neurology, Boston, MA 02118, United States. Electronic address: pria2@bu.edu.

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

Neurology
Chaudhry F, **Bulka H**, **Rathnam AS**, Said OM, Lin J, **Lorigan H**, Bernitsas E, Rube J, Korzeniewski SJ, **Memon AB**, Levy PD, **Schultz L**, Javed A, Lisak R, and **Cerghet M**. COVID-19 in multiple sclerosis patients and risk factors for severe infection. *J Neurol Sci* 2020; 418:117147. PMID: 32980780. Full Text

Department of Neurology, Henry Ford Health System, Detroit, MI, United States of America; Wayne State University School of Medicine, Detroit, MI, United States of America. Electronic address: gf9603@wayne.edu.
Department of Neurology, Henry Ford Health System, Detroit, MI, United States of America.
Wayne State University School of Medicine, Detroit, MI, United States of America.
Wayne State University School of Medicine, Detroit, MI, United States of America; Department of Neurology, Detroit Medical Center, Detroit, MI, United States of America.
Department of Neurology, Henry Ford Health System, Detroit, MI, United States of America; Wayne State University School of Medicine, Detroit, MI, United States of America.
Department of Neurology, Henry Ford Health System, Detroit, MI, United States of America; Department of Public Health Sciences, Henry Ford Hospital, Detroit, MI, United States of America.
Department of Neurology, University of Chicago, Chicago, IL, USA.

Multiple sclerosis (MS) patients have been considered a higher-risk population for COVID-19 due to the high prevalence of disability and disease-modifying therapy use; however, there is little data identifying clinical characteristics of MS associated with worse COVID-19 outcomes. Therefore, we conducted a multicenter prospective cohort study looking at the outcomes of 40 MS patients with confirmed COVID-19. Severity of COVID-19 infection was based on hospital course, where a mild course was defined as the patient not requiring hospital admission, moderate severity was defined as the patient requiring hospital

admission to the general floor, and most severe was defined as requiring intensive care unit admission and/or death. 19/40(47.5%) had mild courses, 15/40(37.5%) had moderate courses, and 6/40(15%) had severe courses. Patients with moderate and severe courses were significantly older than those with a mild course (57[50-63] years old and 66[58.8-69.5] years old vs 48[40-51.5] years old, P = 0.0121, P = 0.0373). There was differing prevalence of progressive MS phenotype in those with more severe courses (severe:2/6[33.3%]primary-progressing and 0/6[0%]secondary-progressing, moderate:1/14[7.14%] and 5/14[35.7%] vs mild:0/19[0%] and 1/19[5.26%], P = 0.0075, 1 unknown). Significant disability was found in 1/19(5.26%) mild course-patients, but was in 9/15(60%, P = 0.00435) of moderate course-patients and 2/6(33.3%, P = 0.200) of severe course-patients. Disease-modifying therapy prevalence did not differ among courses (mild:17/19[89.5%], moderate:12/15[80%] and severe:3/6[50%], P = 0.123). MS patients with more severe COVID-19 courses tended to be older, were more likely to suffer from progressive phenotype, and had a higher degree of disability. However, disease-modifying therapy use was not different among courses.

Neurology

Larivière S, Rodríguez-Cruces R, Royer J, Caligiuri ME, Gambardella A, Concha L, Keller SS, Cendes F, Yasuda C, Bonilha L, Gleichgerrcht E, Focke NK, Domin M, von Podewills F, Langner S, Rummel C, Wiest R, Martin P, Kotikalapudi R, O'Brien TJ, Sinclair B, Vivash L, Desmond PM, 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, Tortora D, Hatton SN, Vos SB, Duncan JS, Whelan CD, Thompson PM, Sisodiya SM, Bernasconi A, Labate A, McDonald CR, Bernasconi N, and Bernhardt BC. Network-based atrophy modeling in the common epilepsies: A worldwide ENIGMA study. *Sci Adv* 2020; 6(47). PMID: 33208365. Full Text

Multimodal Imaging and Connectome Analysis Laboratory, McConnell Brain Imaging Centre, Montreal Neurological Institute and Hospital, McGill University, Montreal, QC, Canada.
Neuroscience Research Center, University Magna Græcia, Catanzaro, CZ, Italy.
Institute of Neurology, University Magna Græcia, Catanzaro, CZ, Italy.
Institute of Neurobiology, Universidad Nacional Autónoma de México, Querétaro, México.
Institute of Systems, Molecular and Integrative Biology, University of Liverpool, Liverpool, UK.
Walton Centre NHS Foundation Trust, Liverpool, UK.
Department of Neurology, University of Campinas-UNICAMP, Campinas, São Paulo, Brazil.
Department of Neurology, Medical University of South Carolina, Charleston, SC, USA.
Department of Clinical Neurophysiology, University of Medicine Göttingen, Göttingen, Germany.
Institute of Diagnostic Radiology and Neuroradiology, Functional Imaging Unit, University Medicine Greifswald, Greifswald, Germany.
Department of Neurology, University Medicine Greifswald, Greifswald, Germany.
Institute of Diagnostic Radiology and Neuroradiology, University Medicine Greifswald, Greifswald, Germany.
Support Center for Advanced Neuroimaging (SCAN), University Institute of Diagnostic and Interventional Neuroradiology, University Hospital Bern, Bern, Switzerland.
Department of Neurology and Epileptology, Hertie Institute for Clinical Brain Research, University of Tübingen, Tübingen, Germany.
Department of Neuroscience, Central Clinical School, Alfred Hospital, Monash University, Melbourne, Victoria, Australia.
Departments of Medicine and Radiology, The Royal Melbourne Hospital, The University of Melbourne, Parkville, Victoria, Australia.
Department of Molecular and Cellular Therapeutics, The Royal College of Surgeons in Ireland, Dublin, Ireland.
Department of Neurology, Yale University School of Medicine, New Haven, CT, USA.
Department of Neurology, St. James' Hospital, Dublin, Ireland.
FutureNeuro SFI Research Centre, Dublin, Ireland.
Epilepsy Center, Neuro Center, Kuopio University Hospital, European Reference Network for Rare and Complex Epilepsies EpiCARE, Kuopio, Finland.

Faculty of Health Sciences, School of Medicine, Institute of Clinical Medicine, University of Eastern Finland, Kuopio, Finland.
Florey Institute of Neuroscience and Mental Health, University of Melbourne, Melbourne, Victoria 3010, Australia.
Neuroradiology Research Program, Meyer Children Hospital of Florence, University of Florence, Florence, Italy.
Translational and Clinical Research Institute, Newcastle University, Newcastle upon Tyne, UK.
Control and Intelligent Processing Center of Excellence (CIPCE), School of Electrical and Computer Engineering, University of Tehran, Tehran, Iran.
Departments of Research Administration and Radiology, Henry Ford Health System, Detroit, MI, USA.
Department of Neurology, Henry Ford Health System, Detroit, MI, USA.
Cognitive Science Department, Xiamen University, Xiamen, China.
Child Neurology Unit and Laboratories, Neuroscience Department, Children's Hospital A. Meyer-University of Florence, Italy.
Functional and Epilepsy Neurosurgery Unit, Neurosurgery Department, Children's Hospital A. Meyer-University of Florence, Italy.
USL Centro Toscana, Neurology Unit, Nuovo Ospedale Santo Stefano, Prato, Italy.
Cardiff University Brain Research Imaging Centre (CUBRIC), College of Biomedical Sciences, Cardiff University, Cardiff, UK.
Welsh Epilepsy Unit, Department of Neurology, University Hospital of Wales, Cardiff, UK.
Institute of Experimental Epileptology and Cognition Research, University Hospital Bonn, Bonn, Germany.
Department of Neurology, Hôpital Erasme, Université Libre de Bruxelles, Brussels, Belgium.
Department of Radiology, Hôpital Erasme, Université Libre de Bruxelles, Brussels, Belgium.
Division of Neuroscience, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK.
Department of Neurology, NYU Grossman School of Medicine, New York, NY, USA.
IRCCS Istituto Giannina Gaslini, Genova, Italy.
Department of Neurosciences, Center for Multimodal Imaging and Genetics, University of California San Diego, La Jolla, CA, USA.
Department of Clinical and Experimental Epilepsy, UCL Institute of Neurology, London, UK.
Chalfont Centre for Epilepsy, Bucks, UK.
Centre for Medical Image Computing, University College London, London, UK.
Imaging Genetics Center, Mark and Mary Stevens Institute for Neuroimaging and Informatics, USC Keck School of Medicine, Los Angeles, CA, USA.
Neuroimaging of Epilepsy Laboratory, McConnell Brain Imaging Centre, Montreal Neurological Institute and Hospital, McGill University, Montreal, QC, Canada.
Department of Psychiatry, Center for Multimodal Imaging and Genetics, University of California San Diego, La Jolla, CA, USA.
Multimodal Imaging and Connectome Analysis Laboratory, McConnell Brain Imaging Centre, Montreal Neurological Institute and Hospital, McGill University, Montreal, QC, Canada. boris.bernhardt@mcgill.ca.

Epilepsy is increasingly conceptualized as a network disorder. In this cross-sectional mega-analysis, we integrated neuroimaging and connectome analysis to identify network associations with atrophy patterns in 1021 adults with epilepsy compared to 1564 healthy controls from 19 international sites. In temporal lobe epilepsy, areas of atrophy colocalized with highly interconnected cortical hub regions, whereas idiopathic generalized epilepsy showed preferential subcortical hub involvement. These morphological abnormalities were anchored to the connectivity profiles of distinct disease epicenters, pointing to temporo-limbic cortices in temporal lobe epilepsy and fronto-central cortices in idiopathic generalized epilepsy. Negative effects of age on atrophy further revealed a strong influence of connectome architecture in temporal lobe, but not idiopathic generalized, epilepsy. Our findings were reproduced across individual sites and single patients and were robust across different analytical methods. Through worldwide collaboration in ENIGMA-Epilepsy, we provided deeper insights into the macroscale features that shape the pathophysiology of common epilepsies.

Neurology

Lima M, Siokas V, Aloizou AM, Liampas I, Mentis AA, Tsouris Z, Papadimitriou A, **Mitsias PD**, Tsatsakis A, Bogdanos DP, Baloyannis SJ, and Dardiotis E. Unraveling the Possible Routes of SARS-COV-2 Invasion into the Central Nervous System. *Curr Treat Options Neurol* 2020; 22(11):37. PMID: 32994698. Full Text

Department of Neurology, Laboratory of Neurogenetics, University of Thessaly, University Hospital of Larissa, Larissa, Greece. GRID: grid.411299.6
Public Health Laboratories, Hellenic Pasteur Institute, Athens, Greece. GRID: grid.418497.7
Department of Neurology, School of Medicine, University of Crete, 71003 Heraklion, Greece. GRID: grid.8127.c. ISNI: 0000 0004 0576 3437
Department of Neurology, Henry Ford Hospital, Detroit, MI 48202 USA. GRID: grid.413103.4. ISNI: 0000 0001 2160 8953
School of Medicine, Wayne State University, Detroit, MI 48202 USA. GRID: grid.254444.7. ISNI: 0000 0001 1456 7807
Laboratory of Toxicology, School of Medicine, University of Crete, 71003 Heraklion, Greece. GRID: grid.8127.c. ISNI: 0000 0004 0576 3437
Department of Rheumatology and clinical Immunology, University General Hospital of Larissa, Faculty of Medicine, School of Health Sciences, University of Thessaly, Larissa, Greece. GRID: grid.410558.d. ISNI: 0000 0001 0035 6670
Research Institute for Alzheimer's Disease, Aristotelian University of Thessaloniki, Thessaloniki, Greece. GRID: grid.4793.9. ISNI: 0000000109457005

PURPOSE OF REVIEW: To describe the possible neuroinvasion pathways of Severe Acute Respiratory Syndrome-related Coronavirus-2 (SARS-CoV-2), the virus responsible for the Coronavirus disease-19 (Covid-19) pandemic. RECENT FINDINGS: We present data regarding the family of Coronaviruses (CoVs) and the central nervous system (CNS), and describe parallels between SARS-CoV-2 and other members of the family, which have been investigated in more depth and combine these findings with the recent advancements regarding SARS-CoV-2. SUMMARY: SARS-CoV-2 like other CoVs is neuroinvasive, neurotropic and neurovirulent. Two main pathways of CNS penetration seem to be the strongest candidates, the hematogenous and the neuronal. The olfactory route in particular appears to play a significant role in neuroinvasion of coronaviruses and SARS-CoV-2, as well. However, existing data suggest that other routes, involving the nasal epithelium in general, lymphatic tissue and the CSF may also play roles in SARS-CoV-2 invasion into the CNS.

Neurology

Wagley N, Lajiness-O'Neill R, Hay JSF, **Bowyer SM**, Ugolini M, Kovelman I, and Brennan JR. Predictive processing during a naturalistic statistical learning task in ASD. *eNeuro* 2020; Epub ahead of print. PMID: 33199412. Full Text

Department of Psychology & Human Development, Vanderbilt University Nashville, TN 37205 neelima.wagley@vanderbilt.edu jobrenn@umich.edu.
Department of Psychology, University of Michigan Ann Arbor, MI 48109.
Department of Psychology, Eastern Michigan University Ypsilanti, MI, USA 48197.
Department of Psychology, University of Tennessee Knoxville, TN 37996.
Department of Neurology, Henry Ford Hospital Detroit, Michigan 48202.
Department of Linguistics, University of Michigan Ann Arbor, MI 48109 neelima.wagley@vanderbilt.edu jobrenn@umich.edu.

Children's sensitivity to regularities within the linguistic stream, such as the likelihood that syllables co-occur, is foundational to speech segmentation and language acquisition. Yet, little is known about the neurocognitive mechanisms underlying speech segmentation in typical development and in neurodevelopmental disorders that impact language acquisition such as Autism Spectrum Disorder (ASD). Here, we investigate the neural signals of statistical learning in 15 human participants (children ages 8-12) with a clinical diagnosis of ASD and 14 age- and gender-matched typically developing peers. We tracked the evoked neural responses to syllable sequences in a naturalistic statistical learning corpus

using magnetoencephalography (MEG) in the left primary auditory cortex, posterior superior temporal gyrus, and inferior frontal gyrus, across three repetitions of the passage. In typically developing children, we observed a neural index of learning in all three regions of interest, measured by the change in evoked response amplitude as a function of syllable surprisal across passage repetitions. As surprisal increased, the amplitude of the neural response increased; this sensitivity emerged after repeated exposure to the corpus. Children with ASD did not show this pattern of learning in all three regions. We discuss two possible hypotheses related to children's sensitivity to bottom-up sensory deficits and difficulty with top-down incremental processing.Significance Statement Language acquisition involves segmenting the continuous speech stream into sounds, syllables, and words. Learning these units relies on both the properties of the input, as well as emerging high-order cognitive mechanisms that guide learning from the top-down. We examined the neurobiology underlying the integration of top-down and bottom-up information in statistical speech segmentation in children with and without ASD. We offer evidence of neural and behavioral effects of syllable-to-syllable processing in speech segmentation that differ in typically developing children from children with a clinical diagnosis of ASD. Our findings inform developmental and cognitive theories of language acquisition by examining the computational nature of speech segmentation across different populations of learners.

Neurology
Wasade VS, and **Schultz L**. Reply to: Effect of seizure timing on long-term survival in brain tumor patients. *Epilepsy Behav* 2020; Epub ahead of print. PMID: 33239218. Full Text

Department of Neurosciences, Henry Ford Health System, Detroit, MI, USA; Wayne State University, School of Medicine, MI, USA. Electronic address: vwasade1@hfhs.org.
Department of Neurosciences, Henry Ford Health System, Detroit, MI, USA; Department of Public Health Sciences, Henry Ford Health System, Detroit, MI, USA.

Neurology
Zhang Y, **Qin Y**, **Chopp M**, **Li C**, **Kemper A**, **Liu X**, **Wang X**, **Zhang L**, and **Zhang ZG**. Ischemic Cerebral Endothelial Cell-Derived Exosomes Promote Axonal Growth. *Stroke* 2020; 51(12):3701-3712. PMID: 33138691. Full Text

Department of Neurology (Y.Z., Y.Q., M.C., C.L., X.L., X.W., L.Z., Z.G.Z.), Henry Ford Hospital, Detroit, MI.
Department of Physics, Oakland University, Rochester, MI (M.C.).
Department of Pathology (A.K.), Henry Ford Hospital, Detroit, MI.

BACKGROUND AND PURPOSE: Cerebral endothelial cells (CECs) and axons of neurons interact to maintain vascular and neuronal homeostasis and axonal remodeling in normal and ischemic brain, respectively. However, the role of exosomes in the interaction of CECs and axons in brain under normal conditions and after stroke is unknown. METHODS: Exosomes were isolated from CECs of nonischemic rats and is chemic rats (nCEC-exos and isCEC-exos), respectively. A multicompartmental cell culture system was used to separate axons from neuronal cell bodies. RESULTS: Axonal application of nCEC-exos promotes axonal growth of cortical neurons, whereas isCEC-exos further enhance axonal growth than nCEC-exos. Ultrastructural analysis revealed that CEC-exos applied into distal axons were internalized by axons and reached to their parent somata. Bioinformatic analysis revealed that both nCEC-exos and isCEC-exos contain abundant mature miRNAs; however, isCEC-exos exhibit more robust elevation of select miRNAs than nCEC-exos. Mechanistically, axonal application of nCEC-exos and isCEC-exos significantly elevated miRNAs and reduced proteins in distal axons and their parent somata that are involved in inhibiting axonal outgrowth. Blockage of axonal transport suppressed isCEC-exo-altered miRNAs and proteins in somata but not in distal axons. CONCLUSIONS: nCEC-exos and isCEC-exos facilitate axonal growth by altering miRNAs and their target protein profiles in recipient neurons.

Neurology

Zillgitt A, **Barkley GL**, and **Bowyer SM**. Visual Mapping With Magnetoencephalography: An Update on the Current State of Clinical Research and Practice With Considerations for Clinical Practice Guidelines. *J Clin Neurophysiol* 2020; 37(6):585-591. PMID: 33165231. Full Text

Department of Neurology, Henry Ford Health System, Detroit, Michigan, U.S.A.
Department of Neurology, Wayne State University, Detroit, Michigan, U.S.A.
Department of Physics, Oakland University, Rochester, Michigan, U.S.A.

Using visual evoked fields (VEFs) to differentiate healthy, normal brain function from dysfunctional cortex has been demonstrated to be both valid and reliable. Currently, VEFs are widely implemented to guide intracranial surgeries for epilepsy and brain tumors. There are several areas of possible future clinical use of VEFs, including early identification of disorders, such as multiple sclerosis, Parkinson's disease, stroke, and human immunodeficiency virus-associated neurocognitive disorders. These studies have suggested that VEFs could be used to study disease pathophysiology or as a biomarker for early identification of a disorder. The current clinical practice guidelines of the American Clinical Magnetoencephalography Society for VEFs are sufficient. At this time, VEFs should be used clinically to identify visual cortex and potentially tailor surgical resections.

Neurosurgery

Anand SK, and **Macki M**. What have we learned from C5 palsy - A short communication. *J Clin Neurosci* 2020; 81:111-112. PMID: 33222897. Full Text

Wayne State University School of Medicine, 540 East Canfield, Detroit, MI 48201 USA.
Department of Neurosurgery, Henry Ford Hospital, 2799 West Grand Boulevard, Royal Oak, MI 48202, USA. Electronic address: mmacki22@gmail.com.

A study group on C5 palsy retrospectively reviewed 1001 cervical operations at their institutions in order to understand the incidence, prognosticators, pathogenesis, and outcome of C5 palsy after cervical operations. Three studies are summarized. C5 palsy was higher after posterior versus anterior operations. C4-C5 foraminotomy and age were the strongest predictors of C5 palsy after posterior surgeries and anterior cervical decompression-fusion, respectively. Among patients undergoing C4-C5 posterior laminoforaminotomy with instrumented fusion, cord shift on postoperative imaging was thought to be implicated in the pathogenesis of C5 palsy. Among affected patients, 81.4% recovered. Median time to resolution of C5 palsy was between 6 months to 1 year.

Neurosurgery

Anand SK, **Macki M**, Culver LG, **Wasade VS**, Hendren S, and **Schwalb JM**. Patient navigation in epilepsy care. *Epilepsy Behav* 2020; 113:107530. PMID: 33232897. Full Text

Wayne State University School of Medicine, 540 E Canfield St., Detroit, MI, USA. Electronic address: asharath@med.wayne.edu.
Department of Neurosurgery, Henry Ford Hospital, 2799 W Grand Blvd, Detroit, MI, USA.
Wayne State University School of Medicine, 540 E Canfield St., Detroit, MI, USA.
Department of Neurology, Henry Ford Hospital, 2799 W Grand Blvd, Detroit, MI, USA; Department of Neurology, Wayne State University School of Medicine, 540 E Canfield St., Detroit, MI, USA.
Division of Colorectal Surgery, Department of Surgery, University of Michigan, 1500 E Medical Center Dr., Ann Arbor, MI, USA.
Department of Neurosurgery, Henry Ford Hospital, 2799 W Grand Blvd, Detroit, MI, USA; Center for Health Policy and Health Services Research, Henry Ford Health System, 2799 W Grand Blvd, Detroit MI 48202, USA.

The concept of patient navigation was first introduced in 1989 by the American Cancer Society and was first implemented in 1990 by Dr. Harold Freeman in Harlem, NY. The role of a patient navigator (PN) is to coordinate care between the care team, the patient, and their family while also providing social support. In the last 30 years, patient navigation in oncological care has expanded internationally and has been shown

to significantly improve patient care experience, especially in the United States cancer care system. Like oncology care, patients who require epilepsy care face socioeconomic and healthcare system barriers and are at significant risk of morbidity and mortality if their care needs are not met. Although shortcomings in epilepsy care are longstanding, the COVID-19 pandemic has exacerbated these issues as both patients and providers have reported significant delays in care secondary to the pandemic. Prior to the pandemic, preliminary studies had shown the potential efficacy of patient navigation in improving epilepsy care. Considering the evidence that such programs are helpful for severely disadvantaged cancer patients and in enhancing epilepsy care, we believe that professional societies should support and encourage PN programs for coordinated and comprehensive care for patients with epilepsy.

Neurosurgery

Benzil DL, Muraszko KM, Soni P, **Air EL**, Orrico KO, and Rutka JT. Toward an understanding of sexual harassment in neurosurgery. *J Neurosurg* 2020;1-10. Epub ahead of print. PMID: 33171438. Full Text

1Department of Neurosurgery, Cleveland Clinic, Cleveland, Ohio.
2Department of Neurosurgery, University of Michigan, Ann Arbor, Michigan.
3Department of Neurosurgery, Henry Ford Health System, Detroit, Michigan.
4Washington Office, American Association of Neurological Surgeons/Congress of Neurological Surgeons, Washington, DC; and.
5Department of Neurosurgery, The Hospital for Sick Children, University of Toronto, Ontario, Canada.

OBJECTIVE: The goal of this study was the creation and administration of a survey to assess the depth and breadth of sexual harassment across neurosurgery. METHODS: A survey was created to 1) assess perceived attitudes toward systemic issues that might be permissive of sexual harassment; 2) measure the reported prevalence and severity of sexual harassment; and 3) determine the populations at highest risk and those most likely to perpetrate sexual harassment. Demographic information was also included to facilitate further analysis. The SurveyMonkey platform was used, and a request to complete the survey was sent to all Society of Neurological Surgeons and Congress of Neurological Surgeons (CNS) active and resident members as well as CNS transitional, emeritus, and inactive members. Data were analyzed using RStudio version 1.2.5019. RESULTS: Nearly two-thirds of responders indicated having witnessed sexual harassment in some form (62%, n = 382). Males were overwhelmingly identified as the offenders in allegations of sexual harassment (72%), with individuals in a "superior position" identified as offenders in 86%. Less than one-third of responders addressed the incidents of sexual harassment when they happened (yes 31%, no 62%, unsure 7%). Of those who did report, most felt there was either no impact or a negative one (negative: 34%, no impact: 38%). Almost all (85%) cited barriers to taking action about sexual harassment, including retaliation/retribution (87%), impact on future career (85%), reputation concerns (72%), and associated stress (50%). Female neurosurgeons were statistically more likely than male neurosurgeons to report witnessing or experiencing sexual harassment, as well as assessing it as a problem. CONCLUSIONS: This study demonstrates that neurosurgeons report significant sexual harassment across all ages and practice settings. Sexual harassment impacts both men and women, with more than half personally subjected to this behavior and two-thirds having witnessed it. Male dominance, a hierarchical environment, and a permissive environment remain prevalent within the neurosurgical community. This is not just a historical problem, but it continues today. A change of culture will be required for neurosurgery to shed this mantle, which must include zero tolerance of this behavior, new policies, awareness of unconscious bias, and commitment to best practices to enhance diversity. Above all, it will require that all neurosurgeons and neurosurgical leaders develop an awareness of sexual harassment in the workplace and establish consistent mechanisms to mitigate against its highly deleterious effects in the specialty.

Neurosurgery

Chhina AK, **Loyd GE**, **Szymanski TJ**, **Nowak KA**, **Peruzzi WT**, **Yeldo NS**, **Han X**, **Kerzabi LS**, **Galusca DM**, **Cazacu S**, **Brodie C**, and **Penning DH**. Frequency and Analysis of Unplanned Extubation in Coronavirus Disease 2019 Patients. *Crit Care Explor* 2020; 2(12):e0291. PMID: 33251520. Full Text

Department of Anesthesiology, Pain Management and Perioperative Medicine, Henry Ford Hospital, Detroit, MI.

Department of Public Health Sciences, Henry Ford Hospital, Detroit, MI.
Department of Neurosurgery, Henry Ford Hospital, Detroit, MI.

OBJECTIVES: To determine if patients with coronavirus disease 2019 had a greater number of unplanned extubations resulting in reintubations than in patients without coronavirus disease 2019. DESIGN: Retrospective cohort study comparing the frequency of unplanned extubations resulting in reintubations in a group of coronavirus disease 2019 patients to a historical (noncoronavirus disease 2019) control group. SETTING: This study was conducted at Henry Ford Hospital, an academic medical center in Detroit, MI. The historical noncoronavirus disease 2019 patients were treated in the 68 bed medical ICU. The coronavirus disease 2019 patients were treated in the coronavirus disease ICU, which included the 68 medical ICU beds, 18 neuro-ICU beds, 32 surgical ICU beds, and 40 cardiovascular ICU beds, as the medical ICU was expanded to these units at the peak of the pandemic in Detroit, MI. PATIENTS: The coronavirus disease 2019 cohort included patients diagnosed with coronavirus disease 2019 who were intubated for respiratory failure from March 12, 2020, to April 13, 2020. The historic control (noncoronavirus disease 2019) group consisted of patients who were admitted to the medical ICU in the year spanning from November 1, 2018 to October 31, 2019, with a need for mechanical ventilation that was not related to surgery or a neurologic reason. INTERVENTIONS: None. MEASUREMENTS AND MAIN RESULTS: To identify how many patients in each cohort had unplanned extubations, an electronic medical records query for patients with two intubations within 30 days was performed, in addition to a review of our institutional quality and safety database of reported self-extubations. Medical charts were manually reviewed by board-certified anesthesiologists to confirm each event was an unplanned extubation followed by a reintubation within 24 hours. There was a significantly greater incidence of unplanned extubations resulting in reintubation events in the coronavirus disease 2019 cohort than in the noncoronavirus disease 2019 cohort (coronavirus disease 2019 cohort: 167 total admissions with 22 events-13.2%; noncoronavirus disease 2019 cohort: 326 total admissions with 14 events-4.3%; $p < 0.001$). When the rate of unplanned extubations was expressed per 100 intubated days, there was not a significant difference between the groups (0.88 and 0.57, respectively; $p = 0.269$). CONCLUSIONS: Coronavirus disease 2019 patients have a higher incidence of unplanned extubation that requires reintubation than noncoronavirus disease 2019 patients. Further study is necessary to evaluate the variables that contribute to this higher incidence and clinical strategies that can reduce it.

Neurosurgery
Redjal N, Nahed BV, Dietrich J, **Kalkanis SN**, and Olson JJ. Congress of neurological surgeons systematic review and evidence-based guidelines update on the role of chemotherapeutic management and antiangiogenic treatment of newly diagnosed glioblastoma in adults. *J Neurooncol* 2020; 150(2):165-213. PMID: 33215343. Full Text

Department of Neurosurgery, Capital Health Institute for Neurosciences, Capital Health Institute for Neurosciences, Two Capital Way, Pennington, NJ, 08534, USA. nredjal@capitalhealth.org.
Department of Neurosurgery, Massachusetts General Hospital, Boston, MA, USA.
Department of Neurology, Massachusetts General Hospital, Boston, MA, USA.
Department of Neurosurgery, Henry Ford Health System, Detroit, MI, USA.
Department of Neurosurgery, Emory University School of Medicine, Atlanta, GA, USA.

QUESTION: What is the role of temozolomide in the management of adult patients (aged 65 and under) with newly diagnosed glioblastoma? TARGET POPULATION: These recommendations apply to adult patients diagnosed with newly diagnosed glioblastoma. RECOMMENDATION: Level I: Concurrent and post-irradiation Temozolomide (TMZ) in combination with radiotherapy and post-radiotherapy as described by Stupp et al. is recommended to improve both PFS and OS in adult patients with newly diagnosed GBM. There is no evidence that alterations in the dosing regimen have additional beneficial effect. QUESTION: Is there benefit to adjuvant temozolomide treatment in elderly patients (> 65 years old?). TARGET POPULATION: These recommendations apply to adult patients diagnosed with newly diagnosed glioblastoma. RECOMMENDATION: Level III: Adjuvant TMZ treatment is suggested as a treatment option to improve PFS and OS in adult patients (over 70 years of age) with newly diagnosed GBM. QUESTION: What is the role of local regional chemotherapy with BCNU biodegradable polymeric wafers in adult patients with newly diagnosed glioblastoma? TARGET POPULATION: These

recommendations apply to adult patients diagnosed with newly diagnosed glioblastoma. RECOMMENDATION: Level III: There is insufficient evidence for the use of BCNU wafers following resection in patients with newly diagnosed glioblastoma who undergo the Stupp protocol after surgery. Further studies of higher quality are suggested to understand the role of BCNU wafer and other locoregional therapy in the setting of Stupp Protocol. QUESTION: What is the role of bevacizumab in the adult patient with newly diagnosed glioblastoma? TARGET POPULATION: These recommendations apply to adult patients diagnosed with newly diagnosed glioblastoma. RECOMMENDATION: Level I: Bevacizumab in general is not recommended in the initial treatment of adult patients with newly diagnosed GBM. It continues to be strongly recommended that patients with newly diagnosed GBM be enrolled in properly designed clinical trials to assess the benefit of novel chemotherapeutic agents compared to standard therapy.

Orthopaedics/Bone and Joint Center

Armstrong AD, Agel J, Beal MD, Bednar MS, Caird MS, Carpenter JE, **Guthrie ST**, Juliano P, Karam M, LaPorte D, Marsh JL, Patt JC, Peabody TD, Wu K, Martin DF, Harrast JJ, and Van Heest AE. Use of the Behavior Assessment Tool in 18 Pilot Residency Programs. *JB JS Open Access* 2020; 5(4). PMID: 33244509. Full Text

Department of Orthopaedics and Rehabilitation, Bone and Joint Institute, Penn State Milton S. Hershey Medical Center, Hershey, Pennsylvania.
Department Orthopaedics and Sports Medicine, Harborview Medical Center, Seattle, Washington.
Department of Orthopaedic Surgery, North Western University, Chicago, Illinois.
Department of Orthopaedic Surgery and Rehabilitation, Loyola University Medical Center, Chicago, Illinois.
Department of Orthopaedic Surgery, University of Michigan, Ann Arbor, Michigan.
Department of Orthopaedic Surgery, Sports Medicine, Med Sport, Ann Arbor, Michigan.
Henry Ford Orthopaedics, Henry Ford Hospital, Detroit, Michigan.
Department of Orthopaedics and Rehabilitation, University of Iowa, Iowa City, Iowa.
Department of Orthopaedic Surgery, Johns Hopkins Medicine, Baltimore, Maryland.
CMC Orthopaedic Surgery, University of North Carolina School of Medicine, Charlotte, North Carolina.
Department of Orthopaedic Surgery, Wake Forest Baptist Health, Winston-Salem, North Carolina.
Data Harbor Solutions, Chicago, Illinois.
Department of Orthopaedic Surgery, University of Minnesota, Minneapolis, Minnesota.

BACKGROUND: The purpose of this study was to determine the feasibility and evaluate the effectiveness of the American Board of Orthopaedic Surgery Behavior Tool (ABOSBT) for measuring professionalism. METHODS: Through collaboration between the American Board of Orthopaedic Surgery and American Orthopaedic Association's Council of Residency Directors, 18 residency programs piloted the use of the ABOSBT. Residents requested assessments from faculty at the end of their clinical rotations, and a 360° request was performed near the end of the academic year. Program Directors (PDs) rated individual resident professionalism (based on historical observation) at the outset of the study, for comparison to the ABOSBT results. RESULTS: Nine thousand eight hundred ninety-two evaluations were completed using the ABOSBT for 449 different residents by 1,012 evaluators. 97.6% of all evaluations were scored level 4 or 5 (high levels of professional behavior) across all of the 5 domains. In total, 2.4% of all evaluations scored level 3 or below reflecting poorer performance. Of 431 residents, the ABOSBT identified 26 of 32 residents who were low performers (2 or more < level 3 scores in a domain) and who also scored "below expectations" by the PD at the start of the pilot project (81% sensitivity and 57% specificity), including 13 of these residents scoring poorly in all 5 domains. Evaluators found the ABOSBT was easy to use (96%) and that it was an effective tool to assess resident professional behavior (81%). CONCLUSIONS: The ABOSBT was able to identify 2.4% low score evaluations (<level 3) for all residents. The tool was concordant with the PD for 81% of the residents considered low performers or "outliers" for professional behavior. The 5-domain construct makes it an effective actionable tool that can be used to help develop performance improvement plans for residents. LEVEL OF EVIDENCE: Level II.

Orthopaedics/Bone and Joint Center

Bernstein DN, **Franovic S**, **Smith DG**, **Hessburg L**, **Yedulla N**, **Moutzouros V**, and **Makhni EC**. Pediatric PROMIS Computer Adaptive Tests Are Highly Correlated With Adult PROMIS Computer Adaptive Tests in Pediatric Sports Medicine Patients. *Am J Sports Med* 2020; Epub ahead of print. PMID: 33175563. Full Text

Institute for Strategy & Competitiveness, Harvard Business School, Boston, Massachusetts, USA.
Department of Orthopedic Surgery, Henry Ford Health System, Detroit, Michigan, USA.

BACKGROUND: The Patient-Reported Outcomes Measurement Information System (PROMIS) is a powerful set of patient-reported outcome measures (PROMs) that are gaining popularity throughout orthopaedic surgery. The use of both adult and pediatric PROMIS questionnaires in orthopaedic sports medicine limits the value of the PROMIS in routine sports medicine clinical care, research, and quality improvement. Because orthopaedic sports medicine surgeons see patients across a wide age range, simplifying the collection of PROMIS computer adaptive tests (CATs) to a single set of questionnaires, regardless of age, is of notable value. PURPOSE/HYPOTHESIS: The purpose was to determine the strength of the correlation between the pediatric and adult PROMIS questionnaires. We hypothesized that there would be a high correlation between the adult and pediatric versions for each PROMIS domain, thereby justifying the use of only the adult version for most sports medicine providers, regardless of patient age. STUDY DESIGN: Cohort study (Diagnosis); Level of evidence, 2. METHODS: Between December 2018 and December 2019, all pediatric sports medicine patients presenting to a single, academic, orthopaedic sports medicine clinic were asked to participate in the present study with their parents' consent. Patients were asked to complete a set of adult PROMIS domains (Physical Function and/or Upper Extremity, Pain Interference, and Depression) as well as a set of pediatric PROMIS domains (Mobility and/or Upper Extremity, Pain Interference, and Depressive Symptoms). Concurrent validity was assessed using Pearson correlation coefficients (r). Ceiling and floor effects were determined. RESULTS: A total of 188 patients met our inclusion criteria. The correlation between the adult and pediatric PROMIS Upper Extremity, Physical Function and Mobility, Pain Interference, and Depression and Depressive Symptoms forms were high-moderate ($r = 0.68$; $P < .01$), high-moderate ($r = 0.69$; $P < .01$), high ($r = 0.78$; $P < .01$), and high ($r = 0.85$; $P < .01$), respectively. Both adult and pediatric depression-related PROMIS domains demonstrated notable floor effects (adult: 38%; pediatric: 24%). The pediatric PROMIS Upper Extremity domain demonstrated a ceiling effect (20%). CONCLUSION: Adult PROMIS CATs may be used in an orthopaedic sports medicine clinic for both adult and pediatric patients. Our findings will help decrease the amount of resources needed for the implementation and use of PROMs for patient care, research, and quality improvement in orthopaedic sports medicine clinics.

Orthopaedics/Bone and Joint Center

Forsythe B, Lavoie-Gagne O, Patel BH, Lu Y, Ritz E, Chahla J, **Okoroha KR**, Allen AA, and Nwachukwu BU. Efficacy of Arthroscopic Surgery in the Management of Adhesive Capsulitis: A Systematic Review and Network Meta-analysis of Randomized Controlled Trials. *Arthroscopy* 2020; Epub ahead of print. PMID: 33221429. Full Text

Midwest Orthopaedics at Rush, Rush University Medical Center, Chicago, IL. Electronic address: brian.forsythe@rushortho.com.
Midwest Orthopaedics at Rush, Rush University Medical Center, Chicago, IL.
Department of Orthopaedic Surgery, University of Illinois at Chicago, Chicago, IL.
Bioinformatics and Biostatistics Core, Rush University Medical Center, Chicago, IL.
Department of Orthopaedic Surgery, Henry Ford Health System, Detroit, MI.
Department of Orthopaedic Surgery, Hospital for Special Surgery, New York, NY.

PURPOSE: To perform a network meta-analysis of randomized controlled trials in order to determine which interventions optimize clinical outcomes in adhesive capsulitis. METHODS: A systematic review was conducted of all clinical trials on adhesive capsulitis published since 2008. Patient cohorts were grouped into treatment categories and data collected included range of motion (ROM) and patient-reported outcome measures (PROMs). Interventions were compared across groups by means of arm-based Bayesian network meta-analysis in a random-effects model. RESULTS: Sixty-six studies

comprising 4042 shoulders (57.6% females, mean age 54.8 ± 3.2 years) were included. The most commonly studied interventions were physical therpay (PT) or shoulder injections. Network meta-analysis demonstrated that arthroscopic surgical capsular release was the most effective treatment in increasing ROM - this effect was apparent in forward flexion [effect difference vs. placebo, or ED (95% CI), 44° (31°-58°], abduction [ED 58° (45°-71°)], internal rotation [ED 34° (24°-44°)], and external rotation [ED 59° (37°-80°)]. Interventions most effective for pain relief included PT supplemented with either medical [ED -4.50 (-9.80-2.80)] or ultrasound therapy [ED -5.10 (-5.10- -1.40)]. Interventions most effective for improvement of functional status included PT, manipulation under anaesthesia (MUA), intra-articular or subacromial steroid injection, surgical capsular release, and supplementation of PT with alternative therapy. CONCLUSIONS: There was not one treatment that emerged superior in regards to range of motion, pain symptoms, and functional status. Surgery, after failure of conservative treatment, ranked highest across all ROM domains. Treatments that ranked highest for treatment of pain included PT supplemented with either medications or ultrasound. Finally, treatments ranked highest for improvements in functional status included MUA, PT with medical therapy, surgical intervention, PT with ultrasound, PT with injection, and injection alone.

Orthopaedics/Bone and Joint Center
Jildeh TR, Shkokani L, **Meta F**, **Tramer JS**, and **Okoroha KR**. Concussion Management for the Orthopaedic Surgeon. *JBJS Rev* 2020; 8(11):e2000055. PMID: 33186210. Full Text

Department of Orthopaedic Surgery, Henry Ford Health System, Detroit, Michigan.
Wayne State University School of Medicine, Detroit, Michigan.

Orthopaedics/Bone and Joint Center
Karnuta JM, Luu BC, Haeberle HS, Saluan PM, Frangiamore SJ, Stearns KL, Farrow LD, Nwachukwu BU, Verma NN, **Makhni EC**, Schickendantz MS, and Ramkumar PN. Machine Learning Outperforms Regression Analysis to Predict Next-Season Major League Baseball Player Injuries: Epidemiology and Validation of 13,982 Player-Years From Performance and Injury Profile Trends, 2000-2017. *Orthop J Sports Med* 2020; 8(11). PMID: 33241060. Full Text

Orthopaedic Machine Learning Laboratory, Cleveland Clinic, Cleveland, Ohio, USA.
Department of Orthopedic Surgery, Baylor College of Medicine, Houston, Texas, USA.
Hospital for Special Surgery, New York, New York, USA.
Rush University Medical Center, Chicago, Illinois, USA.
Department of Orthopedics, Henry Ford Health System, West Bloomfield, Michigan, USA.

BACKGROUND: Machine learning (ML) allows for the development of a predictive algorithm capable of imbibing historical data on a Major League Baseball (MLB) player to accurately project the player's future availability. PURPOSE: To determine the validity of an ML model in predicting the next-season injury risk and anatomic injury location for both position players and pitchers in the MLB. STUDY DESIGN: Descriptive epidemiology study. METHODS: Using 4 online baseball databases, we compiled MLB player data, including age, performance metrics, and injury history. A total of 84 ML algorithms were developed. The output of each algorithm reported whether the player would sustain an injury the following season as well as the injury's anatomic site. The area under the receiver operating characteristic curve (AUC) primarily determined validation. RESULTS: Player data were generated from 1931 position players and 1245 pitchers, with a mean follow-up of 4.40 years (13,982 player-years) between the years of 2000 and 2017. Injured players spent a total of 108,656 days on the disabled list, with a mean of 34.21 total days per player. The mean AUC for predicting next-season injuries was 0.76 among position players and 0.65 among pitchers using the top 3 ensemble classification. Back injuries had the highest AUC among both position players and pitchers, at 0.73. Advanced ML models outperformed logistic regression in 13 of 14 cases. CONCLUSION: Advanced ML models generally outperformed logistic regression and demonstrated fair capability in predicting publicly reportable next-season injuries, including the anatomic region for position players, although not for pitchers.

Orthopaedics/Bone and Joint Center

Koolmees D, Bernstein DN, and **Makhni EC**. Time-Driven Activity-Based Costing Provides a Lower and More Accurate Assessment of Costs in the Field of Orthopaedic Surgery as Compared to Traditional Accounting Methods. *Arthroscopy* 2020; Epub ahead of print. PMID: 33232748. Full Text

Henry Ford Health System. Electronic address: Dylan.Koolmees@wayne.edu.
Harvard Business School. Electronic address: dbernstein@hbs.edu.
Henry Ford Health System. Electronic address: emakhni1@hfhs.org.

PURPOSE: The purpose of this article was to analyze the implementation and benefits of Time-Driven Activity-Based Costing (TDABC) in the field of orthopaedic surgery. METHODS: We performed a search of PubMed, Google Scholar, and Embase in March 2020, using the following terms: "Time-Driven Activity-Based Costing" "TDABC" "Orthopaedic Surgery" "Cost." Then we selected the studies that used the TDABC methodology to generate costs for a particular aspect of orthopaedic surgery. The included studies were divided into the following 5 main categories for ease of analysis: joint arthroplasty, trauma, hand, EMR implementation, and pediatric. We analyzed the overall ability of TDABC in the field of orthopaedic surgery, compared to the standard costing methods. RESULTS: We included a total of 19 studies that implemented the TDABC methodology to generate a cost, which was compared to traditional accounting methods. The orthopaedic subspecialty with the most amount of TDABC implementation has been the field of joint arthroplasty. In these studies, the authors have noted that TDABC has provided a more granular breakdown of the costs, and it has calculated a lower cost when compared to traditional accounting methods. CONCLUSION: TDABC is a powerful cost analysis method that has demonstrated benefit over the ABC approach in determining a lower and more accurate cost of orthopaedic procedures. Furthermore, the TDABC method generates an average cost reduction of $10,000 and $12,000 for THA and TKA, respectively.

Orthopaedics/Bone and Joint Center

Tran G, **Khalil LS**, **Wrubel A**, **Klochko CL**, **Davis JJ**, and **Soliman SB**. Incidental findings detected on preoperative CT imaging obtained for robotic-assisted joint replacements: clinical importance and the effect on the scheduled arthroplasty. *Skeletal Radiol* 2020; Epub ahead of print. PMID: 33140168. Full Text

Division of Musculoskeletal Radiology, Department of Radiology, Henry Ford Hospital, Detroit, MI, USA.
Division of Orthopedic Surgery, Department of Orthopedics, Henry Ford Hospital, Detroit, MI, USA.
Division of Musculoskeletal Radiology, Department of Radiology, Henry Ford Hospital, Detroit, MI, USA. stevens@rad.hfh.edu.

OBJECTIVE: To determine the type and frequency of incidental findings detected on preoperative computed tomography (CT) imaging obtained for robotic-assisted joint replacements and their effect on the planned arthroplasty. MATERIALS AND METHODS: All preoperative CT examinations performed for a robotic-assisted knee or total hip arthroplasty were obtained. This resulted in 1432 examinations performed between September 2016 and February 2020 at our institution. These examinations were initially interpreted by 1 of 9 fellowship-trained musculoskeletal radiologists. Using a diagnosis search, the examination reports were then reviewed to catalog all incidental findings and further classify as significant or non-significant findings. Demographic information was obtained. In those with significant findings, a chart review was performed to record the relevant workup, outcomes, and if the planned arthroplasty was affected. RESULTS: Incidental findings were diagnosed in 740 (51.7%) patients. Of those with incidental findings, 41 (5.5%) were considered significant. A significant finding was more likely to be detected in males (P = 0.007) and on the hip protocol CT (P = 0.014). In 8 patients, these diagnoses resulted in either delay or cancelation of the arthroplasty. A planned total hip arthroplasty was more likely to be altered as compared to a knee arthroplasty (P = 0.018). CONCLUSION: Incidental findings are commonly detected by radiologists on preoperative CT imaging obtained for robotic-assisted joint replacement. Several were valuable findings and resulted in a delay or even cancelation of the planned arthroplasty after the detection of critical diagnoses, which if not identified may have resulted in devastating outcomes.

Otolaryngology
Goosmann M, **Chang S**, and **Craig J**. Treating sinonasal crusting and infection after palatal and sinonasal cancer resection with topical antibiotic irrigations. *Oral Oncol* 2020; Epub ahead of print. PMID: 33243563. Full Text

Henry Ford Health System, Department of Otolaryngology-Head and Neck Surgery, United States. Electronic address: mgoosma1@hfhs.org.
Henry Ford Health System, Department of Otolaryngology-Head and Neck Surgery, United States.

Otolaryngology
Ibrahim S, Byrd C, and **Kubek D**. Cervical chrondrocutaneous branchial remnant: A case report. *Otolaryngology Case Reports* 2020; 17. PMID: Not assigned. Full Text

S. Ibrahim, West Virginia School of Osteopathic Medicine, Lewisburg, WV, United States

Cervical chondrocutaneous branchial remnants (CCBR) are rare benign masses of the neck that arise from anomalies in embryological branchial arch development. They present as a painless, flesh-toned exophytic nodule of the neck. They are most commonly seen on the lower third of the neck, anterior to the sternocleidomastoid muscle. CCBRs are harmless and asymptomatic, but the presence of these lesions in infants should prompt further evaluation for associated anomalies. Histopathologic examination of CCBRs show ectopic cartilaginous tissue with normal overlying epidermis. Treatment includes elective surgical excision. A case of an 18 year old male with a left-sided CCBR is reported.

Otolaryngology
Law RH, Bazzi TD, **Van Harn M**, **Craig JR**, and **Deeb RH**. Predictors of Long-Term Nasal Obstruction Symptom Evaluation Score Stability Following Septoplasty With Inferior Turbinate Reduction. *Laryngoscope* 2020; Epub ahead of print. PMID: 33141435. Full Text

Department of Otolaryngology-Head and Neck Surgery, Henry Ford Hospital, Detroit, Michigan, U.S.A.
Department of Otolaryngology-Head and Neck Surgery, Wayne State University School of Medicine, Detroit, Michigan, U.S.A.
Department of Public Health Sciences, Henry Ford Health System, Detroit, Michigan, U.S.A.

OBJECTIVES/HYPOTHESIS: Determine the postoperative Nasal Obstruction Symptom Evaluation (NOSE) score stability between 1 and ≥6 months after septoplasty with inferior turbinate reduction (ITR). Education level and occupation were evaluated to determine their effects on NOSE score stability during the postoperative period. STUDY DESIGN: Retrospective case series. METHODS: This was a retrospective case series. Patients were included if they underwent septoplasty with ITR for nasal obstruction due to septal deviation and inferior turbinate hypertrophy. NOSE scores were collected preoperatively, and at 1 and ≥6 months postoperatively. Education level and occupation were collected postoperatively via telephone survey. Changes in NOSE scores were compared between the different time points. Education level and occupation were analyzed to determine if they affected NOSE scores. RESULTS: There were 98 patients included, and 56 were male (57.1%). Mean NOSE scores preoperatively and at 1 and ≥6 months postoperatively were 72.1, 17.1, and 12.0, respectively. Patients demonstrated a statistically and clinically significant reduction in NOSE score at 1 month (-54.9, $P < .001$) and at ≥6 months postoperatively (-60.0, $P < .001$). The mean 6.2-point decrease in NOSE score from 1 to ≥6 months was statistically, but not clinically significant. There were no significant differences in NOSE score changes based on educational level and occupation. CONCLUSIONS: Patients achieved statistically and clinically significant reductions in NOSE scores at 1 months, with no clinically significant differences in NOSE scores at ≥6 months, suggesting NOSE score stability between these postoperative time points. Neither education level nor occupation influenced NOSE scores. LEVEL OF EVIDENCE: 4. Laryngoscope, 2020.

Otolaryngology

Plawecki AM, **Singer MC**, **Peterson EL**, **Yaremchuk KL**, and **Deeb RH**. Impact of a specialty trained billing team on an academic otolaryngology practice. *Am J Otolaryngol* 2020; 41(6):102720. PMID: 32977062. Full Text

Department of Otolaryngology - Head & Neck Surgery, Henry Ford Hospital, 2799 W. Grand Blvd, Detroit, MI 48202, USA.
Department of Public Health Sciences, Henry Ford Health System, One Ford Place, Detroit, MI 48202, USA.
Department of Otolaryngology - Head & Neck Surgery, Henry Ford Hospital, 2799 W. Grand Blvd, Detroit, MI 48202, USA. Electronic address: Rdeeb1@hfhs.org.

PURPOSE: To determine how the incorporation of specialty specific training for coders within a focused billing team affected revenue, efficiency, time to reimbursement, and physician satisfaction in an academic otolaryngology practice. MATERIALS AND METHODS: Our academic otolaryngology department recently implemented a new billing system, which incorporated additional training in otolaryngology surgical procedures for medical coders. A mixed model analysis of variance was used to compare billing outcomes for the 6 months before and 6 months after this new approach was initiated. The following metrics were analyzed: Current Procedural Terminology codes, total charges, time between services rendered and billing submission, and time to reimbursement. A survey of department physicians assessing satisfaction with the system was reviewed. RESULTS: There were 4087 Current Procedural Terminology codes included in the analysis. In comparing the periods before and after implementation of the new system, statistically significant decreases were found in the mean number of days to coding completion (19.3 to 12.0, respectively, $p < 0.001$), days to posting of charges (27.0 to 15.2, $p < 0.001$), days to final reimbursement (54.5 to 27.2, $p < 0.001$), and days to closure of form (179.2 to 76.6, $p < 0.001$). Physician satisfaction with communication and coder feedback increased from 36% to 64% after initiation of the new program. CONCLUSIONS: The implementation of additional specialty training for medical coders in the otolaryngology department of a large medical system was associated with improved revenue cycle efficiency. Additionally, this model appears to improve physician satisfaction and confidence with the coding system.

Otolaryngology

Tam S, **Wu VF**, **Williams AM**, **Girgis M**, **Sheqwara JZ**, **Siddiqui F**, and **Chang SS**. Disparities in the Uptake of Telemedicine During the COVID-19 Surge in a Multidisciplinary Head and Neck Cancer Population by Patient Demographic Characteristics and Socioeconomic Status. *JAMA Otolaryngol Head Neck Surg* 2020; Epub ahead of print. PMID: 33151289. Full Text

Department of Otolaryngology-Head and Neck Surgery, Henry Ford Health System and Henry Ford Cancer Institute, Detroit, Michigan.
Department of Hematology/Medical Oncology, Henry Ford Health System and Henry Ford Cancer Institute, Detroit, Michigan.
Department of Radiation Oncology, Henry Ford Health System and Henry Ford Cancer Institute, Detroit, Michigan.

This cohort study examines the association between patient demographic characteristics and socioeconomic status and engagement in telemedicine during the COVID-19 pandemic.

Pathology and Laboratory Medicine

Antar AI, **Otrock ZK**, Abou Dalle I, El-Cheikh J, and Bazarbachi A. Pharmacologic Therapies to Prevent Relapse of Acute Myeloid Leukemia After Allogeneic Hematopoietic Stem Cell Transplantation. *Front Oncol* 2020; 10:596134. PMID: 33224890. Full Text

Almoosa Specialist Hospital, Department of Internal Medicine, Division of Hematology-Oncology, Al-Ahsa, Saudi Arabia.
Department of Hematology and Oncology, Hammoud Hospital University Medical Center, Saida, Lebanon.

Department of Pathology and Laboratory Medicine, Henry Ford Hospital, Detroit, MI, United States.
Bone Marrow Transplantation Program, Department of Internal Medicine, American University of Beirut Medical Center, Beirut, Lebanon.

Relapse is the main cause of mortality in patients with acute myeloid leukemia (AML) after allogeneic hematopoietic stem cell transplantation (allo-HSCT). Adverse cytogenetic or molecular risk factors, as well as refractory disease or persistent measurable residual disease (MRD) at the time of transplantation are associated with an increased risk of recurrence. Salvage therapy for AML relapse after allo-HSCT is often limited to chemotherapy, donor lymphocyte infusions and/or second transplants and is rarely successful. Effective post-transplant preventive intervention in high risk AML may be crucial. The most frequent and promising approach is the use of post-transplant maintenance with hypomethylating agents or with FLT3 tyrosine kinase inhibitors when the target is present. Moreover, IDH1/IDH2 inhibitors and BCL-2 inhibitors in combination with other strategies are promising approaches in the maintenance setting. Here we summarize the current knowledge about the preemptive and prophylactic use of pharmacologic agents after allo-HSCT to prevent relapse of AML.

Pathology and Laboratory Medicine
Warrington JS, Swanson K, Dodd M, Lo SY, Haghamad A, Duque TB, and **Cook B**. Measuring What Matters: How the Laboratory Contributes Value in the Opioid Crisis. *J Appl Lab Med* 2020; 5(6):1378-1390. PMID: 33147341. Full Text

Department of Pathology and Laboratory Medicine, University of Vermont, Burlington, VT.
Laboratory 2.0 Strategic Services, LLC, Salt Lake City, UT.
TriCore Laboratories, Albuquerque, NM.
Geisinger Health Laboratories, Geisinger Health System, Danville, PA.
Department of Pathology and Laboratory Medicine, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead, NY.
Henry Ford Laboratories, Henry Ford Health System, Detroit, MI.

With over 20 years of the opioid crisis, our collective response has evolved to address the ongoing needs related to the management of opioid use and opioid use disorder. There has been an increasing recognition of the need for standardized metrics to evaluate organizational management and stewardship. The clinical laboratory, with a wealth of objective and quantitative health information, is uniquely poised to support opioid stewardship and drive valuable metrics for opioid prescribing practices and opioid use disorder (OUD) management. To identify laboratory-related insights that support these patient populations, a collection of 5 independent institutions, under the umbrella of the Clinical Laboratory 2.0 movement, developed and prioritized metrics. Using a structured expert panel review, laboratory experts from 5 institutions assessed possible metrics as to their relative importance, usability, feasibility, and scientific acceptability based on the National Quality Forum criteria. A total of 37 metrics spanning the topics of pain and substance use disorder (SUD) management were developed with consideration of how laboratory insights can impact clinical care. Monitoring these metrics, in the form of summative reports, dashboards, or embedded in laboratory reports themselves may support the clinical care teams and health systems in addressing the opioid crisis. The clinical insights and standardized metrics derived from the clinical laboratory during the opioid crisis exemplifies the value proposition of clinical laboratories shifting into a more active role in the healthcare system. This increased participation by the clinical laboratories may improve patient safety and reduce healthcare costs related to OUD and pain management.

Pathology and Laboratory Medicine
Zhang Y, **Qin Y**, **Chopp M**, **Li C**, **Kemper A**, **Liu X**, **Wang X**, **Zhang L**, and **Zhang ZG**. Ischemic Cerebral Endothelial Cell-Derived Exosomes Promote Axonal Growth. *Stroke* 2020; 51(12):3701-3712. PMID: 33138691. Full Text

Department of Neurology (Y.Z., Y.Q., M.C., C.L., X.L., X.W., L.Z., Z.G.Z.), Henry Ford Hospital, Detroit, MI.
Department of Physics, Oakland University, Rochester, MI (M.C.).

Department of Pathology (A.K.), Henry Ford Hospital, Detroit, MI.

BACKGROUND AND PURPOSE: Cerebral endothelial cells (CECs) and axons of neurons interact to maintain vascular and neuronal homeostasis and axonal remodeling in normal and ischemic brain, respectively. However, the role of exosomes in the interaction of CECs and axons in brain under normal conditions and after stroke is unknown. METHODS: Exosomes were isolated from CECs of nonischemic rats and is chemic rats (nCEC-exos and isCEC-exos), respectively. A multicompartmental cell culture system was used to separate axons from neuronal cell bodies. RESULTS: Axonal application of nCEC-exos promotes axonal growth of cortical neurons, whereas isCEC-exos further enhance axonal growth than nCEC-exos. Ultrastructural analysis revealed that CEC-exos applied into distal axons were internalized by axons and reached to their parent somata. Bioinformatic analysis revealed that both nCEC-exos and isCEC-exos contain abundant mature miRNAs; however, isCEC-exos exhibit more robust elevation of select miRNAs than nCEC-exos. Mechanistically, axonal application of nCEC-exos and isCEC-exos significantly elevated miRNAs and reduced proteins in distal axons and their parent somata that are involved in inhibiting axonal outgrowth. Blockage of axonal transport suppressed isCEC-exo-altered miRNAs and proteins in somata but not in distal axons. CONCLUSIONS: nCEC-exos and isCEC-exos facilitate axonal growth by altering miRNAs and their target protein profiles in recipient neurons.

Pharmacy

Ali D, Barra ME, Blunck J, Brophy GM, Brown CS, Caylor M, Clark SL, Hensler D, **Jones M**, Lamer-Rosen A, Levesque M, Mahmoud LN, Mahmoud SH, May C, Nguyen K, Panos N, Roels C, Shewmaker J, Smetana K, Traeger J, Shadler A, and Cook AM. Stress-Related Gastrointestinal Bleeding in Patients with Aneurysmal Subarachnoid Hemorrhage: A Multicenter Retrospective Observational Study. *Neurocrit Care* 2020; Epub ahead of print. PMID: 33150575. Full Text

University of Kentucky HealthCare, Lexington, USA. Dina.ali@uky.edu.
Massachusetts General Hospital, Boston, USA.
Saint Luke's Health System-Kansas City, Kansas City, USA.
Virginia Commonwealth University, Richmond, USA.
Mayo Clinic, Rochester, USA.
Hospital of the University of Pennsylvania, Philadelphia, USA.
University of Michigan Hospital, Ann Arbor, USA.
Henry Ford Hospital, Detroit, USA.
Cedars-Sinai Hospital, Los Angeles, USA.
Tampa General Hospital, Tampa, USA.
Lifespan/Rhode Island Hospital, Providence, USA.
University of Alberta, Edmonton, Canada.
Ohio State Wexner Medical Center, Columbus, USA.
Edward-Elmhurst Hospital, Chicago, USA.
Rush University Medical Center, Chicago, USA.
Novant Health, Winston-Salem, USA.
University Hospitals, Shaker Heights, USA.
University of Kentucky College of Pharmacy, Lexington, USA.
University of Kentucky HealthCare, Lexington, USA.

BACKGROUND/OBJECTIVE: Stress-related mucosal bleeding (SRMB) occurs in approximately 2-4% of critically ill patients. Patients with aneurysmal subarachnoid hemorrhage (aSAH) have a (diffuse) space-occupying lesion, are critically ill, often require mechanical ventilation, and frequently receive anticoagulation or antiplatelet therapy after aneurysm embolization, all of which may be risk factors for SRMB. However, no studies have evaluated SRMB in patients with aSAH. Aims of the study were to determine the incidence of SRMB in aSAH patients, evaluate the effect of acid suppression on SRMB, and identify specific risk factors for SRMB. METHODS: This was a multicenter, retrospective, observational study conducted across 17 centers. Each center reviewed up to 50 of the most recent cases of aSAH. Patients with length of stay (LOS) < 48 h or active GI bleeding on admission were excluded. Variables related to demographics, aSAH severity, gastrointestinal (GI) bleeding, provision of

SRMB prophylaxis, adverse events, intensive care unit (ICU), and hospital LOS were collected for the first 21 days of admission or until hospital discharge, whichever came first. Descriptive statistics were used to analyze the data. A multivariate logistic regression modeling was utilized to examine the relationship between specific risk factors and the incidence of clinically important GI bleeding in patients with aSAH. RESULTS: A total of 627 patients were included. The overall incidence of clinically important GI bleeding was 4.9%. Of the patients with clinically important GI bleeding, 19 (61%) received pharmacologic prophylaxis prior to evidence of GI bleeding, while 12 (39%) were not on pharmacologic prophylaxis at the onset of GI bleeding. Patients who received an acid suppressant agent were less likely to experience GI bleeding than patients who did not receive pharmacologic prophylaxis prior to evidence of bleeding (OR 0.39, 95% CI 0.18-0.83). The multivariate regression analysis identified any instance of elevated intracranial pressure, creatinine clearance < 60 ml/min and the incidence of cerebral vasospasm as specific risk factors associated with GI bleeding. Cerebral vasospasm has not previously been described as a risk for GI bleeding (OR 2.5 95% CI 1.09-5.79). CONCLUSIONS: Clinically important GI bleeding occurred in 4.9% of patients with aSAH, similar to the general critical care population. Risk factors associated with GI bleeding were prolonged mechanical ventilation (> 48 h), creatinine clearance < 60 ml/min, presence of coagulopathy, elevation of intracranial pressure, and cerebral vasospasm. Further prospective research is needed to confirm this observation within this patient population.

Pharmacy

Hutton MA, Sundaram A, **Perri MB**, **Zervos MJ**, and **Herc ES**. Assessment of invitrosynergy of daptomycin or vancomycin plus ceftaroline for daptomycin non-susceptible Staphylococcus aureus. *Diagn Microbiol Infect Dis* 2020; 98(3):115126. PMID: 32861155. Full Text

Department of Pharmacy, Henry Ford Health System, 2799 West Grand Boulevard, Detroit, MI 48202. Electronic address: mary.hutton@imail.org.
Wayne State University, 540 E Canfield St, Detroit, MI 48201.
Division of Infectious Diseases, Henry Ford Hospital, 2799 West Grand Boulevard, Detroit, MI 48202.
Wayne State University, 540 E Canfield St, Detroit, MI 48201; Division of Infectious Diseases, Henry Ford Hospital, 2799 West Grand Boulevard, Detroit, MI 48202.
Wayne State University, 540 E Canfield St, Detroit, MI 48201; Division of Infectious Diseases, Henry Ford Hospital, 2799 West Grand Boulevard, Detroit, MI 48202. Electronic address: eherc1@hfhs.org.

The combination of vancomycin or daptomycin plus ceftaroline has showed synergistic results in vitro. This study aimed to investigate in vitro synergy of vancomycin or daptomycin plus ceftaroline for seven patients with daptomycin non-susceptible Staphylococcus aureus (SA) bacteremia Thirteen isolates from seven patients were evaluated: two methicillin-susceptible and five methicillin-resistant SA infections. All patients were treated with daptomycin and became non-susceptible (minimum inhibitory concentration (MIC) >1 μg/mL) with therapy or had resistant strains initially. Time kill experiments were completed with 0.25 × MIC, 0.5 × MIC, and 0.75 × MIC concentrations. No synergy was seen at 0.25 × MIC. Synergy was observed for 4 isolates with vancomycin plus ceftaroline and with daptomycin plus ceftaroline for 2 isolates at 0.5 × MIC. These results are in accordance with literature that supports synergistic combinations of daptomycin or vancomycin with ceftaroline for SA bacteremia. Daptomycin non-susceptible SA bacteremia presents a treatment challenge.

Public Health Sciences

Chaudhry F, **Bulka H**, **Rathnam AS**, Said OM, Lin J, **Lorigan H**, Bernitsas E, Rube J, Korzeniewski SJ, **Memon AB**, Levy PD, **Schultz L**, Javed A, Lisak R, and **Cerghet M**. COVID-19 in multiple sclerosis patients and risk factors for severe infection. *J Neurol Sci* 2020; 418:117147. PMID: 32980780. Full Text

Department of Neurology, Henry Ford Health System, Detroit, MI, United States of America; Wayne State University School of Medicine, Detroit, MI, United States of America. Electronic address: gf9603@wayne.edu.
Department of Neurology, Henry Ford Health System, Detroit, MI, United States of America.
Wayne State University School of Medicine, Detroit, MI, United States of America.

Wayne State University School of Medicine, Detroit, MI, United States of America; Department of Neurology, Detroit Medical Center, Detroit, MI, United States of America.
Department of Neurology, Henry Ford Health System, Detroit, MI, United States of America; Wayne State University School of Medicine, Detroit, MI, United States of America.
Department of Neurology, Henry Ford Health System, Detroit, MI, United States of America; Department of Public Health Sciences, Henry Ford Hospital, Detroit, MI, United States of America.
Department of Neurology, University of Chicago, Chicago, IL, USA.

Multiple sclerosis (MS) patients have been considered a higher-risk population for COVID-19 due to the high prevalence of disability and disease-modifying therapy use; however, there is little data identifying clinical characteristics of MS associated with worse COVID-19 outcomes. Therefore, we conducted a multicenter prospective cohort study looking at the outcomes of 40 MS patients with confirmed COVID-19. Severity of COVID-19 infection was based on hospital course, where a mild course was defined as the patient not requiring hospital admission, moderate severity was defined as the patient requiring hospital admission to the general floor, and most severe was defined as requiring intensive care unit admission and/or death. 19/40(47.5%) had mild courses, 15/40(37.5%) had moderate courses, and 6/40(15%) had severe courses. Patients with moderate and severe courses were significantly older than those with a mild course (57[50-63] years old and 66[58.8-69.5] years old vs 48[40-51.5] years old, P = 0.0121, P = 0.0373). There was differing prevalence of progressive MS phenotype in those with more severe courses (severe:2/6[33.3%]primary-progressing and 0/6[0%]secondary-progressing, moderate:1/14[7.14%] and 5/14[35.7%] vs mild:0/19[0%] and 1/19[5.26%], P = 0.0075, 1 unknown). Significant disability was found in 1/19(5.26%) mild course-patients, but was in 9/15(60%, P = 0.00435) of moderate course-patients and 2/6(33.3%, P = 0.200) of severe course-patients. Disease-modifying therapy prevalence did not differ among courses (mild:17/19[89.5%], moderate:12/15[80%] and severe:3/6[50%], P = 0.123). MS patients with more severe COVID-19 courses tended to be older, were more likely to suffer from progressive phenotype, and had a higher degree of disability. However, disease-modifying therapy use was not different among courses.

Public Health Sciences

Chhina AK, **Loyd GE**, **Szymanski TJ**, **Nowak KA**, **Peruzzi WT**, **Yeldo NS**, **Han X**, **Kerzabi LS**, **Galusca DM**, **Cazacu S**, **Brodie C**, and **Penning DH**. Frequency and Analysis of Unplanned Extubation in Coronavirus Disease 2019 Patients. *Crit Care Explor* 2020; 2(12):e0291. PMID: 33251520. Full Text

Department of Anesthesiology, Pain Management and Perioperative Medicine, Henry Ford Hospital, Detroit, MI.
Department of Public Health Sciences, Henry Ford Hospital, Detroit, MI.
Department of Neurosurgery, Henry Ford Hospital, Detroit, MI.

OBJECTIVES: To determine if patients with coronavirus disease 2019 had a greater number of unplanned extubations resulting in reintubations than in patients without coronavirus disease 2019. DESIGN: Retrospective cohort study comparing the frequency of unplanned extubations resulting in reintubations in a group of coronavirus disease 2019 patients to a historical (noncoronavirus disease 2019) control group. SETTING: This study was conducted at Henry Ford Hospital, an academic medical center in Detroit, MI. The historical noncoronavirus disease 2019 patients were treated in the 68 bed medical ICU. The coronavirus disease 2019 patients were treated in the coronavirus disease ICU, which included the 68 medical ICU beds, 18 neuro-ICU beds, 32 surgical ICU beds, and 40 cardiovascular ICU beds, as the medical ICU was expanded to these units at the peak of the pandemic in Detroit, MI. PATIENTS: The coronavirus disease 2019 cohort included patients diagnosed with coronavirus disease 2019 who were intubated for respiratory failure from March 12, 2020, to April 13, 2020. The historic control (noncoronavirus disease 2019) group consisted of patients who were admitted to the medical ICU in the year spanning from November 1, 2018 to October 31, 2019, with a need for mechanical ventilation that was not related to surgery or a neurologic reason. INTERVENTIONS: None. MEASUREMENTS AND MAIN RESULTS: To identify how many patients in each cohort had unplanned extubations, an electronic medical records query for patients with two intubations within 30 days was performed, in addition to a review of our institutional quality and safety database of reported self-extubations. Medical charts were manually reviewed by board-certified anesthesiologists to confirm each event was an unplanned

extubation followed by a reintubation within 24 hours. There was a significantly greater incidence of unplanned extubations resulting in reintubation events in the coronavirus disease 2019 cohort than in the noncoronavirus disease 2019 cohort (coronavirus disease 2019 cohort: 167 total admissions with 22 events-13.2%; noncoronavirus disease 2019 cohort: 326 total admissions with 14 events-4.3%; $p < 0.001$). When the rate of unplanned extubations was expressed per 100 intubated days, there was not a significant difference between the groups (0.88 and 0.57, respectively; $p = 0.269$). CONCLUSIONS: Coronavirus disease 2019 patients have a higher incidence of unplanned extubation that requires reintubation than noncoronavirus disease 2019 patients. Further study is necessary to evaluate the variables that contribute to this higher incidence and clinical strategies that can reduce it.

Public Health Sciences

Cocco MP, **White E**, **Xiao S**, Hu D, Mak A, Sleiman P, **Yang M**, **Bobbitt KR**, **Gui H**, **Levin AM**, **Hochstadt S**, **Whitehouse K**, **Rynkowski D**, Barczak AJ, Abecasis G, Blackwell TW, Kang HM, Nickerson DA, Germer S, Ding J, **Lanfear DE**, Gilliland F, Gauderman WJ, Kumar R, Erle DJ, Martinez F, Hakonarson H, Burchard EG, and **Williams LK**. Asthma and its relationship to mitochondrial copy number: Results from the Asthma Translational Genomics Collaborative (ATGC) of the Trans-Omics for Precision Medicine (TOPMed) program. *PLoS One* 2020; 15(11):e0242364. PMID: 33237978. Full Text

Center for Individualized and Genomic Medicine Research (CIGMA), Department of Internal Medicine, Henry Ford Health System, Detroit, Michigan, United States of America.
Department of Medicine, University of California San Francisco, San Francisco, California, United States of America.
Center for Applied Genomics, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, United States of America.
Department of Pediatrics, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, United States of America.
Department of Public Health Sciences, Henry Ford Health System, Detroit, Michigan, United States of America.
Lung Biology Center and UCSF CoLabs, University of California San Francisco, San Francisco, California, United States of America.
Center for Statistical Genetics, University of Michigan, Ann Arbor, Michigan, United States of America.
Regeneron Pharmaceuticals, Inc., Tarrytown, New York, United States of America.
Department of Genome Sciences, University of Washington, Seattle, Washington, United States of America.
Northwest Genomics Center, Seattle, Washington, United States of America.
Brotman Baty Institute, Seattle, Washington, United States of America.
New York Genome Center, New York, New York, United States of America.
Human Statistical Genetics Unit, Laboratory of Genetics and Genomics, National Institute on Aging, National Institutes of Health, Bethesda, Maryland, United States of America.
Department of Preventive Medicine, Keck School of Medicine, University of Southern California, Los Angeles, California, United States of America.
Department of Pediatrics, Northwestern University Feinberg School of Medicine, Chicago, Illinois, United States of America.
Arizona Respiratory Center and Department of Pediatrics, University of Arizona, Tucson, Arizona, United States of America.
Department of Bioengineering & Therapeutic Sciences, University of California San Francisco, San Francisco, California, United States of America.

BACKGROUND: Mitochondria support critical cellular functions, such as energy production through oxidative phosphorylation, regulation of reactive oxygen species, apoptosis, and calcium homeostasis. OBJECTIVE: Given the heightened level of cellular activity in patients with asthma, we sought to determine whether mitochondrial DNA (mtDNA) copy number measured in peripheral blood differed between individuals with and without asthma. METHODS: Whole genome sequence data was generated as part of the Trans-Omics for Precision Medicine (TOPMed) Program on participants from the Study of Asthma Phenotypes and Pharmacogenomic Interactions by Race-ethnicity (SAPPHIRE) and the Study of African Americans, Asthma, Genes, & Environment II (SAGE II). We restricted our analysis to individuals

who self-identified as African American (3,651 asthma cases and 1,344 controls). Mitochondrial copy number was estimated using the sequencing read depth ratio for the mitochondrial and nuclear genomes. Respiratory complex expression was assessed using RNA-sequencing. RESULTS: Average mitochondrial copy number was significantly higher among individuals with asthma when compared with controls (SAPPHIRE: 218.60 vs. 200.47, P<0.001; SAGE II: 235.99 vs. 223.07, P<0.001). Asthma status was significantly associated with mitochondrial copy number after accounting for potential explanatory variables, such as participant age, sex, leukocyte counts, and mitochondrial haplogroup. Despite the consistent relationship between asthma status and mitochondrial copy number, the latter was not associated with time-to-exacerbation or patient-reported asthma control. Mitochondrial respiratory complex gene expression was disproportionately lower in individuals with asthma when compared with individuals without asthma and other protein-encoding genes. CONCLUSIONS: We observed a robust association between asthma and higher mitochondrial copy number. Asthma having an effect on mitochondria function was also supported by lower respiratory complex gene expression in this group.

Public Health Sciences

Hoffert M, **Kerr H**, **Hegab S**, **Whitehouse S**, **Kokas M**, **MacLean L**, **Van Harn MG**, and **Baker-Genaw K**. Designing a Yoga Intervention Program to Improve Well-Being for Physician Trainees: Challenges and Lessons Learned. *Int J Yoga Therap* 2020; Epub ahead of print. PMID: 33157552. Full Text

Department of Medical Education, Henry Ford Hospital, Detroit, Mich.
Department of Dermatology, Henry Ford Hospital, Detroit, Mich.
Division of Pulmonary and Critical Care Medicine, Henry Ford Hospital, Detroit, Mich.
Behavioral Health Services, Henry Ford Hospital, Detroit, Mich.
Public Health Science Division of Biostatistics, Henry Ford Hospital, Detroit, Michigan.
Department of Medical Education and Department of Internal Medicine, Henry Ford Hospital, Detroit, Mich.

Well-being activities may help to counteract physician burnout. Yoga is known to enhance well-being, but there are few studies of yoga as an intervention for physicians in training. This prospective methodology-development study aimed to explore how to establish a yoga-based well-being intervention for physician trainees in a large urban training hospital. We aimed to identify factors that contribute to trainee participation and explore an instrument to measure changes in self-reported well-being after yoga. Cohorts included a required-attendance group, a voluntary-attendance group, and an unassigned walk-in yoga group. Weekly 1-hour yoga sessions were led by a qualified yoga instructor for 4 weeks. The seven-question Resident Physician Well-Being Index (RPWBI) was used to measure resident well-being before yoga, after 4 weeks of yoga, and 6 months post-yoga. Trainees attending each session ranged from 17 for required yoga to 0-2 for voluntary yoga, 2-9 for lunchtime walk-in yoga, and 1-7 for evening walk-in yoga. In the required-yoga group (n = 17), overall RPWBI mean scores did not change significantly across the three query times, and participation in the survey declined over time. The mean baseline RPWBI score for the required group before yoga was in the non-distressed range and answers to the seven individual questions varied. Requiring a yoga activity for medical trainees may be a good strategy for promoting participation in yoga. The RPWBI may have limited utility for measuring changes in overall group well-being after a yoga intervention.

Public Health Sciences

Law RH, Bazzi TD, **Van Harn M**, **Craig JR**, and **Deeb RH**. Predictors of Long-Term Nasal Obstruction Symptom Evaluation Score Stability Following Septoplasty With Inferior Turbinate Reduction. *Laryngoscope* 2020; Epub ahead of print. PMID: 33141435. Full Text

Department of Otolaryngology-Head and Neck Surgery, Henry Ford Hospital, Detroit, Michigan, U.S.A.
Department of Otolaryngology-Head and Neck Surgery, Wayne State University School of Medicine, Detroit, Michigan, U.S.A.
Department of Public Health Sciences, Henry Ford Health System, Detroit, Michigan, U.S.A.

OBJECTIVES/HYPOTHESIS: Determine the postoperative Nasal Obstruction Symptom Evaluation (NOSE) score stability between 1 and ≥6 months after septoplasty with inferior turbinate reduction (ITR).

Education level and occupation were evaluated to determine their effects on NOSE score stability during the postoperative period. STUDY DESIGN: Retrospective case series. METHODS: This was a retrospective case series. Patients were included if they underwent septoplasty with ITR for nasal obstruction due to septal deviation and inferior turbinate hypertrophy. NOSE scores were collected preoperatively, and at 1 and ≥6 months postoperatively. Education level and occupation were collected postoperatively via telephone survey. Changes in NOSE scores were compared between the different time points. Education level and occupation were analyzed to determine if they affected NOSE scores. RESULTS: There were 98 patients included, and 56 were male (57.1%). Mean NOSE scores preoperatively and at 1 and ≥6 months postoperatively were 72.1, 17.1, and 12.0, respectively. Patients demonstrated a statistically and clinically significant reduction in NOSE score at 1 month (-54.9, P < .001) and at ≥6 months postoperatively (-60.0, P < .001). The mean 6.2-point decrease in NOSE score from 1 to ≥6 months was statistically, but not clinically significant. There were no significant differences in NOSE score changes based on educational level and occupation. CONCLUSIONS: Patients achieved statistically and clinically significant reductions in NOSE scores at 1 months, with no clinically significant differences in NOSE scores at ≥6 months, suggesting NOSE score stability between these postoperative time points. Neither education level nor occupation influenced NOSE scores. LEVEL OF EVIDENCE: 4. Laryngoscope, 2020.

Public Health Sciences

Lu M, Bowlus CL, Lindor K, Rodriguez-Watson CV, Romanelli RJ, Haller IV, Anderson H, VanWormer JJ, Boscarino JA, Schmidt MA, Daida YG, Sahota A, Vincent J, **Li J**, Trudeau S, **Rupp LB**, and **Gordon SC**. Validity of an Automated Algorithm to Identify Cirrhosis Using Electronic Health Records in Patients with Primary Biliary Cholangitis. *Clin Epidemiol* 2020; 12:1261-1267. PMID: 33204167. Full Text

Department of Public Health Sciences, Henry Ford Health System, Detroit, MI, USA.
University of California Davis School of Medicine, Sacramento, CA, USA.
College of Health Solutions, Arizona State University, Phoenix, AZ, USA.
Center for Health Research Kaiser Permanente Mid-Atlantic Research Institute, Rockville, MD; Reagan-Udall Foundation for the FDA, Washington, DC, USA.
Palo Alto Medical Foundation Research Institute, Palo Alto, CA, USA.
Essentia Institute of Rural Health, Essentia Health, Duluth, MN, USA.
Skaggs School of Pharmacy and Pharmaceutical Sciences, University of Colorado Anschutz Medical Campus, Aurora, CO, USA.
Marshfield Clinic Research Foundation, Marshfield, WI, USA.
Department of Population Health Sciences, Geisinger Clinic, Danville, PA, USA.
Center for Health Research, Kaiser Permanente Northwest, Portland, OR, USA.
Center for Integrated Health Care Research, Kaiser Permanente Hawai'i, Honolulu, HI, USA.
Department of Research and Evaluation, Kaiser Permanente Southern California, Los Angeles, CA, USA.
Baylor, Scott & White Research Institute, Temple, TX, USA.
Center for Health Policy and Health Services Research, Henry Ford Health System, Detroit, MI, USA.
Division of Gastroenterology and Hepatology, Henry Ford Health System; and Wayne State University School of Medicine, Detroit, MI, USA.

BACKGROUND: Biopsy remains the gold standard for determining fibrosis stage in patients with primary biliary cholangitis (PBC), but it is unavailable for most patients. We used data from the 11 US health systems in the FibrOtic Liver Disease Consortium to explore a combination of biochemical markers and electronic health record (EHR)-based diagnosis/procedure codes (DPCs) to identify the presence of cirrhosis in PBC patients. METHODS: Histological fibrosis staging data were obtained from liver biopsies. Variables considered for the model included demographics (age, gender, race, ethnicity), total bilirubin, alkaline phosphatase, albumin, aspartate aminotransferase (AST) to platelet ratio index (APRI), Fibrosis 4 (FIB4) index, AST to alanine aminotransferase (ALT) ratio, and >100 DPCs associated with cirrhosis/decompensated cirrhosis, categorized into ten clusters. Using least absolute shrinkage and selection operator regression (LASSO), we derived and validated cutoffs for identifying cirrhosis. RESULTS: Among 4328 PBC patients, 1350 (32%) had biopsy data; 121 (9%) were staged F4 (cirrhosis). DPC clusters (including codes related to cirrhosis and hepatocellular carcinoma diagnoses/procedures), Hispanic ethnicity, ALP, AST/ALT ratio, and total bilirubin were retained in the final model (AUROC=0.86

and 0.83 on learning and testing data, respectively); this model with two cutoffs divided patients into three categories (no cirrhosis, indeterminate, and cirrhosis) with specificities of 81.8% (for no cirrhosis) and 80.3% (for cirrhosis). A model excluding DPCs retained ALP, AST/ALT ratio, total bilirubin, Hispanic ethnicity, and gender (AUROC=0.81 and 0.78 on learning and testing data, respectively). CONCLUSION: An algorithm using laboratory results and DPCs can categorize a majority of PBC patients as cirrhotic or noncirrhotic with high accuracy (with a small remaining group of patients' cirrhosis status indeterminate). In the absence of biopsy data, this EHR-based model can be used to identify cirrhosis in cohorts of PBC patients for research and/or clinical follow-up.

Public Health Sciences

Lu M, **Wu KH**, **Trudeau S**, Jiang M, Zhao J, and Fan E. A genomic signature for accurate classification and prediction of clinical outcomes in cancer patients treated with immune checkpoint blockade immunotherapy. *Sci Rep* 2020; 10(1):20575. PMID: 33239757. Full Text

Department of Public Health Sciences, Henry Ford Health System, 3E One Ford Place, Detroit, MI, 48202, USA. mlu1@hfhs.org.
Division of Data Analytics, Northern Medical Center, Middletown, NY, USA. mlu1@hfhs.org.
Department of Public Health Sciences, Henry Ford Health System, 3E One Ford Place, Detroit, MI, 48202, USA.
Department of Computational Medicine and Bioinformatics, University of Michigan, Ann Arbor, MI, USA.
Division of Data Analytics, Northern Medical Center, Middletown, NY, USA.

Tumor mutational burden (TMB) is associated with clinical response to immunotherapy, but application has been limited to a subset of cancer patients. We hypothesized that advanced machine-learning and proper modeling could identify mutations that classify patients most likely to derive clinical benefits. Training data: Two sets of public whole-exome sequencing (WES) data for metastatic melanoma. Validation data: One set of public non-small cell lung cancer (NSCLC) data. Least Absolute Shrinkage and Selection Operator (LASSO) machine-learning and proper modeling were used to identify a set of mutations (biomarker) with maximum predictive accuracy (measured by AUROC). Kaplan-Meier and log-rank methods were used to test prediction of overall survival. The initial model considered 2139 mutations. After pruning, 161 mutations (11%) were retained. An optimal threshold of 0.41 divided patients into high-weight (HW) or low-weight (LW) TMB groups. Classification for HW-TMB was 100% (AUROC = 1.0) on melanoma learning/testing data; HW-TMB was a prognostic marker for longer overall survival. In validation data, HW-TMB was associated with survival (p = 0.0057) and predicted 6-month clinical benefit (AUROC = 0.83) in NSCLC. In conclusion, we developed and validated a 161-mutation genomic signature with "outstanding" 100% accuracy to classify melanoma patients by likelihood of response to immunotherapy. This biomarker can be adapted for clinical practice to improve cancer treatment and care.

Public Health Sciences

Plawecki AM, **Singer MC**, **Peterson EL**, **Yaremchuk KL**, and **Deeb RH**. Impact of a specialty trained billing team on an academic otolaryngology practice. *Am J Otolaryngol* 2020; 41(6):102720. PMID: 32977062. Full Text

Department of Otolaryngology - Head & Neck Surgery, Henry Ford Hospital, 2799 W. Grand Blvd, Detroit, MI 48202, USA.
Department of Public Health Sciences, Henry Ford Health System, One Ford Place, Detroit, MI 48202, USA.
Department of Otolaryngology - Head & Neck Surgery, Henry Ford Hospital, 2799 W. Grand Blvd, Detroit, MI 48202, USA. Electronic address: Rdeeb1@hfhs.org.

PURPOSE: To determine how the incorporation of specialty specific training for coders within a focused billing team affected revenue, efficiency, time to reimbursement, and physician satisfaction in an academic otolaryngology practice. MATERIALS AND METHODS: Our academic otolaryngology department recently implemented a new billing system, which incorporated additional training in otolaryngology surgical procedures for medical coders. A mixed model analysis of variance was used to

compare billing outcomes for the 6 months before and 6 months after this new approach was initiated. The following metrics were analyzed: Current Procedural Terminology codes, total charges, time between services rendered and billing submission, and time to reimbursement. A survey of department physicians assessing satisfaction with the system was reviewed. RESULTS: There were 4087 Current Procedural Terminology codes included in the analysis. In comparing the periods before and after implementation of the new system, statistically significant decreases were found in the mean number of days to coding completion (19.3 to 12.0, respectively, $p < 0.001$), days to posting of charges (27.0 to 15.2, $p < 0.001$), days to final reimbursement (54.5 to 27.2, $p < 0.001$), and days to closure of form (179.2 to 76.6, $p < 0.001$). Physician satisfaction with communication and coder feedback increased from 36% to 64% after initiation of the new program. CONCLUSIONS: The implementation of additional specialty training for medical coders in the otolaryngology department of a large medical system was associated with improved revenue cycle efficiency. Additionally, this model appears to improve physician satisfaction and confidence with the coding system.

Public Health Sciences

Prabhakar D, **Peterson EL**, **Hu Y**, **Chawa S**, Rossom RC, Lynch FL, Lu CY, Waitzfelder BE, Owen-Smith AA, **Williams LK**, Beck A, Simon GE, and Ahmedani BK. Serious Suicide Attempts and Risk of Suicide Death. *Crisis* 2020;1-8. Epub ahead of print. PMID: 33151092. Request Article

Sheppard Pratt, Baltimore, MD, USA.
Department of Public Health Sciences, Henry Ford Health System, Detroit, MI, USA.
Center for Health Policy and Health Services Research (CHSR), Henry Ford Health System, Detroit, MI, USA.
Behavioral Health Sciences, Henry Ford Health System, Detroit, MI, USA.
Health Partners Institute, University of Minnesota, Minneapolis, MN, USA.
Center for Health Research, Kaiser Permanente Northwest, Portland, OR, USA.
Department of Population Medicine, Harvard Medical School, Boston, MA, USA.
Center for Health Research, Kaiser Permanente, Honolulu, HI, USA.
Center for Research and Evaluation, Kaiser Permanente Georgia, Atlanta, GA, USA.
Center of Individualized and Genomic Medicine Research (CIGMA), Department of Internal Medicine, Henry Ford Health System, Detroit, MI, USA.
Institute for Health Research, Kaiser Permanente Colorado, Denver, CO, USA.
Health Research Institute, Kaiser Permanente, Seattle, WA, USA.

Background: In the US, more than one million people attempt suicide each year. History of suicide attempt is a significant risk factor for death by suicide; however, there is a paucity of data from the US general population on this relationship. Aim: The objective of this study was to examine suicide attempts needing medical attention as a risk for suicide death. Method: We conducted a case-control study involving eight US healthcare systems. A total of 2,674 individuals who died by suicide from 2000 to 2013 were matched to 267,400 individuals by year and location. Results: Prior suicide attempt associated with a medical visit increases risk for suicide death by 39.1 times, particularly for women (OR = 79.2). However, only 11.3% of suicide deaths were associated with an attempt that required medical attention. The association was the strongest for children 10-14 years old (OR = 98.0). Most suicide attempts were recorded during the 20-week period prior to death. Limitations: Our study is limited to suicide attempts for which individuals sought medical care. Conclusion: In the US, prior suicide attempt is associated with an increased risk of suicide death; the risk is high especially during the period immediately following a nonlethal attempt.

Public Health Sciences

Sitarik AR, Arora M, Austin C, Bielak LF, Eggers S, **Johnson CC**, Lynch SV, Kyun Park S, **Hank Wu KH**, Yong GJM, and **Cassidy-Bushrow AE**. Fetal and early postnatal lead exposure measured in teeth associates with infant gut microbiota. *Environ Int* 2020; 144:106062. PMID: 32871381. Full Text

Department of Public Health Sciences, Henry Ford Health System, Detroit, USA. Electronic address: asitari1@hfhs.org.

Senator Frank R Lautenberg Environmental Health Sciences Laboratory, Department of Environmental Medicine and Public Health, Icahn School of Medicine at Mount Sinai, New York City, USA. Electronic address: manish.arora@mssm.edu.
Senator Frank R Lautenberg Environmental Health Sciences Laboratory, Department of Environmental Medicine and Public Health, Icahn School of Medicine at Mount Sinai, New York City, USA. Electronic address: christine.austin@mssm.edu.
Department of Epidemiology, University of Michigan, Ann Arbor, USA. Electronic address: lfbielak@umich.edu.
Senator Frank R Lautenberg Environmental Health Sciences Laboratory, Department of Environmental Medicine and Public Health, Icahn School of Medicine at Mount Sinai, New York City, USA. Electronic address: shoshannah.eggers@mssm.edu.
Department of Public Health Sciences, Henry Ford Health System, Detroit, USA. Electronic address: cjohnso1@hfhs.org.
Division of Gastroenterology, Department of Medicine, University of California, San Francisco, USA. Electronic address: Susan.Lynch@ucsf.edu.
Department of Epidemiology, University of Michigan, Ann Arbor, USA; Department of Environmental Health Sciences, University of Michigan, Ann Arbor, USA. Electronic address: sungkyun@umich.edu.
Department of Public Health Sciences, Henry Ford Health System, Detroit, USA. Electronic address: wukh@umich.edu.
Division of Gastroenterology, Department of Medicine, University of California, San Francisco, USA. Electronic address: Germaine.Yong@ucsf.edu.
Department of Public Health Sciences, Henry Ford Health System, Detroit, USA. Electronic address: acassid1@hfhs.org.

BACKGROUND: Lead (Pb) is an environmentally ubiquitous heavy metal associated with a wide range of adverse health effects in children. Both lead exposure and the early life microbiome- which plays a critical role in human development-have been linked to similar health outcomes, but it is unclear if the adverse effects of lead are partially driven by early life gut microbiota dysbiosis. The objective of this study was to examine the association between in utero and postnatal lead levels (measured in deciduous baby teeth) and early life bacterial and fungal gut microbiota in the first year of life. METHODS: Data from the Wayne County Health, Environment, Allergy and Asthma Longitudinal Study (WHEALS) birth cohort were analyzed. Tooth lead levels during the 2nd and 3rd trimesters and postnatally (<1 year of age) were quantified using high-resolution microspatial mapping of dentin growth rings. Early life microbiota were measured in stool samples collected at approximately 1 and 6 months of age, using both 16S rRNA (bacterial) and ITS2 (fungal) sequencing. Of the 1,258 maternal-child pairs in WHEALS, 146 had data on both tooth metals and early life microbiome. RESULTS: In utero tooth lead levels were significantly associated with gut fungal community composition at 1-month of age, where higher levels of 2nd trimester tooth lead was associated with lower abundances of Candida and Aspergillus and higher abundances of Malassezia and Saccharomyces; 3rd trimester lead was also associated with lower abundances of Candida. Though lead did not significantly associate with the overall structure of the infant gut bacterial community, it associated with the abundance of some specific bacterial taxa, including the increased abundance of Collinsella and Bilophila and a decreased abundance of Bacteroides taxa. CONCLUSIONS: The observed associations between lead exposure and infant gut microbiota could play a role in the impact of lead on childhood development. Given the paucity of research examining these associations in humans-particularly for fungal microbiota-further investigation is needed.

Public Health Sciences

Upson K, Harmon QE, Heffron R, Hall JE, Wise LA, **Wegienka G**, Tokar EJ, and Baird DD. Depot Medroxyprogesterone Acetate Use and Blood Lead Levels in a Cohort of Young Women. *Environ Health Perspect* 2020; 128(11):117004. PMID: 33206002. Full Text

Department of Epidemiology and Biostatistics, College of Human Medicine, Michigan State University, East Lansing, Michigan, USA.
Epidemiology Branch, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina, USA.
Department of Global Health, University of Washington, Seattle, Washington, USA.

Department of Epidemiology, University of Washington, Seattle, Washington, USA.
Clinical Research Branch, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina, USA.
Department of Epidemiology, Boston University School of Public Health, Boston, Massachusetts, USA.
Department of Public Health Sciences, Henry Ford Health System, Detroit, Michigan, USA.
Stem Cells Toxicology Group, National Toxicology Program Laboratory, Division of the National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina, USA.

BACKGROUND: Injectable contraceptive use is common, with 74 million users worldwide. Use of the injectable contraceptive depot medroxyprogesterone acetate (DMPA) is associated with bone mineral density loss. We hypothesize that increased bone resorption with DMPA use allows for mobilization of the toxic metal lead stored in bone to blood, presenting users with increased systemic exposure to lead. OBJECTIVE: The objective of our study was to investigate the association between current DMPA use and blood lead concentrations. METHODS: We conducted a cross-sectional analysis using enrollment data from the Study of Environment, Lifestyle & Fibroids (SELF), a cohort of 1,693 African-American women who were 23-35 years of age. Data on DMPA use were collected by computer-assisted telephone interview. Blood lead concentrations were measured in whole blood samples among 1,548 participants (91% of cohort). We estimated the adjusted percent difference in blood lead concentrations and 95% confidence intervals (CI) between current DMPA users and nonusers using multivariable linear regression. RESULTS: Geometric mean blood lead concentration was 0.69 µg/dL (95% CI: 0.67, 0.71). After adjustment, current DMPA users (7% of cohort) had blood lead concentrations that were 18% higher than those of nonusers (95% CI: 8%, 29%). Similar associations were observed with additional analyses to assess for potential bias from smoking, DMPA-induced amenorrhea, use of estrogen-containing contraceptives, having given birth in the prior year, and history of medical conditions or current medication use associated with bone loss. DISCUSSION: Our results indicate that current DMPA use is associated with increased blood lead concentrations. Further research, particularly in populations highly exposed to lead, is warranted to consider tradeoffs between the adverse effects of lead on human health and the importance of DMPA as a contraceptive option to prevent unintended pregnancy. https://doi.org/10.1289/EHP7017.

Public Health Sciences

Varma A, **Trudeau S**, **Zhou Y**, **Jafri SM**, **Krajenta R**, **Lamerato L**, **Brown K**, Luzzi V, **Lu M**, and **Gordon SC**. African Americans Demonstrate Significantly Lower Serum Alanine Aminotransferase Compared to Non-African Americans. *J Racial Ethn Health Disparities* 2020; Epub ahead of print. PMID: 33230736. Request Article

Department of Gastroenterology and Hepatology, Henry Ford Health System, 3E One Ford Place, Detroit, MI, 48202, USA.
Department of Public Health Sciences, Henry Ford Health System, Detroit, MI, USA.
Providence Health and Services Regional Laboratory, Portland, OR, USA.
Department of Gastroenterology and Hepatology, Henry Ford Health System, 3E One Ford Place, Detroit, MI, 48202, USA. sgordon3@hfhs.org.

BACKGROUND AND AIMS: Normal ranges of serum alanine aminotransferase (ALT) may vary by race. However, results from research studies are contradictory, and many of these studies have included only small numbers of African Americans. We investigated ALT values in patients without evidence of liver disease to determine whether normal ranges differ across race groups. We also evaluated whether a race- and sex-dependent upper limit of normal (ULN) would improve the ability of ALT to predict liver disease compared to the sex-dependent ULN currently in use. METHODS: We identified ICD9 codes for liver conditions and diabetes in medical records from a sample of 6719 patients. Analysis of variance (ANOVA) was used to assess differences in ALT log-transformed distributions by race. Logistic regression was used to evaluate whether the addition of race to the current sex-dependent ULN improves the ability of ALT to predict liver disease (assessed by area under the receiver operating characteristic curve (AUROC)). RESULTS: Among 1200 patients with BMI 18.5 < 25 and no evidence of liver disease or type 2 diabetes in their medical record, African Americans demonstrated significantly lower ALT

(23.47 IU/L; 95% CL 22.87-24.10) than a combined group of Asian American/White/Other patients (25.71 IU/L; 95% CL 24.69-26.77). This difference remained across BMI categories. The race- and sex-dependent model demonstrated significantly better predictive ability than the sex-dependent model (AUROC = 66.6% versus 59.6%, respectively; $p < 0.0001$). CONCLUSIONS: In a large, racially diverse sample, African Americans demonstrated significantly lower ALT compared to non-African Americans; this difference remained as BMI increased. The establishment of race-specific normal ranges for ALT could contribute to better screening and care for African American patients.

Public Health Sciences

Wasade VS, and **Schultz L**. Reply to: Effect of seizure timing on long-term survival in brain tumor patients. *Epilepsy Behav* 2020; Epub ahead of print. PMID: 33239218. Full Text

Department of Neurosciences, Henry Ford Health System, Detroit, MI, USA; Wayne State University, School of Medicine, MI, USA. Electronic address: vwasade1@hfhs.org.
Department of Neurosciences, Henry Ford Health System, Detroit, MI, USA; Department of Public Health Sciences, Henry Ford Health System, Detroit, MI, USA.

Pulmonary and Critical Care Medicine

Hoffert M, **Kerr H**, **Hegab S**, **Whitehouse S**, **Kokas M**, **MacLean L**, **Van Harn MG**, and **Baker-Genaw K**. Designing a Yoga Intervention Program to Improve Well-Being for Physician Trainees: Challenges and Lessons Learned. *Int J Yoga Therap* 2020; Epub ahead of print. PMID: 33157552. Full Text

Department of Medical Education, Henry Ford Hospital, Detroit, Mich.
Department of Dermatology, Henry Ford Hospital, Detroit, Mich.
Division of Pulmonary and Critical Care Medicine, Henry Ford Hospital, Detroit, Mich.
Behavioral Health Services, Henry Ford Hospital, Detroit, Mich.
Public Health Science Division of Biostatistics, Henry Ford Hospital, Detroit, Michigan.
Department of Medical Education and Department of Internal Medicine, Henry Ford Hospital, Detroit, Mich.

Well-being activities may help to counteract physician burnout. Yoga is known to enhance well-being, but there are few studies of yoga as an intervention for physicians in training. This prospective methodology-development study aimed to explore how to establish a yoga-based well-being intervention for physician trainees in a large urban training hospital. We aimed to identify factors that contribute to trainee participation and explore an instrument to measure changes in self-reported well-being after yoga. Cohorts included a required-attendance group, a voluntary-attendance group, and an unassigned walk-in yoga group. Weekly 1-hour yoga sessions were led by a qualified yoga instructor for 4 weeks. The seven-question Resident Physician Well-Being Index (RPWBI) was used to measure resident well-being before yoga, after 4 weeks of yoga, and 6 months post-yoga. Trainees attending each session ranged from 17 for required yoga to 0-2 for voluntary yoga, 2-9 for lunchtime walk-in yoga, and 1-7 for evening walk-in yoga. In the required-yoga group (n = 17), overall RPWBI mean scores did not change significantly across the three query times, and participation in the survey declined over time. The mean baseline RPWBI score for the required group before yoga was in the non-distressed range and answers to the seven individual questions varied. Requiring a yoga activity for medical trainees may be a good strategy for promoting participation in yoga. The RPWBI may have limited utility for measuring changes in overall group well-being after a yoga intervention.

Pulmonary and Critical Care Medicine

Kim HS, Khemasuwan D, **Diaz-Mendoza J**, and Mehta AC. Management of tracheo-oesophageal fistula in adults. *Eur Respir Rev* 2020; 29(158). PMID: 33153989. Full Text

Division of Pulmonary and Critical Care, St Elizabeth Medical Center, Boston, MA, USA hyun.kim@steward.org.
Division of Pulmonary and Critical Care, St Elizabeth Medical Center, Boston, MA, USA.
Pulmonary and Critical Care Medicine, Henry Ford Hospital/Wayne State University, Detroit, MI, USA.

Dept of Medicine, Lerner College of Medicine, Respiratory Institute, Cleveland Clinic, Cleveland, OH, USA.

Tracheo-oesophageal fistula (TOF) is a pathological connection between the trachea and the oesophagus that is associated with various underlying conditions including malignancies, infections, inhalation injuries and traumatic damage. As the condition spans multiple organ systems with varying aetiologies and acuities, TOF poses unique diagnostic and management challenges to pulmonologists, gastroenterologists and thoracic surgeons alike. Although stents have been a cornerstone in the management of TOF, there exists a large gap in our understanding of their efficacy and precise methodology, making stenting procedure both art and science. TOFs relating to underlying oesophageal or tracheal malignancies require advanced understanding of the airway and digestive tract anatomy, dimensions of the fistula, stent characteristics and types, and the interplay between the oesophageal stent and the airway stent if dual stenting procedure is elected. In this review article, we review the most up-to-date data on risk factors, clinical manifestations, diagnostic approaches, management methods and prognosis. Consequently, this article serves to evaluate current therapeutic strategies and the future directions in the areas of 3D-printed stents, over-the-scope clipping systems, tissue matrices and atrial septal closure devices.

Pulmonary and Critical Care Medicine

Reaume M, Duong T, **Song T**, and **Diaz-Mendoza J**. The pulmonary nodule following lung transplantation. *Clin Imaging* 2020; 72:37-41. PMID: 33202293. Full Text

Department of Pulmonary and Critical Care Medicine, Henry Ford Hospital, Detroit, MI, United States of America.
Department of Medicine, Weiss Memorial Hospital, Chicago, IL, United States of America.
Department of Radiology, Henry Ford Hospital, Detroit, MI, United States of America.
Department of Pulmonary and Critical Care Medicine, Henry Ford Hospital, Detroit, MI, United States of America; Department of Medicine, Wayne State University, Detroit, MI, United States of America. Electronic address: Jdiaz1@hfhs.org.

The clinical scenario of a pulmonary nodule following lung transplantation is one with limited experience and no supporting guidelines for the approach to diagnosis and management. Given the broad differential diagnosis for pulmonary nodules in this setting, most of which are life-threatening without appropriate treatment, aggressive evaluation is required. Here we present a case of a 70-year-old female with the development of a large pulmonary nodule in the native lung four years following a single lung transplant. She underwent bronchoscopy with endobronchial ultrasound to achieve a tissue diagnosis which showed small cell lung carcinoma. The patient was started on chemotherapy and has shown clinical and radiographic improvement at most recent follow up seven months after the initial diagnosis. In this report we discuss the differential diagnosis and corresponding imaging findings for the pulmonary nodule following lung transplantation to aid in guiding clinicians navigate this challenging clinical situation.

Radiation Oncology

Bagher-Ebadian H, and **Chetty IJ**. Technical Note: ROdiomX: A Validated Software for Radiomics Analysis of Medical Images in Radiation Oncology. *Med Phys* 2020; Epub ahead of print. PMID: 33169367. Full Text

Department of Radiation Oncology, Henry Ford Health System, USA.

PURPOSE: This study introduces an in-house-designed software platform (ROdiomX) for the radiomics analysis of medical images in radiation oncology. ROdiomX is a MATLAB-based framework for the computation of radiomic features and feature aggregation techniques in compliance with the Image-Biomarker-Standardization-Initiative (IBSI) guidelines, which includes pre-processing protocols and quantitative benchmark results for analysis of computational phantom images. METHODS AND MATERIALS: The ROdiomX software system consists of a series of computation cores implemented on the basis of the guidelines proposed by the IBSI. It is capable of quantitative computation of the following 11 different feature categories: Local-Intensity, Intensity-Histogram, Intensity-Based-Statistical, Intensity-

Volume-Histogram, Gray-Level-Co-occurrence, Gray-Level-Run-Length, Gray-Level-Size-Zone, Gray-Level-Distance-Zone, Neighborhood-Grey-Tone-Difference, Neighboring-Grey-Level-Dependence, and Morphological feature. ROdiomX was validated against benchmark values for the IBSI 3D digital phantom, as well as one designed in-house (HFH). The Intra-class correlation coefficient (ICC) for estimating the degree of absolute agreement between ROdiomX computation and benchmark values for different features at the 95% confidence level (CL) was used for comparison. RESULTS: Among the 11 feature categories with 151 total features including 10 different feature aggregation methods (following the IBSI guidelines), the percent difference between absolute feature values computed by the ROdiomX software and benchmark values reported for IBSI and HFH digital phantoms were 0.14% ± 0.43% and 0.11% ± 0.27% respectively. The ICC values were ≥0.997 for all ten feature categories for both the IBSI and HFH digital phantoms. CONCLUSION: The authors successfully developed a platform for computation of quantitative radiomic features. The image preprocessing and computational software cores were designed following the procedures specified by the IBSI. Benchmarking testing was in excellent agreement against the IBSI and HFH-designed computational phantoms.

Radiation Oncology

Chun SG, Simone CB, 2nd, Amini A, **Chetty IJ**, Donington J, Edelman MJ, Higgins KA, Kestin LL, **Movsas B**, Rodrigues GB, Rosenzweig KE, Slotman BJ, **Rybkin, II**, Wolf A, and Chang JY. American Radium Society Appropriate Use Criteria: Radiation Therapy for Limited-Stage SCLC 2020. *J Thorac Oncol* 2020; Epub ahead of print. PMID: 33166720. Full Text

Department of Radiation Oncology, The University of Texas, MD Anderson Cancer Center, Houston, Texas. Electronic address: sgchun@mdanderson.org.
New York Proton Center, New York, New York.
Department of Radiation Oncology, City of Hope Comprehensive Cancer Center, Duarte, California.
Department of Radiation Oncology, Henry Ford Cancer Institute, Detroit, Michigan.
Department of Surgery, The University of Chicago, Chicago, Illinois.
Department of Hematology and Oncology, Fox Chase Comprehensive Cancer Center, Philadelphia, Pennsylvania.
Department of Radiation Oncology, Emory University Winship Cancer Institute, Atlanta, Georgia.
MHP Radiation Oncology Institute/GenesisCare USA, Farmington Hills, Michigan.
Department of Radiation Oncology, London Health Sciences Centre, London, Ontario, Canada.
Department of Radiation Oncology, Mount Sinai School of Medicine, New York, New York.
Department of Radiation Oncology, Amsterdam University Medical Center, Amsterdam, The Netherlands.
Department of Hematology and Oncology, Henry Ford Cancer Institute, Detroit, Michigan.
Department of Thoracic Surgery, Mount Sinai School of Medicine, New York, New York.
Department of Radiation Oncology, The University of Texas, MD Anderson Cancer Center, Houston, Texas.

INTRODUCTION: Combined modality therapy with concurrent chemotherapy and radiation has long been the standard of care for limited-stage SCLC (LS-SCLC). However, there is controversy over best combined modality practices for LS-SCLC. To address these controversies, the American Radium Society (ARS) Thoracic Appropriate Use Criteria (AUC) Committee have developed updated consensus guidelines for the treatment of LS-SCLC. METHODS: The ARS AUC are evidence-based guidelines for specific clinical conditions that are reviewed by a multidisciplinary expert panel. The guidelines include a review and analysis of current evidence with application of consensus methodology (modified Delphi) to rate the appropriateness of treatments recommended by the panel for LS-SCLC. Agreement or consensus was defined as less than or equal to 3 rating points from the panel median. The consensus ratings and recommendations were then vetted by the ARS Executive Committee and subject to public comment before finalization. RESULTS: The ARS Thoracic AUC committee developed multiple consensus recommendations for LS-SCLC. There was strong consensus that patients with unresectable LS-SCLC should receive concurrent chemotherapy with radiation delivered either once or twice daily. For medically inoperable T1-T2N0 LS-SCLC, either concurrent chemoradiation or stereotactic body radiation followed by adjuvant chemotherapy is a reasonable treatment option. The panel continues to recommend whole-brain prophylactic cranial irradiation after response to chemoradiation for LS-SCLC. There was panel agreement that prophylactic cranial irradiation with hippocampal avoidance and programmed cell

death protein-1/programmed death-ligand 1-directed immune therapy should not be routinely administered outside the context of clinical trials at this time. CONCLUSIONS: The ARS Thoracic AUC Committee provide consensus recommendations for LS-SCLC that aim to provide a groundwork for multidisciplinary care and clinical trials.

Radiation Oncology

Tam S, **Wu VF**, **Williams AM**, **Girgis M**, **Sheqwara JZ**, **Siddiqui F**, and **Chang SS**. Disparities in the Uptake of Telemedicine During the COVID-19 Surge in a Multidisciplinary Head and Neck Cancer Population by Patient Demographic Characteristics and Socioeconomic Status. *JAMA Otolaryngol Head Neck Surg* 2020; Epub ahead of print. PMID: 33151289. Full Text

Department of Otolaryngology-Head and Neck Surgery, Henry Ford Health System and Henry Ford Cancer Institute, Detroit, Michigan.
Department of Hematology/Medical Oncology, Henry Ford Health System and Henry Ford Cancer Institute, Detroit, Michigan.
Department of Radiation Oncology, Henry Ford Health System and Henry Ford Cancer Institute, Detroit, Michigan.

This cohort study examines the association between patient demographic characteristics and socioeconomic status and engagement in telemedicine during the COVID-19 pandemic.

Research Administration

Larivière S, Rodríguez-Cruces R, Royer J, Caligiuri ME, Gambardella A, Concha L, Keller SS, Cendes F, Yasuda C, Bonilha L, Gleichgerrcht E, Focke NK, Domin M, von Podewills F, Langner S, Rummel C, Wiest R, Martin P, Kotikalapudi R, O'Brien TJ, Sinclair B, Vivash L, Desmond PM, 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, Tortora D, Hatton SN, Vos SB, Duncan JS, Whelan CD, Thompson PM, Sisodiya SM, Bernasconi A, Labate A, McDonald CR, Bernasconi N, and Bernhardt BC. Network-based atrophy modeling in the common epilepsies: A worldwide ENIGMA study. *Sci Adv* 2020; 6(47). PMID: 33208365. Full Text

Multimodal Imaging and Connectome Analysis Laboratory, McConnell Brain Imaging Centre, Montreal Neurological Institute and Hospital, McGill University, Montreal, QC, Canada.
Neuroscience Research Center, University Magna Græcia, Catanzaro, CZ, Italy.
Institute of Neurology, University Magna Græcia, Catanzaro, CZ, Italy.
Institute of Neurobiology, Universidad Nacional Autónoma de México, Querétaro, México.
Institute of Systems, Molecular and Integrative Biology, University of Liverpool, Liverpool, UK.
Walton Centre NHS Foundation Trust, Liverpool, UK.
Department of Neurology, University of Campinas-UNICAMP, Campinas, São Paulo, Brazil.
Department of Neurology, Medical University of South Carolina, Charleston, SC, USA.
Department of Clinical Neurophysiology, University of Medicine Göttingen, Göttingen, Germany.
Institute of Diagnostic Radiology and Neuroradiology, Functional Imaging Unit, University Medicine Greifswald, Greifswald, Germany.
Department of Neurology, University Medicine Greifswald, Greifswald, Germany.
Institute of Diagnostic Radiology and Neuroradiology, University Medicine Greifswald, Greifswald, Germany.
Support Center for Advanced Neuroimaging (SCAN), University Institute of Diagnostic and Interventional Neuroradiology, University Hospital Bern, Bern, Switzerland.
Department of Neurology and Epileptology, Hertie Institute for Clinical Brain Research, University of Tübingen, Tübingen, Germany.
Department of Neuroscience, Central Clinical School, Alfred Hospital, Monash University, Melbourne, Victoria, Australia.
Departments of Medicine and Radiology, The Royal Melbourne Hospital, The University of Melbourne, Parkville, Victoria, Australia.

Department of Molecular and Cellular Therapeutics, The Royal College of Surgeons in Ireland, Dublin, Ireland.
Department of Neurology, Yale University School of Medicine, New Haven, CT, USA.
Department of Neurology, St. James' Hospital, Dublin, Ireland.
FutureNeuro SFI Research Centre, Dublin, Ireland.
Epilepsy Center, Neuro Center, Kuopio University Hospital, European Reference Network for Rare and Complex Epilepsies EpiCARE, Kuopio, Finland.
Faculty of Health Sciences, School of Medicine, Institute of Clinical Medicine, University of Eastern Finland, Kuopio, Finland.
Florey Institute of Neuroscience and Mental Health, University of Melbourne, Melbourne, Victoria 3010, Australia.
Neuroradiology Research Program, Meyer Children Hospital of Florence, University of Florence, Florence, Italy.
Translational and Clinical Research Institute, Newcastle University, Newcastle upon Tyne, UK.
Control and Intelligent Processing Center of Excellence (CIPCE), School of Electrical and Computer Engineering, University of Tehran, Tehran, Iran.
Departments of Research Administration and Radiology, Henry Ford Health System, Detroit, MI, USA.
Department of Neurology, Henry Ford Health System, Detroit, MI, USA.
Cognitive Science Department, Xiamen University, Xiamen, China.
Child Neurology Unit and Laboratories, Neuroscience Department, Children's Hospital A. Meyer-University of Florence, Italy.
Functional and Epilepsy Neurosurgery Unit, Neurosurgery Department, Children's Hospital A. Meyer-University of Florence, Italy.
USL Centro Toscana, Neurology Unit, Nuovo Ospedale Santo Stefano, Prato, Italy.
Cardiff University Brain Research Imaging Centre (CUBRIC), College of Biomedical Sciences, Cardiff University, Cardiff, UK.
Welsh Epilepsy Unit, Department of Neurology, University Hospital of Wales, Cardiff, UK.
Institute of Experimental Epileptology and Cognition Research, University Hospital Bonn, Bonn, Germany.
Department of Neurology, Hôpital Erasme, Université Libre de Bruxelles, Brussels, Belgium.
Department of Radiology, Hôpital Erasme, Université Libre de Bruxelles, Brussels, Belgium.
Division of Neuroscience, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK.
Department of Neurology, NYU Grossman School of Medicine, New York, NY, USA.
IRCCS Istituto Giannina Gaslini, Genova, Italy.
Department of Neurosciences, Center for Multimodal Imaging and Genetics, University of California San Diego, La Jolla, CA, USA.
Department of Clinical and Experimental Epilepsy, UCL Institute of Neurology, London, UK.
Chalfont Centre for Epilepsy, Bucks, UK.
Centre for Medical Image Computing, University College London, London, UK.
Imaging Genetics Center, Mark and Mary Stevens Institute for Neuroimaging and Informatics, USC Keck School of Medicine, Los Angeles, CA, USA.
Neuroimaging of Epilepsy Laboratory, McConnell Brain Imaging Centre, Montreal Neurological Institute and Hospital, McGill University, Montreal, QC, Canada.
Department of Psychiatry, Center for Multimodal Imaging and Genetics, University of California San Diego, La Jolla, CA, USA.
Multimodal Imaging and Connectome Analysis Laboratory, McConnell Brain Imaging Centre, Montreal Neurological Institute and Hospital, McGill University, Montreal, QC, Canada. boris.bernhardt@mcgill.ca.

Epilepsy is increasingly conceptualized as a network disorder. In this cross-sectional mega-analysis, we integrated neuroimaging and connectome analysis to identify network associations with atrophy patterns in 1021 adults with epilepsy compared to 1564 healthy controls from 19 international sites. In temporal lobe epilepsy, areas of atrophy colocalized with highly interconnected cortical hub regions, whereas idiopathic generalized epilepsy showed preferential subcortical hub involvement. These morphological abnormalities were anchored to the connectivity profiles of distinct disease epicenters, pointing to temporo-limbic cortices in temporal lobe epilepsy and fronto-central cortices in idiopathic generalized epilepsy. Negative effects of age on atrophy further revealed a strong influence of connectome

architecture in temporal lobe, but not idiopathic generalized, epilepsy. Our findings were reproduced across individual sites and single patients and were robust across different analytical methods. Through worldwide collaboration in ENIGMA-Epilepsy, we provided deeper insights into the macroscale features that shape the pathophysiology of common epilepsies.

Sleep Medicine
Cheng P, Casement MD, **Kalmbach DA**, **Castelan AC**, and **Drake CL**. Digital Cognitive Behavioral Therapy for Insomnia Promotes Later Health Resilience During the Coronavirus Disease 19 (COVID-19) Pandemic. *Sleep* 2020; Epub ahead of print. PMID: 33249492. Full Text

Sleep Disorders and Research Center, Henry Ford Health System, Detroit, MI, USA.
Department of Psychology, University of Oregon, Eugene, OR, USA.

STUDY OBJECTIVES: Stressful life events contribute to insomnia, psychosocial functioning, and illness. Though individuals with a history of insomnia may be especially vulnerable during stressful life events, risk may be mitigated by prior intervention. This study evaluated the effect of prior digital cognitive-behavioral therapy for insomnia (dCBT-I) versus sleep education on health resilience during the COVID-19 pandemic. METHODS: COVID impact, insomnia, general- and COVID-related stress, depression, and global health were assessed in April 2020 in adults with a history of insomnia who completed a randomized controlled trial of dCBT-I (n = 102) versus sleep education control (n = 106) in 2016-2017. Regression analyses were used to evaluate the effect of intervention conditions on subsequent stress and health during the pandemic. RESULTS: Insomnia symptoms were significantly associated with COVID-19 related disruptions, and those previously received dCBT-I reported less insomnia symptoms, less general stress and COVID-related cognitive intrusions, less depression, and better global health than those who received sleep education. Moreover, the odds for resurgent insomnia was 51% lower in the dCBT-I versus control condition. Similarly, odds of moderate to severe depression during COVID-19 was 57% lower in the dCBT-I condition. CONCLUSIONS: Those who received dCBT-I had increased health resilience during the COVID-19 pandemic in adults with a history of insomnia and ongoing mild to moderate mental health symptoms. These data provide evidence that dCBT-I is a powerful tool to promote mental and physical health during stressors, including the COVID-19 pandemic.

Surgery
Al-Darzi W, **Alalwan Y**, **Askar F**, **Sadiq O**, **Venkat D**, **Gonzalez H**, **Galusca D**, **Yoshida A**, and **Jafri SM**. Risk Factors and Outcomes of Intracardiac Thrombosis During Orthotopic Liver Transplantation. *Transplant Proc* 2020; Epub ahead of print. PMID: 33246584. Full Text

Division of Cardiology, Henry Ford Hospital, Detroit, Michigan. Electronic address: waleed.aldarzi@gmail.com.
Department of Internal Medicine, Henry Ford Hospital, Detroit, Michigan.
Department of Internal Medicine, Henry Ford Hospital, Detroit, Michigan; School of Medicine, Wayne State University, Detroit, Michigan.
Division of Gastroenterology, Henry Ford Hospital, Detroit, Michigan.
School of Medicine, Wayne State University, Detroit, Michigan; Division of Gastroenterology, Henry Ford Hospital, Detroit, Michigan.
Department of Anesthesiology, Henry Ford Hospital, Detroit, Michigan.
Transplant and Hepatobiliary Surgery, Henry Ford Hospital, Detroit, Michigan.

BACKGROUND: Intracardiac thrombosis incidence during orthotopic liver transplantation is estimated at 0.36% to 6.2% with mortality up to 68%. We aimed to evaluate risk factors and outcomes related to intracardiac thrombosis during orthotopic liver transplantation. MATERIALS AND METHODS: A comprehensive retrospective data review of 388 patients who underwent orthotopic liver transplantation at an urban transplant center from January 2013 to October 2016 was obtained. RESULTS: Six patients were found to have documented intracardiac thrombosis; 4 cases were recognized during the reperfusion stage and 1 during pre-anhepatic stage. All allografts were procured from decreased donors with a median donor age of 44 years (interquartile range, 35.25-49.75) and the cause of death was listed as cerebrovascular accident in 5 donors. Preoperative demographic, clinical, laboratory, and historical risk

factors did not differ in patients with thrombosis. None had a prior history of trans-jugular intrahepatic portosystemic shunt or gastrointestinal bleeding. Three patients had renal injury, but no intraoperative hemodialysis was performed. Transesophageal echocardiographic findings included elevated pulmonary artery pressure (1/6), right ventricular strain (1/6), and pulmonary artery thrombus (1/6). Three patients died intraoperatively. Tissue plasminogen activator alone was given to 1 patient who did not survive, intravenous heparin only to 1 patient with resolution, and a combination of both was used in 2 patients with clot resolution achieved. CONCLUSION: Cardiac thrombosis should be considered in patients having hemodynamic compromise during liver transplantation. Transesophageal echocardiography is a useful diagnostic tool. Intracardiac thrombosis treatment remains challenging; however, using both thrombolytics and heparin could achieve better results.

Surgery
Bergquist JR, **Li AY**, Javadi CS, Chima RS, Frye JS, and Visser BC. Too Big to Fail: Successful Resection of a Large Hepatocellular Carcinoma with Portal Tumor Thrombus. *Dig Dis Sci* 2020; Epub ahead of print. PMID: 33140182. Full Text

Section of Surgical Oncology, Hepatobiliary and Pancreatic Surgery, Department of Surgery, Stanford University Hospital, 300 Pasteur Dr., H3680, Stanford, CA, 94305, USA.
Department of Surgery, General Surgery Residency Program, Henry Ford Hospital, Detroit, MI, USA.
Department of Radiology, Stanford University, Stanford, CA, USA.
Department of Pathology, Stanford University, Stanford, CA, USA.
Section of Surgical Oncology, Hepatobiliary and Pancreatic Surgery, Department of Surgery, Stanford University Hospital, 300 Pasteur Dr., H3680, Stanford, CA, 94305, USA. bvisser@stanford.edu.

Surgery
Brescia AA, Vu JV, He C, Li J, **Harrington SD**, Thompson MP, Norton EC, Regenbogen SE, Syrjamaki JD, Prager RL, and Likosky DS. Determinants of Value in Coronary Artery Bypass Grafting. *Circ Cardiovasc Qual Outcomes* 2020; 13(11):e006374. PMID: 33176461. Full Text

Department of Cardiac Surgery, Michigan Medicine (A.A.B., M.P.T., R.L.P., D.S.L.), School of Public Health, University of Michigan, Ann Arbor.
Center for Healthcare Outcomes and Policy (A.A.B., M.P.T., E.C.N., S.E.R., D.S.L.), School of Public Health, University of Michigan, Ann Arbor.
Department of Surgery (J.V.V., S.E.R., J.D.S.), School of Public Health, University of Michigan, Ann Arbor.
Michigan Society of Thoracic and Cardiovascular Surgeons Quality Collaborative, Ann Arbor (C.H., M.P.T., R.L.P., D.S.L.).
Department of Epidemiology (J.L.), School of Public Health, University of Michigan, Ann Arbor.
Henry Ford Macomb Hospital, Clinton Township, MI (S.D.H.). Michigan Value Collaborative, Ann Arbor (M.P.T., E.C.N., S.E.R., J.D.S.).
Department of Economics (E.C.N.), School of Public Health, University of Michigan, Ann Arbor.
Department of Health Management and Policy (E.C.N.), School of Public Health, University of Michigan, Ann Arbor.

Background Over 180 000 coronary artery bypass grafting (CABG) procedures are performed annually, accounting for $7 to $10 billion in episode expenditures. Assessing tradeoffs between spending and quality contributing to value during 90-day episodes has not been conducted but is essential for success in bundled reimbursement models. We, therefore, identified determinants of variability in hospital 90-day episode value for CABG. Methods Medicare and private payor admissions for isolated CABG from 2014 to 2016 were retrospectively linked to clinical registry data for 33 nonfederal hospitals in Michigan. Hospital composite risk-adjusted complication rates (≥1 National Quality Forum-endorsed, Society of Thoracic Surgeons measure: deep sternal wound infection, renal failure, prolonged ventilation >24 hours, stroke, re-exploration, and operative mortality) and 90-day risk-adjusted, price-standardized episode payments were used to categorize hospitals by value by defining the intersection between complications and spending. Results Among 2573 total patients, those at low- versus high-value hospitals had a higher percentage of prolonged length of stay >14 days (9.3% versus 2.4%, P=0.006), prolonged ventilation

(17.6% versus 4.8%, P<0.001), and operative mortality (4.8% versus 0.6%, P=0.001). Mean total episode payments were $51 509 at low-compared with $45 526 at high-value hospitals (P<0.001), driven by higher readmission ($3675 versus $2177, P=0.005), professional ($7462 versus $6090, P<0.001), postacute care ($7315 versus $5947, P=0.031), and index hospitalization payments ($33 474 versus $30 800, P<0.001). Among patients not experiencing a complication or 30-day readmission (1923/2573, 74.7%), low-value hospitals had higher inpatient evaluation and management payments ($1405 versus $752, P<0.001) and higher utilization of inpatient rehabilitation (7% versus 2%, P<0.001), but lower utilization of home health (66% versus 73%, P=0.016) and emergency department services (13% versus 17%, P=0.034). Conclusions To succeed in emerging bundled reimbursement programs for CABG, hospitals and physicians should identify strategies to minimize complications while optimizing inpatient evaluation and management spending and use of inpatient rehabilitation, home health, and emergency department services.

Surgery
Brown CS, Albright J, Henke PK, Mansour MA, **Weaver M**, and Osborne NH. Modeling the Elective Vascular Surgery Recovery After COVID-19: Implications for Moving Forward. *J Vasc Surg* 2020; Epub ahead of print. PMID: 33248121. Full Text

Section of Vascular Surgery, Department of Surgery, University of Michigan, Ann Arbor, Michigan. Section of Vascular Surgery, Department of Surgery, Spectrum Health, Grand Rapids, Michigan. Section of Vascular Surgery, Department of Surgery, Henry Ford Health System, Detroit, Michigan.

OBJECTIVE: Delays in elective surgery caused by the COVID-19 pandemic have resulted in a substantial backlog of cases. In the current study, we sought to determine the estimated time to recovery for vascular surgery procedures delayed due to COVID-19 in a regional health system METHODS: Utilizing data from a 35-hospital regional vascular surgical collaborative consisting of all hospitals performing vascular surgery in the state of Michigan, a 35-hospital regional health collaborative consisting of all hospitals completing vascular surgery procedures within the state of Michigan, we estimated delayed surgical cases for adults undergoing carotid endarterectomy, carotid stenting, endovascular and open abdominal aortic aneurysm repair, and lower extremity bypass. We utilized Seasonal Autoregressive Integrated Moving Average (ARIMA) models to predict surgical volume in the absence of the COVID-19 pandemic and utilized historical data to predict elective surgical recovery time. RESULTS: Median statewide monthly vascular surgical volume for the study period was 439 procedures, with a maximum statewide monthly case volume of 519 procedures. For the month of April 2020, elective vascular surgery procedural volume decreased by approximately 90%. Significant variability was seen in estimated hospital capacity as well as estimated backlogged cases, with the recovery of elective cases estimated to take approximately 8 months. If hospitals across the collaborative share the burden of backlogged cases, the recovery could be shortened to approximately 3 months. CONCLUSION: In this study of vascular surgical volume in a regional health collaborative, elective surgical procedures decreased by 90% resulting in a backlog of over 700 cases. Recovery time if all hospitals in the collaborative share the burden of backlogged cases would be reduced from 8 months to 3 months, underscoring the necessity of regional and statewide policies to minimize patient harm due to delays in recovery for elective surgery.

Surgery
Ehlers AP, Thumma JR, Finks JF, **Carlin AM**, Ghaferi AA, and Varban OA. Evaluation of Patient Reported Gastroesophageal Reflux Severity at Baseline and at One-Year after Bariatric Surgery. *Ann Surg* 2020; Epub ahead of print. PMID: 33214432. Full Text

Center for Healthcare Outcomes & Policy, Ann Arbor, MI.
Department of Surgery, Henry Ford Health System, Detroit, MI.

OBJECTIVE: To assess patient-reported gastroesophageal reflux disease (GERD) severity before and after sleeve gastrectomy (SG) and Roux-en-Y gastric bypass (RYGB). SUMMARY BACKGROUND DATA: Development of new-onset or worsening GERD symptoms following bariatric surgery varies by procedure, but there is a lack of patient-reported data to help guide decision-making. METHODS: Retrospective cohort study of patients undergoing bariatric surgery in a statewide quality collaborative

between 2013-2017. We used a validated GERD survey with symptom scores ranging from 0 (no symptoms) to 5 (severe daily symptoms) and included patients who completed surveys both at baseline and one-year after surgery (n = 10,451). We compared the rates of improved and worsened GERD symptoms after SG and RYGB. RESULTS: Within our study cohort, 8,680 (83%) underwent SG and 1,771 (17%) underwent RYGB. Mean baseline score for all patients was 0.94. Patients undergoing SG experienced similar improvement in GERD symptoms when compared to RYGB (30.4% vs 30.8%, p = 0.7015). However, SG patients also reported higher rates of worsening symptoms (17.8% vs 7.5%, p < 0.0001) even though they were more likely to undergo concurrent hiatal hernia repair (35.1% vs 20.0%, p < 0.0001). More than half of patients (53.5%) did not report a change in their score. CONCLUSIONS: Although SG patients reported higher rates of worsening GERD symptoms when compared to RYGB, the majority of patients (>80%) in this study experienced improvement or no change in GERD regardless of procedure. Using clinically relevant patient-reported outcomes can help guide decisions about procedure choice in bariatric surgery for patients with GERD.

Surgery

Miller-Matero LR, **Hamann A**, **LaLonde L**, **Martens KM**, Son J, **Clark-Sienkiewicz S**, **Sata M**, **Coleman JP**, **Hecht LM**, **Braciszewski JM**, and **Carlin AM**. Predictors of Alcohol Use after Bariatric Surgery. *J Clin Psychol Med Settings* 2020; Epub ahead of print. PMID: 33205321. Full Text

Behavioral Health, Henry Ford Health System, 1 Ford Place, 3A, Detroit, MI, 48202, USA. Lmatero1@hfhs.org.
Center for Health Policy and Health Services Research, Henry Ford Health System, Detroit, MI, USA. Lmatero1@hfhs.org.
Behavioral Health, Henry Ford Health System, 1 Ford Place, 3A, Detroit, MI, 48202, USA.
Department of Surgery, Henry Ford Health System, Detroit, MI, USA.
Wayne State University School of Medicine, Henry Ford Health System, Detroit, MI, USA.
Center for Health Policy and Health Services Research, Henry Ford Health System, Detroit, MI, USA.

Patients undergoing bariatric surgery are at risk for devloping an alcohol use disorder (AUD). The purpose of this study was to investigate pre-surgical psychosocial risk factors for post-surgical alcohol consumption and hazardous drinking. Participants (N = 567) who underwent bariatric surgery between 2014 and 2017 reported their post-surgical alcohol use. Information was collected from the pre-surgical evaluation including history of alcohol use, psychiatric symptoms, and maladaptive eating behaviors (i.e., binge eating, purging, and emotional eating). Younger age and pre-surgical alcohol use predicted post-surgical alcohol use and hazardous drinking. In addition, higher levels of depressive symptoms and maladaptive eating patterns predicted post-surgical binge drinking. Clinicians conducting pre-surgical psychosocial evaluations should be aware of the multiple risk factors related to post-surgical problematic alcohol use. Future research should evaluate whether preventive interventions for high-risk patients decrease risk for post-surgical alcohol misuse.

Surgery

Perinjelil V, Haake RS, **Ahmed A**, Al-Daoud F, Maraqa T, Mercer L, Wong K, Morris S, Scholten D, and Sachwani-Daswani G. A Single Center Review of the Dangers of Recreational Fires in the Pediatric Population. *J Burn Care Res* 2020; Epub ahead of print. PMID: 33200770. Full Text

Hurley Medical Center, Flint, Michigan.
Michigan State University, East Lansing, Michigan.
Henry Ford Wyandotte Hospital, Wyandotte, Michigan.

The increasing trend of admissions due to recreational fires prompted a 5-year review. The retrospective chart review of pediatric burn injuries from campfires or bonfires treated at a single medical center's burn unit. The study included children within the ages of 0 to 15 admitted or transferred from January 2012 to December 2016 with first, second, and/or third degree burns by bonfires. These patients accrued burns due to active fires as well as postfire ember contact. Two hundred-eighty nine (289) were pediatric admissions out of which 66 (22.8%) were pediatric admissions associated with recreational fires. The mean annual admission for campfire or bonfire burns was 13 ± .98. The mean age was 4 ± 2.47 years.

Gender distribution revealed 21 female and 45 male pediatric patients under the age of 15. From the available data, 8 (12%) of these burns occurred at home in the backyard and 16 (24%) at a public camp or park. Injury mechanisms were more commonly a result of direct contact with hot coals and embers (65%). Falls into open flame accounted for 23% (n = 15) of injuries, and flash flames accounted for 12% of injuries (n = 8). The presence of supervision was unknown in 56%; however, lack of supervision was a factor in 14% of our study population. By gaining a better understanding of the type of injury, mechanism of injury, and the demographic of recreational fire burn victims, policy, and awareness campaigns were instituted in an effort to reduce the incidence of recreational fire burns.

Surgery

Varban OA, Thumma JR, **Carlin AM**, Ghaferi AA, Dimick JB, and Finks JF. Evaluating the Impact of Surgeon Self-Awareness by Comparing Self vs Peer Ratings of Surgical Skill and Outcomes for Bariatric Surgery. *Ann Surg* 2020; Epub ahead of print. PMID: 33201111. Full Text

Department of Surgery, University of Michigan, MI.
Center for Healthcare Outcomes and Policy, University of Michigan, MI.
Department of Surgery, Henry Ford Health System, MI.

OBJECTIVE: To evaluate variation in self vs. peer-assessments of surgical skill using surgical videos and compare surgeon-specific outcomes with bariatric surgery. SUMMARY BACKGROUND DATA: Prior studies have demonstrated that surgeons with lower peer-reviewed ratings of surgical skill had higher complication rates after bariatric surgery. METHODS: This is a retrospective cohort study of 25 surgeons who voluntarily submitted a video of a typical laparoscopic sleeve gastrectomy (SG) between 2015-2016. Videos were self and peer-rated using a validated instrument based on a 5-point Likert scale (5="master surgeon" and 1="surgeon-in-training"). Risk adjusted 30-day complication rates were compared between surgeons who over-rated and under-rated their skill based on data from 24,186 SG cases as well as 12,888 gastric bypass (GBP) cases. RESULTS: Individual overall self-rating of surgical skill varied between 2.5 to 5. Surgeons in the top quartile for self:peer ratings (n=6, ratio 1.58) had lower overall mean peer-scores (2.98 vs 3.79, p = 0.0150) than surgeons in the lowest quartile (n = 6, ratio 0.94). Complication rates between top and bottom quartiles were similar after SG, however leak rates were higher with GBP among surgeons who over-rated their skill with sleeve gastrectomy (0.65 vs 0.27, p = 0.0181). Surgeon experience was similar between comparison groups. CONCLUSIONS AND RELEVANCE: Self-perceptions of surgical skill varied widely. Surgeons who over-rated their skill had higher leak rates for more complex procedures. Video assessments can help identify surgeons with poor self-awareness who may benefit from a surgical coaching program.

Surgery

Witkowski P, Philipson L, Kaufman DB, Ratner L, **Abouljoud MS**, Bellin M, Buse J, Kandeel F, Stock P, Mulligan D, Markmann JF, Kozlowski T, Andreoni K, Alejandro R, Baidal D, Hardy MA, Wickrema A, Mirmira RG, Fung J, Becker Y, Josephson MA, Bachul PJ, Pyda JS, Charlton M, Millis JM, Gaglia J, Stratta RJ, Fridell JA, Niederhaus S, Forbes RC, Jayant K, Robertson RP, Odorico J, Levy M, Harland R, Abrams PL, Olaitan OK, Kandaswamy R, Wellen J, Japour AJ, Desai CS, Naziruddin B, Balamurugan AN, Barth RN, and Ricordi C. The Demise of Islet Allotransplantation in the US: A Call for an Urgent Regulatory Update The "ISLETS FOR US" Collaborative. *Am J Transplant* 2020; Epub ahead of print. PMID: 33251712. Full Text

Transplantation Institute, Department of Surgery, University of Chicago, Chicago, IL, USA.
Kovler Diabetes Center, University of Chicago, Chicago, IL, USA.
Division of Transplantation, Department of Surgery, University of Wisconsin, School of Medicine and Public Health, Madison, WI, USA.
Department of Surgery, Columbia University College of Physicians and Surgeons, New York, NY, USA.
Transplant and Hepatobiliary Surgery, Henry Ford Hospital, Detroit, MI, USA.
Schulze Diabetes Institute, Department of Surgery, University of Minnesota, Minneapolis, MN, USA.
Division of Endocrinology, Department of Medicine, University of North Carolina School of Medicine, Chapel Hill, NC, USA.

Department of Translational Research and Cellular Therapeutics, Diabetes and Metabolism Research Institute, Beckman Research Institute of City of Hope, Duarte, CA, USA.
Division of Transplant Surgery, Department of Surgery, University of California-San Francisco, San Francisco, CA, USA.
Department of Surgery, Transplantation and Immunology, Yale University, CT, USA.
Division of Transplantation, Department of Surgery, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA.
Division of Transplantation, Department of Surgery, The University of Oklahoma College of Medicine, Oklahoma City, OK, USA.
Department of Surgery, University of Florida, College of Medicine, Gainesville, FL, USA.
Diabetes Research Institute and Cell Transplant Center, University of Miami, Miami, FL, USA.
Department of Medicine, Section of Hematology and Oncology, University of Chicago, Chicago, IL, USA.
Department of Medicine, Translational Research Center, University of Chicago, Chicago, IL, USA.
Department of Surgery, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA.
Joslin Diabetes Center, Harvard Medical School, Boston, MA, USA.
Department of Surgery, Section of Transplantation, Wake Forest School of Medicine, Winston-Salem, NC, USA.
Department of Surgery, Indiana University School of Medicine, Indianapolis, IN, USA.
Department of Surgery, University of Maryland Medical Center, Baltimore, MD, USA.
Division of Kidney and Pancreas Transplantation, Department of Surgery, Vanderbilt University Medical Center, Nashville, TN, USA.
Division of Endocrinology and Metabolism, Department of Internal Medicine, University of Washington, Seattle, WA, USA.
Division of Transplantation, Hume-Lee Transplant Center, Virginia Commonwealth University School of Medicine, Richmond, VA, USA.
Department of Surgery, University of Arizona, Tucson, AZ, USA.
MedStar Georgetown Transplant Institute, Washington, DC, USA.
Department of Surgery, Rush University Medical Center, Chicago, IL, USA.
Department of Surgery, University of Minnesota, Minneapolis, MN, USA.
Department of Surgery, Washington University, St Louis, MO, USA.
AdvancedDx Biological Laboratories, USA.
Department of Surgery, Section of Transplantation, University of North Carolina at Chapel Hill, NC, USA.
Transplantation Institute, Baylor University Medical Center, Dallas, TX, USA.
Division of Pediatric General and Thoracic Surgery, Cincinnati Children's Hospital Medical Center, Department of Surgery, University of Cincinnati, Cincinnati, OH, USA.

Islet allotransplantation in the United States (US) is facing an imminent demise. Despite nearly three decades of progress in the field, an archaic regulatory framework has stymied US clinical practice. Current regulations do not reflect the state-of-the-art in clinical or technical practices. In the US, islets are considered biologic drugs and "more than minimally manipulated" human cell and tissue products (HCT/Ps). Across the world, human islets are appropriately defined as "minimally manipulated tissue" which has led to islet transplantation becoming a standard-of-care procedure for patients with type 1 diabetes mellitus and problematic hypoglycemia. As a result of the outdated US regulations, only eleven patients underwent allo-ITx in the US between 2011-2016 and all in the setting of a clinical trial. Herein, we describe the current regulations pertaining to islet transplantation in the United States. We explore the progress which has been made in the field and demonstrate why the regulatory framework must be updated to both, better reflect our current clinical practice and to deal with upcoming challenges. We propose specific updates to current regulations which are required for the renaissance of ethical, safe, effective, and affordable allo-ITx in the United States.

Urology

Bronkema C, **Arora S**, **Keeley J**, **Rakic N**, **Sood A**, **Dalela D**, **Jamil M**, **Peabody JO**, **Rogers CG**, **Menon M**, and **Abdollah F**. Impact of treatment modality on overall survival in localized ductal prostate adenocarcinoma: A national cancer database analysis. *Urol Oncol* 2020; Epub ahead of print. PMID: 33223370. Full Text

VCORE - Vattikuti Urology Institute Center for Outcomes Research, Analytics and Evaluation, Henry Ford Hospital, Detroit, MI; Wayne State University School of Medicine, Detroit, MI.
VCORE - Vattikuti Urology Institute Center for Outcomes Research, Analytics and Evaluation, Henry Ford Hospital, Detroit, MI.
VCORE - Vattikuti Urology Institute Center for Outcomes Research, Analytics and Evaluation, Henry Ford Hospital, Detroit, MI. Electronic address: fabdoll1@hfhs.org.

PURPOSE: Ductal adenocarcinoma is considered a rare histological variant of prostate adenocarcinoma (PCa). Given the rarity of this subtype, optimal treatment strategies for men with nonmetastatic ductal PCa is largely unknown. We aimed to describe the impact of surgery, radiotherapy, systemic therapy, and observation on overall survival (OS) in men with nonmetastatic ductal PCa. MATERIALS AND METHODS: We selected 1,656 cases of nonmetastatic ductal PCa, diagnosed between 2004 and 2015, within the National Cancer Database. Covariates included age, race, Charlson comorbidity score, clinical T stage, clinical lymph node stage, serum prostate specific antigen (PSA), income, hospital type, insurance status, year of diagnosis, and location of residence. Cox regression analysis tested the impact of treatment (surgery, radiotherapy, systemic therapy, and observation) on OS. RESULTS: In men with nonmetastatic ductal PCa, median (interquartile range [IQR]) age and PSA were 67 (60-73) years and 6.2 (4.2-10.7) ng/ml, respectively. Advanced local stage (≥cT3a) was most frequently observed in patients initially treated with systemic therapy (34.8%), followed by those treated with radiotherapy (18.1%), surgery (7.1%) and observation (6.4%, P< 0.001). Serum PSA at presentation was highest in the systemic therapy cohort (median 16.0 ng/ml, IQR: 4.9-37.7), followed by the radiotherapy cohort (median 7.2 ng/ml, IQR: 4.1-12.2), observation cohort (median 7.0 ng/ml, IQR: 4.3-13.3) and surgery cohort (median 5.9 ng/ml, IQR: 4.3-9.2, P< 0.001). Multivariable analysis showed that in comparison to men treated surgically, OS was significantly lower for patients receiving radiotherapy (HR 2.2; 95% CI: 1.5-3.2), under observation (HR 4.6; 95% CI: 2.8-7.6) and receiving systemic therapy (HR 5.2; 95% CI: 3.0-9.1) as an initial course of treatment. CONCLUSIONS: While limited by its retrospective nature, our study shows that starting treatment with surgery is associated with more favorable long-term OS outcomes than radiotherapy, systemic therapy or observation.

Urology
Dalela D, **Sood A**, **Keeley J**, **Rogers C**, **Menon M**, and **Abdollah F**. Generalizability of prostate-specific antigen (PSA) screening trials in a "real world" setting: a nationwide survey analysis. *Urology* 2020; Epub ahead of print. PMID: 33221417. Full Text

VUI Center for Outcomes Research, Analytics and Evaluation, Vattikuti Urology Institute, Henry Ford Hospital, Detroit, MI USA.
VUI Center for Outcomes Research, Analytics and Evaluation, Vattikuti Urology Institute, Henry Ford Hospital, Detroit, MI USA. Electronic address: firas_abdollah@gmail.com.

Urology
Kahali B, Chen Y, Feitosa MF, Bielak LF, O'Connell JR, Musani SK, Hegde Y, Chen Y, Stetson LC, Guo X, Fu YP, Smith AV, Ryan KA, Eiriksdottir G, Cohain AT, Allison M, Bakshi A, Bowden DW, Budoff MJ, Carr JJ, **Carskadon S**, Chen YI, Correa A, Crudup BF, Du X, Harris TB, Yang J, Kardia SLR, Launer LJ, Liu J, Mosley TH, Norris JM, Terry JG, **Palanisamy N**, Schadt EE, O'Donnell CJ, Yerges-Armstrong LM, Rotter JI, Wagenknecht LE, Handelman SK, Gudnason V, Province MA, Peyser PA, Halligan B, Palmer ND, and Speliotes EK. A noncoding variant near PPP1R3B promotes liver glycogen storage and MetS, but protects against myocardial infarction. *J Clin Endocrinol Metab* 2020; Epub ahead of print. PMID: 33231259. Full Text

Department of Internal Medicine, University of Michigan, Ann Arbor, MI, USA.
Centre for Brain Research, Indian Institute of Science, Bangalore, India.
Division of Statistical Genomics, Department of Genetics, Washington University School of Medicine, St. Louis, MO, USA.
School of Public Health, Department of Epidemiology, University of Michigan, Ann Arbor, MI, USA.

Department of Endocrinology, Diabetes, and Nutrition, University of Maryland-Baltimore, Baltimore, MD, USA.
Department of Medicine, University of Mississippi Medical Center, Jackson, MS, USA.
Institute for Translational Genomics and Population Sciences, LABioMed and Department of Pediatrics at Harbor-UCLA, Torrance, CA, USA.
Framingham Heart Study, NHLBI, NIH, Framingham, MA, USA.
Office of Biostatistics Research, Division of Cardiovascular Diseases, NHLBI, NIH, Bethesda, MD, USA.
School of Public Health, Department of Biostatistics, University of Michigan, Ann Arbor, MI, USA.
Icelandic Heart Association, Kopavogur, Iceland.
Department of Genetics and Genomics Sciences, Icahn School of Medicine, New York, NY, USA.
Department of Family Medicine and Public Health, University of California, San Diego, CA, USA.
Queensland Brain Institute, The University of Queensland, Brisbane, Queensland, Australia.
Department of Biochemistry, Wake Forest School of Medicine, Winston-Salem, NC, USA.
Department of Internal Medicine, LA Biomedical Research Institute at Harbor-UCLA, Torrance, CA, USA.
Department of Radiology, Vanderbilt University School of Medicine, Nashville, TN, USA.
Department of Urology, Henry Ford Health System, Detroit, MI, USA.
Laboratory of Epidemiology and Population Sciences, National Institute of Aging, Bethesda, MD, USA.
Institute for Molecular Bioscience, The University of Queensland, Brisbane, Queensland, Australia.
Brigham and Women's Hospital, Havard University, Boston, MA, USA.
Department of Medicine, Division of Geriatrics, University of Mississippi Medical Center, Jackson, MS, USA.
Department of Preventive Medicine and Biometrics, University of Colorado at Denver Health Sciences Center, Aurora, CO, USA.
Cardiology Section, Department of Medicine, Boston Veteran's Administration Healthcare, Boston, MA, USA.
Target Sciences, GlaxoSmithKline, Collegeville, PA, USA.
Division of Public Health Sciences, Wake Forest School of Medicine, Winston-Salem, NC, USA.
Department of Medicine, University of Iceland, Reykjavik, Iceland.
Department of Computational Medicine and Bioinformatics, University of Michigan, Ann Arbor, MI, USA.

CONTEXT: Glycogen storage diseases are rare. Increased glycogen in the liver results in increased attenuation. OBJECTIVE: Investigate the association and function of a noncoding region associated with liver attenuation but not histologic nonalcoholic fatty liver disease. DESIGN: Genetics of Obesity-associated Liver Disease Consortium. SETTING: Population-based Main Outcome: Computed tomography measured liver attenuation. RESULTS: Carriers of rs4841132-A (frequency 2-19%) do not show increased hepatic steatosis; they have increased liver attenuation indicative of increased glycogen deposition. rs4841132 falls in a noncoding RNA LOC157273 ~190kb upstream of PPP1R3B. We demonstrate that rs4841132-A increases PPP1R3B through a cis genetic effect. Using CRISPR/Cas9 we engineered a 105bp deletion including rs4841132-A in human hepatocarcinoma cells which increases PPP1R3B, decreases LOC157273 and increases glycogen perfectly mirroring the human disease. Overexpression of PPP1R3B or knockdown of LOC157273 increased glycogen but did not result in decreased LOC157273 or increased PPP1R3B, respectively, suggesting that the effects may not all occur via affecting RNA levels. Based on EHR data, rs4841132-A associates with all components of the metabolic syndrome (MetS). However, rs4841132-A associated with decreased low-density lipoprotein (LDL) cholesterol and risk for myocardial infarction (MI). A metabolic signature for rs4841132-A includes increased glycine, lactate, triglycerides and decreased acetoacetate and beta-hydroxybutyrate. CONCLUSIONS: These results show that rs4841132-A promotes a hepatic glycogen storage disease by increasing PPP1R3B and decreasing LOC157273. rs4841132-A promotes glycogen accumulation and development of MetS but lowers LDL cholesterol and risk for MI. These results suggest that elevated hepatic glycogen is one cause of MetS that does not invariably promote MI.

Urology

Tandogdu Z, Collins J, Shaw G, Rohn J, Koves B, Sachdeva A, Ghazi A, Haese A, Mottrie A, Kumar A, Sivaraman A, Tewari A, Challacombe B, Rocco B, Giedelman C, Wagner C, **Rogers CG**, Murphy DG, Pushkar D, Ogaya-Pinies G, Porter J, Ramesh Seetharam K, Graefen M, Orvieto MA, Covas Moschovas M, Schatloff O, Wiklund P, Coelho R, Valero R, de Reijke TM, Ahlering T, Rogers T, van der Poel HG, Patel V, Artibani W, Wagenlehner F, Nathan S, Erik Bjerklund Johansens T, Hawkey P, and Kelly J. Management of patients who opt for radical prostatectomy during the COVID-19 pandemic: An International Accelerated Consensus Statement. *BJU Int* 2020; Epub ahead of print. PMID: 33185026.
Full Text

University College London Hospital, Department of Urology, London, UK.
University College London, Medical School, London, UK.
Department of Urology, Budapest Hospital, Hungary.
Freeman Hospital, Department of Urology, NHS Foundation Trust, Newcastle Upon-Tyne, UK.
University of Rochester, Department of Urology, Rochester, USA.
Leitender Arzt für roboterassistierte Urologie, Martini-Klinik am UKE GmbH, Universitätsklinikum Hamburg-Eppendorf, Germany.
OLV Hospital, Department of Urology, Belgium.
Department Urology ,Robotics and Renal Transplant, Superspeciality Block,Safdarjang Hospital and VMMC, New Delhi, India.
Apollo Hospitals, Department of Urology, Chennai, India.
Icahn School of Medicine at Mount Sinai, Department of Urology, New York, USA.
Guy's and St Thomas' Hospitals, Department of Urology, London, UK.
University of Modena and reggio emilia, department of Urology AOU di Mldena, Italy.
Marly Clinic and the San José Hospital, Bogota, Colombia.
St. Antonius - Hospital Gronau, Head of Robotic Urology, Gronau, Germany.
Department of Urology, Vattikuti Urology Institute, Henry Ford Health System, Detroit, Michigan, USA.
Division of Cancer Surgery, Peter MacCallum Cancer Centre, Melbourne, Australia.
MSMSU, Urology, Moscow, Russia.
Hospital Universitario Rey Juan Carlos, Madrid, Spain.
Swedish Medical Center, Seattle, USA.
Adventhealth Global Robotics Institute, Celebration Place, Florida, USA.
Martini-Klinik, University-Hospital Hamburg-Eppendorf, Hamburg, Germany.
Clinica Alemana, Department of Urology, Santiago, Chile.
Sudmedica Health, Department of Urology, Valparaiso, Chile.
University of São Paulo School of Medicine, São Paulo, Brazil.
Scott Department of Urology, Baylor College of Medicine, Houston, Texas, USA.
Amsterdam UMC, University of Amsterdam, Department of Urology, The Netherlands.
University of California, Irvine Orange, California, USA.
Department of Urology, Netherlands Cancer Institute, Amsterdam, The Netherlands.
University of Verona, Department of Urology, Verona, Italy.
Department of Urology, Pediatric Urology and Andrology, Justus-Liebig-University, Giessen, Germany.
Institute of Clinical Medicine, Department of Urology, University of Oslo, Oslo, Norway.
Institute of Microbiology and Infection, University of Birmingham, Birmingham, UK.
Queen Elizabeth Hospital Birmingham, UK.

BACKGROUND: Coronavirus disease-19 (COVID-19) pandemic caused delays in definitive treatment of patients with prostate cancer. Beyond the immediate delay a backlog for future patients is expected. Such delays can lead to disease progression. OBJECTIVE: We aimed to develop guidance on criteria for prioritization for surgery and reconfiguring management pathways for non-metastatic stage of prostate cancer who opt for surgical treatment. A second aim was to identify the infection prevention and control (IPC) measures to achieve low likelihood of COVID-19 hazard if radical prostatectomy was to be carried out during the outbreak and whilst the disease is endemic. DESIGN, SETTING AND PARTICIPANTS: An accelerated consensus process and systematic review. We conducted a systematic review of the evidence on COVID-19 and reviewed international guidance on prostate cancer. These were presented to an international prostate cancer expert panel (n=34) through an online meeting. The consensus process

underwent three rounds of survey in total. Additions to the second- and third-round surveys were formulated based on the answers and comments from the previous rounds. OUTCOME MEASURES: Consensus opinion was defined as ≥80% agreement, which were used to reconfigure the prostate cancer pathways. RESULTS: Evidence on the delayed management of patients with prostate cancer is scarce. There was 100% agreement that prostate cancer pathways should be reconfigured and develop measures to prevent nosocomial COVID-19 for patients treated surgically. Consensus was reached on prioritization criteria of patients for surgery and management pathways for those who have delayed treatment. IPC measures to achieve a low likelihood of nosocomial COVID-19 were coined as "COVID-19 cold sites". CONCLUSION: Re-configuring management pathways for prostate cancer patients is recommended if significant delay (>3-6 months) in surgical management is unavoidable. The mapped pathways provide guidance for such patients. The IPC processes proposed provide a framework for providing radical prostatectomy within an environment with low COVID-19 risk during the outbreak or when the disease remains endemic. The broader concepts could be adapted to other indications beyond prostate cancer surgery.

Conference Abstracts

Anesthesiology

Naffouj S, **Siddiqui MB**, **Shaikh A**, Shabbir N, Shabbir A, and **Salgia RJ**. THE IMPLICATIONS OF CHRONIC OPIOID USE ON POST-TRANSPLANT CLINICAL OUTCOMES: A SYSTEMATIC REVIEW AND META-ANALYSIS. *Hepatology* 2020; 72:852A-852A.

[Naffouj, Sandra] Henry Ford Hlth Syst, Internal Med, Detroit, MI USA. [Siddiqui, Mohammad B.; Salgia, Reena J.] Henry Ford Hlth Syst, Gastroenterol & Hepatol, Detroit, MI USA. [Shaikh, Amna] Henry Ford Hlth Syst, Anesthesiol, Detroit, MI USA. [Shabbir, Nawal; Shabbir, Aimun] Karachi Med & Dent Coll, Karachi, Pakistan.

Background: Based on current literature, pre-transplant chronic opioid use (COU) for analgesia is highly prevalent among patients awaiting solid-organ transplant. However, there are very few large-scale studies on the effect of COU on post-transplant outcomes. We conducted a systematic review and meta-analysis to evaluate the impact of pre-transplant COU on solid-organ transplantation clinical outcomes. Methods: A comprehensive literature review was conducted by searching the PubMed, Ovid Medline, Embase, Web of Science, and Cochrane databases from inception to April 2020 to identify all studies that evaluated the impact of pre-transplant COU on post-transplant clinical outcomes. COU was defined as >3 months of consecutive opioid use entering transplant listing. The search included studies regarding heart, lung, kidney, and liver transplantation. Our primary outcome was all-cause mortality, and secondary outcomes were graft failure and the one-year readmission rate. A random-effect model was used to estimate the pooled hazard ratios (HR) or odds ratios (OR) of our outcomes. Results: Nine retrospective studies involving 166,765 patients were included in the primary meta- analysis. The all-cause post-transplant mortality rate was significantly higher in patients who were on chronic opioids preceding transplant compared to those who were not (HR 1.42; 95% CI 1.34-1.50). The included studies demonstrated low heterogeneity (Figure 1, part A). Additionally, COU patients had an increased risk of graft failure compared to non-COU patients (HR 1.26; 95% CI (1.13-1.40) (Figure 1, part B). With regards to the one-year readmission rates, and noting that only three studies included data on readmission rates, there was no statistically significant difference in the readmission rate between the two groups (HR 1.78; 95% CI (0.87-3.63). The studies had high heterogeneity (Figure 1, part C). Conclusion: This study demonstrates that pre-transplant COU in solid-organ transplant patients is associated with an increased risk of all-cause mortality and graft failure. Pre- transplant COU may be a surrogate for comorbidities causing chronic pain or psychosocial traits that can contribute to non- compliance post-transplant. These potential risk factors may explain the increased risk of poor outcomes post-transplant. Therefore, a careful evaluation of opioid use patterns and consideration of alternative analgesic strategies is warranted in this population to lessen the reliance on opioid use and associated adverse outcomes.

Center for Health Policy and Health Services Research

Naffouj S, **Selim R**, **Shamaa O**, **Ahmed A**, **Zhou YR**, **Rupp LB**, **Jafri SM**, **Gordon SC**, and **Gonzalez HC**. LIVER TRANSPLANT EVALUATION IN THE PETH ERA. *Hepatology* 2020; 72:176A-176A.

[Naffouj, Sandra; Shamaa, Omar] Henry Ford Hlth Syst, Internal Med, Detroit, MI USA. [Selim, Ranya; Jafri, Syed-Mohammed; Gordon, Stuart C.; Gonzalez, Humberto C.] Henry Ford Hlth Syst, Gastroenterol & Hepatol, Detroit, MI USA. [Ahmed, Abdelwahab; Jafri, Syed-Mohammed; Gordon, Stuart C.; Gonzalez, Humberto C.] Wayne State Univ, Sch Med, Detroit, MI 48202 USA. [Zhou, Yueren] Henry Ford Hlth Syst, Dept Publ Hlth Sci, Detroit, MI USA. [Rupp, Loralee B.] Henry Ford Hlth Syst, Ctr Hlth Policy & Hlth Serv Res, Detroit, MI USA.

Background: Phosphatidylethanol (PEth) is a phospholipid formed in the presence of ethanol with a high sensitivity, specificity, and long half-life compared to other alcohol detection tests. PEth has become a key biomarker in liver transplant (LT) evaluation since 2018. We aimed to determine the impact of PEth on the transplant evaluation process and LT waitlist in alcoholic liver disease. Methods: Candidates referred for LT evaluation 1/1/2017 to 11/12/2019 were captured using Organ Transplant Tracking Record at Henry Ford Hospital, Detroit, MI. 2018 evaluations were excluded (testing transition period). Only

patients with alcoholic liver disease were included. Patients were divided into pre-PEth (2017) and PEth (2019) eras. Demographics, use of PEth and non-PEth (serum ethanol or urine ethyl glucoronide) testing, Child Pugh/MELD scores, insurance and evaluation termination/delisting reasons were captured. PEth+ was defined as a level >10 ng/dL. Rates of terminations/de-listings were compared between groups using Chi-square. Logistic regression was used to identify factors associated with terminations/de-listings (as a composite outcome). Results: There were 375 evaluations for alcoholic liver disease; 157 in pre-PEth era, 210 in PEth era, and 8 excluded due to loss of follow-up. Patient characteristics are shown in Table 1. There were 72(46%) vs 85(41%) terminations (p=0.321) and 11(7%) vs 2(1%) de-listings in pre-PEth vs PEth eras (p=0.002), respectively. Of the terminations/de-listings, there were 5(7%) due to non-PEth+ in 2017 vs 16(19%) due to PEth+ in 2019 (p=0.069). Odds ratios of terminations/delistings due to alcohol use were 0.36 for black vs white race, 0.43 for employed vs unemployed, 0.52 for Medicare vs Medicaid and 1.37 for commercial insurance vs Medicaid (p=0.069, 0.126, and 0.063 for race, employment status, and insurance, respectively). Conclusion: Our results demonstrate that black race, employment, and commercial or Medicare insurance was associated with lower risk of termination/delisting. There were fewer de-listings in the PEth era. Despite the increased detection of surreptitious alcohol use due to PEth, the rates of termination/delisting for alcohol use were similar. We speculate that our results reflect the use of PEth test as a screening tool prior to transplant referral. Additionally, a recent shift toward a more liberal consideration of a) shorter period of sobriety and/or b) select alcoholic hepatitis patients may explain these findings.

Center for Health Policy and Health Services Research

Lu M, **Rupp LB**, Boscarino JA, Schmidt MA, Daida Y, **Zhou YR**, **Trudeau S**, **Li J**, and **Gordon SC**. IMPACT OF HISTORY OF CHRONIC VIRAL HEPATITIS AND LIVER FIBROSIS ON RISK OF HOSPITALIZATION AND DEATH AMONG PATIENTS WITH SARS-COV-2 INFECTION. *Hepatology* 2020; 72:280A-281A.

[Lu, Mei; Zhou, Yueren; Trudeau, Sheri; Li, Jia] Henry Ford Hlth Syst, Dept Publ Hlth Sci, Detroit, MI USA. [Rupp, Loralee B.] Henry Ford Hlth Syst, Ctr Hlth Policy & Hlth Serv Res, Detroit, MI USA. [Boscarino, Joseph A.] Geisinger Med Clin, Dept Populat Hlth Sci, Danville, PA USA. [Schmidt, Mark A.] Kaiser Permanente Northwest, Ctr Hlth Res, Washington, DC USA. [Daida, Yihe] Kaiser Permanente Hawaii, Ctr Integrated Hlth Care Res, Honolulu, HI USA. [Gordon, Stuart C.] Henry Ford Hlth Syst, Div Gastroenterol & Hepatol, Detroit, MI USA. [Gordon, Stuart C.] Wayne State Univ, Med, Sch Med, Detroit, MI 48202 USA.

Background: We investigated factors associated with Covid-19 related hospitalization and death among patients with and without a history of chronic viral hepatitis B or C (CHB/CHC) in a single large, integrated health system located in metropolitan Detroit, Michigan, an area that experienced a significant outbreak of SARS-Cov-2 in Spring 2020. Methods: Baseline data were collected before date of first positive SARS-CoV-2 test or Covid-related hospitalization, whichever was earlier. Risk of hospitalization was analyzed with logistic regression; risk of death with Cox regression. Variables with p-values <0.05 were retained in the final multivariable models. Results: Of 6661 patients that tested SARS-CoV-2 positive from March 12–April 26, 2020, 94 (1.4%) had a history of CHB or CHC. A total of 2604 were hospitalized due to Covid-19, 55 (58.5%) with CHB or CHC and 2549 (38.8%) without CHB/CHC. Among hospitalized patients, 10 (18.2%) CHB/CHC patients and 426 (16.7%) non-hepatitis patients died. In multivariable analyses, viral hepatitis was not a risk factor for hospitalization, but approached significance for death (adjusted Hazard Ratio [aHR] 1.82, 95% Confidence Interval [CI] 0.96–3.46). In addition to recognized risk factors for Covid-19 severity such as increasing age, obesity, type 2 diabetes, and multiple co-morbidities, we found that increasing Fibrosis-4 (FIB4) score (a biomarker for liver fibrosis and cirrhosis) was associated with risk of hospitalization (adjusted Odds Ratio [aOR] 95%CI 1.32, 1.16–1.51). African American and male patients were also at higher risk of hospitalization. Notably, a number of risk factors for hospitalization were not associated with or were associated with reduced risk of death among hospitalized patients; African American patients and those with BMI ≥30 had lower mortality than White patients and those with BMI <25 (aHR 0.73, 95%CI 0.60–0.89; and aHR 0.69, 95%CI 0.54–0.88) respectively. Conclusion: Increasing baseline FIB4 index is associated with higher risk of hospitalization among patients with Covid-19. History of CHB or CHC trended toward increased risk of Covid-related mortality; future studies in larger samples of patients with chronic viral hepatitis are warranted.

Center for Health Policy and Health Services Research

Gordon SC, **Rupp LB**, Boscarino JA, Daida Y, Schmidt MA, **Zhou YR**, **Trudeau S**, **Li J**, and **Lu M**. RISK FACTORS FOR SARS-COV-2 INFECTION AMONG PATIENTS WITH CHRONIC VIRAL HEPATITIS. *Hepatology* 2020; 72:299A-300A.

[Gordon, Stuart C.] Henry Ford Hlth Syst, Div Gastroenterol & Hepatol, Detroit, MI USA. [Gordon, Stuart C.] Wayne State Univ, Sch Med, Med, Detroit, MI 48202 USA. [Rupp, Loralee B.] Henry Ford Hlth Syst, Ctr Hlth Policy & Hlth Serv Res, Detroit, MI USA. [Boscarino, Joseph A.] Geisinger Med Clin, Dept Populat Hlth Sci, Detroit, MI USA. [Daida, Yihe] Kaiser Permanente Hawaii, Ctr Integrated Hlth Care Res, Honolulu, HI USA. [Schmidt, Mark A.] Kaiser Permanente Northwest, Ctr Hlth Res, Washington, DC USA. [Zhou, Yueren; Trudeau, Sheri; Li, Jia; Lu, Mei] Henry Ford Hlth Syst, Dept Publ Hlth Sci, Detroit, MI USA.

Background: We investigated factors associated with risk of SARS-CoV-2 infection among an established cohort of chronic hepatitis B and C (CHB/ CHC) patients at a large, vertically integrated health system located in southeastern Michigan (which includes Detroit), a racially-diverse area that experienced a significant outbreak of COVID-19 during March–May 2020. Methods: Patient characteristics and clinical conditions were collected for the period prior to date of first positive SARS-CoV-2 test, or March 11, 2020 for those who were not SARS-CoV-2 infected. Variables included: age; gender; race; insurance type; household income; BMI; CHC vs. CHB; AST; ALT; liver fibrosis status (as measured by APRI/ FIB4); diagnosis of liver cirrhosis; Charlson-Deyo comorbidity index; select individual comorbidities; and history of antiviral therapy. Patients coinfected with both CHB and CHC were excluded. Logistic regression, univariate followed by multivariable modeling, was performed. Variables with p-values <0.05 were retained in the final model. Results: A total of 13,556 patients with a history of chronic viral hepatitis were included; 94 had a positive SARS-CoV-2 result. In univariate comparisons, there was a significant difference between groups (p<0.05) with regard to type of hepatitis infection (C vs. B), age, race, BMI, insurance type, household income, comorbidity index, AST, ALT, APRI, presence of cirrhosis, type 2 diabetes, chronic heart disease, renal disease, peripheral vascular disease, history of receipt of antiviral therapy, and achievement of sustained viral response (CHC). In the final multivariable model, increased risk of SARS-CoV-2 infection was associated with CHC vs CHB (adjusted Odds Ratio [aOR])=4.00, 95% confidence interval [CI] 1.89–8.47), presence of cirrhosis (aOR=1.66, 95%CI 1.08–2.55), normal AST at baseline (aOR=2.50, 95%CI 1.46–4.27), higher comorbidity index (aOR=1.40, 95%CI 1.19–1.67), Black/ African American vs white race (aOR=18.0, CI 6.59–45.5), and BMI (BMI 25–30 vs <25: aOR=3.82, CI 1.95–7.49; BMI >30 vs <25: aOR=2.85, CI 1.46–5.56). Conclusion: In a cohort of chronic viral hepatitis patients drawn from a geographic area that experienced a significant COVID-19 outbreak, Black/ African American race, BMI>25, cirrhosis, CHC (active or post-SVR) vs. CHB, and higher comorbidity index were associated with higher risk of SARS-CoV-2 infection.

Center for Health Policy and Health Services Research

Gordon SC, **Li J**, Moorman AC, Spradling PR, Teshale EH, Boscarino JA, Daida Y, Schmidt MA, **Zhou YR**, **Rupp LB**, **Trudeau S**, and **Lu M**. PATIENT CHARACTERISTICS AND EFFICACY OF PANGENOTYPIC DIRECT-ACTING ANTIVIRAL REGIMENS AMONG A COHORT OF CHRONIC HEPATITIS C PATIENTS RECEIVING ROUTINE CLINICAL CARE IN THE US. *Hepatology* 2020; 72:540A-541A.

[Gordon, Stuart C.] Henry Ford Hlth Syst, Gastroenterol & Hepatol, Detroit, MI USA. [Gordon, Stuart C.] Wayne State Univ, Sch Med, Med, Detroit, MI 48202 USA. [Li, Jia; Zhou, Yueren; Trudeau, Sheri; Lu, Mei] Henry Ford Hlth Syst, Dept Publ Hlth Sci, Detroit, MI USA. [Moorman, Anne C.; Spradling, Philip R.; Teshale, Eyasu H.] Ctr Dis Control & Prevent, Div Viral Hepatitis, Natl Ctr HIV Hepatitis STD & TB Prevent, Atlanta, GA USA. [Boscarino, Joseph A.] Geisinger Med Clin, Dept Populat Hlth Sci, Danville, PA USA. [Daida, Yihe] Kaiser Permanente Hawaii, Ctr Integrated Hlth Care Res, Honolulu, HI USA. [Schmidt, Mark A.] Kaiser Permanente Northwest, Ctr Integrated Hlth Care Res, Washington, DC USA. [Rupp, Loralee B.] Henry Ford Hlth Syst, Ctr Hlth Policy, Detroit, MI USA. [Rupp, Loralee B.] Henry Ford Hlth Syst, Hlth Serv Res, Detroit, MI USA.

Background: Using recent data from the Chronic Hepatitis Cohort study (CHeCS), we report patient characteristics and “real world” efficacy of three pangenotypic direct-acting antiviral (DAA) regimens used to treat chronic hepatitis C (CHC) patients with a range of HCV genotypes (GT 1-4 and 6) under routine care. Methods: CHeCS CHC patients were followed through mid-2019. Baseline patient characteristics and rates of sustained virological response 12 weeks after end of treatment (SVR12) were compared among the three pangenotypic regimens (SOF/VEL, SOF/VEL/VOX, and GLE/PIB). Results: A total of 1842 patients were included, of which 1019 were treated with SOF/VEL, 753 with GLE/ PIB, and 70 with SOF/VEL/VOX. There were statistically significant differences in patient characteristics among the three groups (p-values <0.05): (1) 46% and 54% of patients treated with SOF/VEL and GLE/PIB were aged 60 years and older, respectively, versus only 25% of those treated with SOF/VEL/VOX; (2) 7% of patients treated with SOF/VEL had decompensated cirrhosis (DCC) while almost none treated with the other regimens had DCC (≤1%); (3) 93% of the SOF/ VEL/VOX-treated group were DAA experienced, compared with only 2-4% in the other treated groups; (4) GT distribution varied among the three regimens (Table). Observed rates of SVR12 were 97%, 98% and 97% with SOF/VEL, GLE/PIB, and SOF/VEL/VOX, respectively, with no significant difference observed (p-values in the range of 0.50 to 0.62 from pairwise comparisons). Among the 48 patients that did not achieve SVR12: (1) 19% were DAA experienced (vs. 6% of those that achieved SVR12); (2) 10% had DCC (vs. 4% of those that achieved SVR12); (3) 21% experienced a toxicity (vs. 11% of those that achieved SVR12); (4) 31% had diabetes and 4% were on proton pump inhibitor therapy at time of DAA initiation (vs. 21% and 1%, respectively, of those that achieved SVR12). Conclusion: Observed rates of SVR12 were very high for all three pangenotypic regimens, with no significant difference between them. A sizeable majority of CHC patients treated with SOF/VEL/VOX and GLE/PIB had GT 1, while the largest proportion of patients treated with SOF/VEL had GT 2. Patients with DCC were mostly treated with SOF/VEL, as would be expected based on treatment guidelines. Patients who did not achieve SVR12 had higher rates of prior DAA experience, DCC, diabetes, and on-treatment toxicities.

Diagnostic Radiology

Caines A, **Mishra K**, **Stanley S**, **Sturza S**, **Abouljoud MS**, and **Salgia RJ**. THE IMPACT OF HCC LOCOREGIONAL THERAPY ON PERI-OPERATIVE AND POST-TRANSPLANT COMPLICATIONS. *Hepatology* 2020; 72:850A-851A.

[Caines, Allyce] Henry Ford Hlth Syst, Detroit, MI USA. [Caines, Allyce] Henry Ford Hlth Syst, Gastroenterol & Hepatol, Detroit, MI USA. [Mishra, Kajali; Stanley, Sara] Henry Ford Hlth Syst, Internal Med, Detroit, MI USA. [Sturza, Scott] Henry Ford Hlth Syst, Intervent & Diagnost Radiol, Detroit, MI USA. [Abouljoud, Marwan S.] Henry Ford Hosp, Transplant & Hepatobiliary Surg, Detroit, MI 48202 USA. [Salgia, Reena J.] Henry Ford Hlth Syst, Hepatol, Detroit, MI USA.

Background: Transplant candidacy in the setting of HCC is largely dependent on a patient falling within Milan criteria. For those who fall outside of Milan criteria or in regions where liver transplant (LT) waiting times are prolonged, locoregional therapies (LRT) are used to decrease tumor burden as a bridge to LT. There is limited amount of data available regarding the effects of LRT on peri-operative LT complications and outcomes. The aim of this study was to examine the effects of LRT for treatment of HCC on peri-operative LT outcomes. Methods: We conducted a retrospective review of patients who underwent LT from 2012 - 2018. Patients with cirrhosis and HCC who were transplanted within the study period and received LRT (drug eluting bead chemoembolization, thermal ablation, SBRT or yttrium-90 glass sphere radioembolization) for HCC prior to LT were compared to a control group of patients who did not receive LRT. Demographic variables and peri-operative data were collected for both groups. Univariate two-group comparisons were performed using 2-sample t-tests and wilcoxon rank sum tests. Results: 160 LRT patients were compared to 200 controls. Patients who received LRT prior to LT were older than the control group (60.95 vs. 56.47; p< 0.001). HCV was more common in the LRT group than controls (69% vs. 26%; p <.001). 11% of the LRT group and 21% of controls had cirrhosis due to alcohol (p<.001). Mean native MELD at time of LT was 23.57 and 25.56 (p = 0.005) for the LRT patients and control groups respectively. The control group had significantly greater intra- operative transfusion requirements and longer hospital stays than the LRT group. There were no significant differences in the occurrence of bile leak, anastomotic biliary stricture or hepatic artery stenosis, post-LT nor total operative time, need for take back to OR or overall post LT mortality between the LRT and control groups. On subgroup analysis we

did not find an increase in complications based on type of LRT or number of LRT treatments received. However, the long-term post LT mortality rate was higher among those who received TARE compared to those who did not receive TARE (33% vs. 12%; p=0.015). Conclusion: We found that the occurrence of LRT for HCC prior to LT did not lead to increased intra-operative transfusion requirements, longer post-LT hospital stay, higher post-LT complications, longer operative times, increased rates of return to the OR or increased overall mortality compared to patients who did not undergo LRT prior to LT.

Diagnostic Radiology

Feldman AM, **Dai Z**, **Zong W**, **Pantelic M**, **Elshaikh MA**, and **Wen N**. Utilizing Semi-Supervised Learning and Image Matting in Combination With Mask R-CNN for Accurate Dominant Intraprostatic Lesion Identification and Segmentation on Multiparametric-MRI. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):e257.

Purpose/Objective(s): Identification of the dominant intraprostatic lesion (DIL) using multiparametric-MRI (mp-MRI) can aid clinicians in the diagnosis, risk stratification, staging and therapeutic options in men with prostate cancer. Deep-learning based segmentation models such as Mask R-CNN are an emerging modality capable of identification and auto-segmentation of these lesions. However, model generation is limited by relatively sparse annotated data and anatomic challenges such as the ambiguous transition zone between the DIL and normal prostate tissue. Here we used a Mask R-CNN backbone in combination with semi-supervised training and image matting in an effort to overcome these limitations and achieve accurate segmentation of the DIL. Materials/Methods: A total of 244 patients, split into 2 cohorts, with biopsy proven prostate adenocarcinoma and mp-MRI imaging, were reviewed. Cohort 1 included 202 patients from the SPIE-AAPM-NCI Prostate MR Gleason Grade Group Challenge (PROSTATEx-2 Challenge). Cohort 2 included 42 patients from our institution. All patients in cohort 2 and 96 patients in cohort 1 had the DIL annotated by two experienced clinicians from our institution on T2-weighted imaging (T2WI) to establish the ground truth. Apparent diffusion coefficient mapping was rigidly registered to T2WI. A base Mask R-CNN model was trained in a supervised fashion using 84 annotated patients gathered from both cohorts. The base model with the most confident label was then used to predict 106 cohort 1 patients without annotations. The 84 annotated patients and 106 self-annotated patients were then used as the training set to train a semi-supervised model. Finally, image matting was applied as a post-processing approach to refine the boundaries of detected lesions. Ten annotated cohort 1 patients were used as the validation set and 23 and 21 cohort 1 and cohort 2 patients, respectively, were used as the testing set. Dice similarity coefficient (DSC) and the 95th percentile Hausdorff distance (95 HD) were used as evaluation metrics. We defined agreement as the degree to which a model's predictions concurred with the ground truth annotations. Results: The DSC, 95HD (mm) and agreement for the validation on the base model were 0.659 ± 0.105, 3.75 ± 1.40, and 90.0%, respectively. For the testing set on the base model, these results were 0.564 ± 0.153, 4.52 ± 2.16 and 78.6%, respectively. When applying the semi-supervised model, the DSC, 95HD (mm) and agreement were 0.635 ± 0.142, 4.31 ± 1.34 and 100.0% for the validation set and 0.585 ± 0.146, 4.83 ± 2.53 and 76.8% on the testing set. Using image mapping, these values were increased to 0.725± 0.116, 3.70 ± 1.09, 100%; and 0.672 ± 0.123, 4.18 ± 1.97, 76.8% on validation and testing sets, respectively. Conclusion: Semi-supervised learning offered limited improvements when applied to the Mask R-CNN backbone model. However, image matting proved to be a powerful tool in improving the segmentation of the DIL.

Gastroenterology

Ashraf T, **Mendiratta V**, **Gill S**, **Ahmed A**, and **Jafri SM**. LONG TERM USE OF URSODIOL IN POST-LIVER TRANSPLANT PATIENTS INCREASES BILIARY COMPLICATIONS. *Hepatology* 2020; 72:821A-822A.

[Ashraf, Taha; Gill, Sonika] Henry Ford Hosp, Internal Med, Detroit, MI 48202 USA. [Mendiratta, Vivek] Henry Ford Hosp, Gastroenterol, Detroit, MI USA. [Ahmed, Abdelwahab] Wayne State Univ, Detroit, MI 48202 USA. [Jafri, Syed-Mohammed] Henry Ford Hosp, Gastroenterol & Hepatol, Detroit, MI 48202 USA.

Background: Studies suggest ursodiol has beneficial effects in reducing liver enzymes during the first 4 weeks after liver transplantation (LT) as well as incidence of biliary casts and sludge in the first year. Hepatologists often continue ursodiol indefinitely despite evidence of improvement in long-term

outcomes. This retrospective study evaluates ursodiol and its effect on LT outcomes over a 3-year period. Methods: A retrospective study of LT candidates transplanted between 5/2014- 10/2016 at our institution was performed. Patients with primary biliary cirrhosis, primary sclerosing cholangitis and autoimmune hepatitis were excluded and a total of 284 patients were recorded. Relevant data collected included: patient demographics, reason for transplantation, cold ischemic time, ursodiol use and dosage, presence and severity of rejection, number of hospitalizations, occurrences of biliary complications and mortality. Biliary complications were defined as strictures or leaks. Statistics were calculated using analysis of variance (ANOVA), chi-square, Fisher's exact test and Wilcoxon Rank Sum Test. Results: 284 liver transplants were performed in 180 males and 104 females with a mean age of 57.5. Ursodiol use was 62% at 6 months, 55% at 12 months, 45.4% at 2 years and 26.8% at 3 years. Univariate analysis showed that in spite of ursodiol use there remained a significant increase in biliary complications when compared to no use at 6 months (28.4% vs 10.3% p = <0.001) and between 6-12 months (10.3% vs 1.9% p= 0.010). This was again seen at 1-2 years (9.2% vs 3.3% p=0.053) and at 2-3 years (10.4% vs 2.8% p=0.055). There was no significant difference in mortality associated with use at 6 months (10.2% vs 8.3% p = 0.597) or 12 months (8.4% vs 8.3% p=0.982). There was consistently no significant difference in the number of hospitalizations, moderate or severe rejections at any time point (Table 1). This was true when analyzing all rejections at 6 months, 12 months, 2 years and 3 years as well (p=0.248, p=0.333, p=0.275 and p=0.100). Conclusion: Our data shows no long-term benefit of ursodiol use on mortality, re-admission rate, or number of rejections at 3 years post-transplant. Ursodiol does not reduce incidence of biliary complications in patients where medication was used for this purpose and instead increases number of biliary complications at 6 and 12 months. This suggests that ursodiol does not have long term protective effects and should be weaned off in the vast majority of patients.

Gastroenterology

Ashraf T, **Mendiratta V**, **Musleh M**, **Parraga T**, **Alangaden G**, **Brown KA**, and **Jafri SM**. PRIMARY CARE VISITS ARE THE KEY FACTOR IN ENSURING HIGHER VACCINATION RATES IN POST-LIVER TRANSPLANT PATIENTS. A SINGLE CENTER STUDY. *Hepatology* 2020; 72:836A-836A.

[Ashraf, Taha; Musleh, Maher] Henry Ford Hosp, Internal Med, Detroit, MI 48202 USA. [Mendiratta, Vivek] Henry Ford Hosp, Gastroenterol, Detroit, MI 48202 USA. [Parraga, Tommy; Alangaden, George] Henry Ford Hosp, Infect Dis, Detroit, MI 48202 USA. [Brown, Kimberly Ann; Jafri, Syed-Mohammed] Henry Ford Hosp, Gastroenterol & Hepatol, Detroit, MI 48202 USA.

Background: Liver transplant recipients are at an increased risk for life threatening vaccine preventable disease. If vaccines are not given pre-transplant, major societal guidelines recommend they are given in the post-transplant period. This retrospective study evaluates vaccination rates in our institution and potential areas for improvement. Methods: A retrospective study of patients transplanted between 1/2015-1/2018 at our institution was performed. Relevant data collected included patient demographics, travel distance to transplant center, primary care provider (PCP) location and PCP and transplant clinic visits. Vaccination status and eligibility for influenza (IV), pneumococcus (PV), Hepatitis-A (HAV) and B (HBV), Tdap and Td vaccines (TdV) were obtained through our electronic medical records and the Michigan Care Improvement Registry. Statistics were calculated using analysis of variance (ANOVA), chi-square, Fisher's exact test and Wilcoxon Rank Sum Test. Results: 406 patients met our inclusion criteria with 83.0% (336) Caucasians, 10.8% (44) African-Americans, 3.7% (15) Hispanics with overall mean age of 59. PCP visitation post-transplant was significantly associated with vaccination of IV (62.9% vs 47.2% p=0.007), HAV (66.7% vs 45.5% p= 0.003), HBV (60.0% vs 50.1% p=0.391), PV (64.6% vs 39.6% p<0.001) and Tdap (75.0% vs 36.4% p<0.001). However with the exception of PV (92.7% vs 88.5% p =0.314) the same was not seen with transplant clinic visits. Patients who were vaccinated were more likely to have their PCP at their transplant center for PV (46.8% vs 27.8% p=0.005), TdAp (67.5% vs 24.7% p<0.001), IV (35.8% vs 33.6% p =0.689) , HAV (43.1% vs 31.7% p=0.093) and HBV (36.8% vs 33.7% p=0.780). Those who received IV post-transplant were significantly younger than those who did not (56.3 ± 9.7 vs 59.9 ± 9.8 p< 0.001). PV uptake trended towards an older age (60.1 ± 8.4 vs 56.9 ± 10.6 p=0.023), there was no association with age for the remaining vaccines. Notably, post-transplant hospital admissions was not significantly associated with uptake and at times trended towards a negative association. Conclusion: Our data highlights multiple areas for improvement in vaccination in the post-transplant period. Physicians should encourage patients to see their PCP and ideally at their transplant

institution. Furthermore, transplant clinics should more attentively prescribe and administer vaccines during visits. The age disparity seen in PV, suggest guidelines for non- immunocompromized patients are erroneously being followed and could be corrected by appropriate education. Finally, our data demonstrates that hospital admissions post-transplant are a missed opportunity to vaccinate eligible patients.

Gastroenterology
Ashraf T, **Siddiqui MB**, **Khorfan K**, and **Moonka D**. LONG-TERM SAFETY OF SIROLIMUS IN LIVER TRANSPLANT RECIPIENTS. *Hepatology* 2020; 72:823A-824A.

[Ashraf, Taha; Khorfan, Kamal] Henry Ford Hosp, Internal Med, Detroit, MI 48202 USA. [Siddiqui, Mohammad B.; Moonka, Dilip] Henry Ford Hosp, Gastroenterol, Detroit, MI 48202 USA.

Background: Sirolimus (SRL) has been used as an alternative to calcineurin inhibitors (CI) to help spare renal function in liver transplant (LT) recipients. SRL received a black-box warning in LT because of concerns about hepatic artery thrombosis (HAT). Prior to this, our center initiated a large number of LT patients on SRL. This study assesses the long-term safety of SRL in LT recipients. Methods: This is a retrospective, single-center study of all LT recipients who initiated SRL from 2001-2006. A group that remained on SRL was compared to a group that discontinued SRL (CNI group) for adverse events. Groups were compared for LT outcomes. Kaplan-Meier analyses with Cox regression models were done to determine risk factors (RF), including SRL use, for death or end-stage renal disease (ESRD). Results: 159 patients were included. 109 (68.5%) remained on SRL and 50 (31.4%) discontinued (CNI). There were no differences between groups in age at transplant, gender, race, etiology of liver disease or time after LT to SRL initiation. The mean and median follow up time for the SRL group was 703.87 and 739.71 weeks respectively and was 703.58 and 757.15 weeks for the CNI group. In comparing SRL to CNI groups, there were no differences in HAT (2.8 vs. 2.0%), CAD (6.4 vs. 10%) or CVA (5.7% vs. 11.9%). Fewer patients on SRL died (47.7% vs. 58.0%) or developed ESRD (19.3 vs. 32.0%) though neither difference was significant (P=0.228: P=0.078). No significant differences were noted in GFR between the two groups up to 10 years after LT. In the evaluation of risk factors to time to ESRD, CNI (SRL discontinuation) had a small trend towards earlier onset ESRD on univariate analysis (HR:1.56, CI:0.78, 3.23, p=0.207 but even less so on multivariate analysis (HR:1.366, CI:0.675-2.763) (Figure 1). In the evaluation of RF for time to death, CNI was associated with greater mortality from time of transplant (HR:1.46, CI: 1.06-2.03, p=0.023) and from time of SRL initiation (HR:1.64, CI:1.06- 2.55, p=0.026) (Figure 1). However, when including age, diabetes and GFR at LT in multivariate analyses, the effect of CNI was no longer significant. Conclusion: The results describe one of the longest follow-up periods for SRL use in LT patients, with mean follow up extending over a decade. The results demonstrate that patients receiving SRL after LT did not have an increased risk of developing diabetes, CAD, CVA or HAT. Furthermore, SRL was at least equivalent to CNI in terms of ESRD and mortality. This suggests that SRL, in appropriate LT patients, is safe and that LT patients currently receiving SRL can continue to do so.
Gastroenterology
Bowlus CL, Assis DN, Wu JL, Levy C, Goldberg DS, Forman L, Schlansky B, Lammert C, Prenner S, Reddy KR, **Gordon SC**, Ahn J, Zepeda JB, Silveira MG, Boyer JL, and Pollock BH. IMPACT OF RACE AND ETHNICITY ON PROGNOSTIC MODELS OF OUTCOMES IN PRIMARY SCLEROSING CHOLANGITIS. *Hepatology* 2020; 72:748A-749A.

[Bowlus, Christopher L.] Univ Calif Davis, Sch Med, Div Gastroenterol & Hepatol, Davis, CA 95616 USA. [Assis, David N.] Yale Univ, Sch Med, Digest Dis, New Haven, CT 06520 USA. [Wu, Jialin] Univ Miami, Schiff Ctr Liver Dis, Coral Gables, FL 33124 USA. [Levy, Cynthia] Univ Miami, Div Gastroenterol & Hepatol, Coral Gables, FL 33124 USA. [Goldberg, David S.] Univ Miami, Sch Med, Coral Gables, FL 33124 USA. [Forman, Lisa] Univ Colorado, Div Gastroenterol Hepatol, Boulder, CO 80309 USA. [Schlansky, Barry] Kaiser Permanente Northwest, Washington, DC USA. [Lammert, Craig] Indiana Univ Sch Med, Gastroenterol & Hepatol, Indianapolis, IN 46202 USA. [Prenner, Stacey] Northwestern Univ, Northwestern Mem Hosp, Evanston, IL 60208 USA. [Reddy, K. Rajender] Univ Penn, Philadelphia, PA 19104 USA. [Gordon, Stuart C.] Henry Ford Hlth Syst, Gastroenterol & Hepatol, Detroit, MI USA. [Gordon, Stuart C.] Wayne State Univ, Sch Med, Med, Detroit, MI 48202 USA. [Ahn, Joseph] Oregon Hlth & Sci Univ, Dept Gastroenterol & Hepatol, Portland, OR 97201 USA. [Zepeda, Joseph Benjamin] Univ

Calif Davis, Sch Med, Gastroenterol & Hepatol, Davis, CA 95616 USA. [Silveira, Marina G.; Boyer, James L.] Yale Univ, Sch Med, Internal Med, New Haven, CT 06520 USA. [Pollock, Brad H.] Univ Calif Davis, Dept Publ Hlth Sci, Davis, CA 95616 USA.

Background: Primary sclerosing cholangitis (PSC) is a chronic cholestatic liver disease with a median time to liver transplant or death (LT/D) of approximately 20 years. The Mayo Risk Score (MRS), Amsterdam-Oxford Model (AOM), and UK-PSC scores predict LT/D in PSC but have not been validated in a racially and ethnically diverse population. We aimed to validate these models in a diverse cohort and determine if race and/or ethnicity affect their performance. Methods: Patients diagnosed with PSC, including small duct PSC and overlap with autoimmune hepatitis (PSC/AIH), alive without liver transplantation after 2008, were enrolled in the Consortium for Autoimmune Liver Diseases (CALiD) registry at 9 U.S. centers. MRS, AOM, UK-PSC (short term), and model for end-stage liver disease (MELD) were calculated from the earliest available data. Time-to-failure analysis was performed from the date of the earliest available score to either LT/D or hepatic decompensation (HD), defined as first variceal bleed, ascites, or encephalopathy. Accuracy of each model was summarized using Harrell's C-index. The effect of race and ethnicity on each model for LT/D and HD was determined by Cox regression. Results: A total of 335 patients with a median follow up 6.4 y were analyzed including 39 (11.6%) Black(B) and 37 (11.0%) Hispanic(H) patients. Characteristics did not differ between non-Hispanic White (NHW), B, and H patients [age of diagnosis (median 40.4, IQR 24.6; p=0.52), male sex (60.3%; p=0.84), PSC type (89.0% large duct, 3.6% small duct, 7.7% PSC/AIH; p=0.57), and IBD (72.2%; p=0.14)]. All models predicted both LT/D and HD (Table). However, MELD score demonstrated poor discrimination for both LT/D and HD (C-index<0.7) and MELD prediction of LT/D was significantly lower than MRS (p = 0.013). MRS, AOM, and UK-PSC had good discrimination for LT/D (C-index>0.7) and did not significantly differ. C-index for HD was generally lower than for LT/D and did not significantly differ between the scores. Notably, B race compared to NHW was independently associated with an increased risk of HD in three of four models. Conclusion: Current PSC-specific models performed similarly and better than MELD in an ethnically and racially diverse patient population. Neither race nor ethnicity impacted any of the models' performance for LT/D, but B race was an independent predictor of HD in some models. Race and ethnicity should be incorporated into new models as they are developed for clinical trials as surrogate endpoints.

Gastroenterology
Caines A, **Mishra K**, **Stanley S**, **Sturza S**, **Abouljoud MS**, and **Salgia RJ**. THE IMPACT OF HCC LOCOREGIONAL THERAPY ON PERI-OPERATIVE AND POST-TRANSPLANT COMPLICATIONS. *Hepatology* 2020; 72:850A-851A.

[Caines, Allyce] Henry Ford Hlth Syst, Detroit, MI USA. [Caines, Allyce] Henry Ford Hlth Syst, Gastroenterol & Hepatol, Detroit, MI USA. [Mishra, Kajali; Stanley, Sara] Henry Ford Hlth Syst, Internal Med, Detroit, MI USA. [Sturza, Scott] Henry Ford Hlth Syst, Intervent & Diagnost Radiol, Detroit, MI USA. [Abouljoud, Marwan S.] Henry Ford Hosp, Transplant & Hepatobiliary Surg, Detroit, MI 48202 USA. [Salgia, Reena J.] Henry Ford Hlth Syst, Hepatol, Detroit, MI USA.

Background: Transplant candidacy in the setting of HCC is largely dependent on a patient falling within Milan criteria. For those who fall outside of Milan criteria or in regions where liver transplant (LT) waiting times are prolonged, locoregional therapies (LRT) are used to decrease tumor burden as a bridge to LT. There is limited amount of data available regarding the effects of LRT on peri-operative LT complications and outcomes. The aim of this study was to examine the effects of LRT for treatment of HCC on peri-operative LT outcomes. Methods: We conducted a retrospective review of patients who underwent LT from 2012 - 2018. Patients with cirrhosis and HCC who were transplanted within the study period and received LRT (drug eluting bead chemoembolization, thermal ablation, SBRT or yttrium-90 glass sphere radioembolization) for HCC prior to LT were compared to a control group of patients who did not receive LRT. Demographic variables and peri-operative data were collected for both groups. Univariate two-group comparisons were performed using 2-sample t-tests and wilcoxon rank sum tests. Results: 160 LRT patients were compared to 200 controls. Patients who received LRT prior to LT were older than the control group (60.95 vs. 56.47; p< 0.001). HCV was more common in the LRT group than controls (69% vs. 26%; p <.001). 11% of the LRT group and 21% of controls had cirrhosis due to alcohol (p<.001).

Mean native MELD at time of LT was 23.57 and 25.56 (p = 0.005) for the LRT patients and control groups respectively. The control group had significantly greater intra- operative transfusion requirements and longer hospital stays than the LRT group. There were no significant differences in the occurrence of bile leak, anastomotic biliary stricture or hepatic artery stenosis, post-LT nor total operative time, need for take back to OR or overall post LT mortality between the LRT and control groups. On subgroup analysis we did not find an increase in complications based on type of LRT or number of LRT treatments received. However, the long-term post LT mortality rate was higher among those who received TARE compared to those who did not receive TARE (33% vs. 12%; p=0.015). Conclusion: We found that the occurrence of LRT for HCC prior to LT did not lead to increased intra-operative transfusion requirements, longer post-LT hospital stay, higher post-LT complications, longer operative times, increased rates of return to the OR or increased overall mortality compared to patients who did not undergo LRT prior to LT.

Gastroenterology
Gordon SC, **Li J**, Moorman AC, Spradling PR, Teshale EH, Boscarino JA, Daida Y, Schmidt MA, **Zhou YR**, **Rupp LB**, **Trudeau S**, and **Lu M**. PATIENT CHARACTERISTICS AND EFFICACY OF PANGENOTYPIC DIRECT-ACTING ANTIVIRAL REGIMENS AMONG A COHORT OF CHRONIC HEPATITIS C PATIENTS RECEIVING ROUTINE CLINICAL CARE IN THE US. *Hepatology* 2020; 72:540A-541A.

[Gordon, Stuart C.] Henry Ford Hlth Syst, Gastroenterol & Hepatol, Detroit, MI USA. [Gordon, Stuart C.] Wayne State Univ, Sch Med, Med, Detroit, MI 48202 USA. [Li, Jia; Zhou, Yueren; Trudeau, Sheri; Lu, Mei] Henry Ford Hlth Syst, Dept Publ Hlth Sci, Detroit, MI USA. [Moorman, Anne C.; Spradling, Philip R.; Teshale, Eyasu H.] Ctr Dis Control & Prevent, Div Viral Hepatitis, Natl Ctr HIV Hepatitis STD & TB Prevent, Atlanta, GA USA. [Boscarino, Joseph A.] Geisinger Med Clin, Dept Populat Hlth Sci, Danville, PA USA. [Daida, Yihe] Kaiser Permanente Hawaii, Ctr Integrated Hlth Care Res, Honolulu, HI USA. [Schmidt, Mark A.] Kaiser Permanente Northwest, Ctr Integrated Hlth Care Res, Washington, DC USA. [Rupp, Loralee B.] Henry Ford Hlth Syst, Ctr Hlth Policy, Detroit, MI USA. [Rupp, Loralee B.] Henry Ford Hlth Syst, Hlth Serv Res, Detroit, MI USA.

Background: Using recent data from the Chronic Hepatitis Cohort study (CHeCS), we report patient characteristics and “real world” efficacy of three pangenotypic direct-acting antiviral (DAA) regimens used to treat chronic hepatitis C (CHC) patients with a range of HCV genotypes (GT 1-4 and 6) under routine care. Methods: CHeCS CHC patients were followed through mid-2019. Baseline patient characteristics and rates of sustained virological response 12 weeks after end of treatment (SVR12) were compared among the three pangenotypic regimens (SOF/VEL, SOF/VEL/VOX, and GLE/PIB). Results: A total of 1842 patients were included, of which 1019 were treated with SOF/VEL, 753 with GLE/ PIB, and 70 with SOF/VEL/VOX. There were statistically significant differences in patient characteristics among the three groups (p-values <0.05): (1) 46% and 54% of patients treated with SOF/VEL and GLE/PIB were aged 60 years and older, respectively, versus only 25% of those treated with SOF/VEL/VOX; (2) 7% of patients treated with SOF/VEL had decompensated cirrhosis (DCC) while almost none treated with the other regimens had DCC (≤1%); (3) 93% of the SOF/ VEL/VOX-treated group were DAA experienced, compared with only 2-4% in the other treated groups; (4) GT distribution varied among the three regimens (Table). Observed rates of SVR12 were 97%, 98% and 97% with SOF/VEL, GLE/PIB, and SOF/VEL/VOX, respectively, with no significant difference observed (p-values in the range of 0.50 to 0.62 from pairwise comparisons). Among the 48 patients that did not achieve SVR12: (1) 19% were DAA experienced (vs. 6% of those that achieved SVR12); (2) 10% had DCC (vs. 4% of those that achieved SVR12); (3) 21% experienced a toxicity (vs. 11% of those that achieved SVR12); (4) 31% had diabetes and 4% were on proton pump inhibitor therapy at time of DAA initiation (vs. 21% and 1%, respectively, of those that achieved SVR12). Conclusion: Observed rates of SVR12 were very high for all three pangenotypic regimens, with no significant difference between them. A sizeable majority of CHC patients treated with SOF/VEL/VOX and GLE/PIB had GT 1, while the largest proportion of patients treated with SOF/VEL had GT 2. Patients with DCC were mostly treated with SOF/VEL, as would be expected based on treatment guidelines. Patients who did not achieve SVR12 had higher rates of prior DAA experience, DCC, diabetes, and on-treatment toxicities.

Gastroenterology

Gordon SC, **Rupp LB**, Boscarino JA, Daida Y, Schmidt MA, **Zhou YR**, **Trudeau S**, **Li J**, and **Lu M**. RISK FACTORS FOR SARS-COV-2 INFECTION AMONG PATIENTS WITH CHRONIC VIRAL HEPATITIS. *Hepatology* 2020; 72:299A-300A.

[Gordon, Stuart C.] Henry Ford Hlth Syst, Div Gastroenterol & Hepatol, Detroit, MI USA. [Gordon, Stuart C.] Wayne State Univ, Sch Med, Med, Detroit, MI 48202 USA. [Rupp, Loralee B.] Henry Ford Hlth Syst, Ctr Hlth Policy & Hlth Serv Res, Detroit, MI USA. [Boscarino, Joseph A.] Geisinger Med Clin, Dept Populat Hlth Sci, Detroit, MI USA. [Daida, Yihe] Kaiser Permanente Hawaii, Ctr Integrated Hlth Care Res, Honolulu, HI USA. [Schmidt, Mark A.] Kaiser Permanente Northwest, Ctr Hlth Res, Washington, DC USA. [Zhou, Yueren; Trudeau, Sheri; Li, Jia; Lu, Mei] Henry Ford Hlth Syst, Dept Publ Hlth Sci, Detroit, MI USA.

Background: We investigated factors associated with risk of SARS-CoV-2 infection among an established cohort of chronic hepatitis B and C (CHB/ CHC) patients at a large, vertically integrated health system located in southeastern Michigan (which includes Detroit), a racially-diverse area that experienced a significant outbreak of COVID-19 during March–May 2020. Methods: Patient characteristics and clinical conditions were collected for the period prior to date of first positive SARS-CoV-2 test, or March 11, 2020 for those who were not SARS-CoV-2 infected. Variables included: age; gender; race; insurance type; household income; BMI; CHC vs. CHB; AST; ALT; liver fibrosis status (as measured by APRI/ FIB4); diagnosis of liver cirrhosis; Charlson-Deyo comorbidity index; select individual comorbidities; and history of antiviral therapy. Patients coinfected with both CHB and CHC were excluded. Logistic regression, univariate followed by multivariable modeling, was performed. Variables with p-values <0.05 were retained in the final model. Results: A total of 13,556 patients with a history of chronic viral hepatitis were included; 94 had a positive SARS-CoV-2 result. In univariate comparisons, there was a significant difference between groups (p<0.05) with regard to type of hepatitis infection (C vs. B), age, race, BMI, insurance type, household income, comorbidity index, AST, ALT, APRI, presence of cirrhosis, type 2 diabetes, chronic heart disease, renal disease, peripheral vascular disease, history of receipt of antiviral therapy, and achievement of sustained viral response (CHC). In the final multivariable model, increased risk of SARS-CoV-2 infection was associated with CHC vs CHB (adjusted Odds Ratio [aOR])=4.00, 95% confidence interval [CI] 1.89–8.47), presence of cirrhosis (aOR=1.66, 95%CI 1.08–2.55), normal AST at baseline (aOR=2.50, 95%CI 1.46–4.27), higher comorbidity index (aOR=1.40, 95%CI 1.19–1.67), Black/ African American vs white race (aOR=18.0, CI 6.59–45.5), and BMI (BMI 25–30 vs <25: aOR=3.82, CI 1.95–7.49; BMI >30 vs <25: aOR=2.85, CI 1.46–5.56). Conclusion: In a cohort of chronic viral hepatitis patients drawn from a geographic area that experienced a significant COVID-19 outbreak, Black/ African American race, BMI>25, cirrhosis, CHC (active or post-SVR) vs. CHB, and higher comorbidity index were associated with higher risk of SARS-CoV-2 infection.

Gastroenterology

Kitajima T, **Kuno Y**, **Sukkarieh N**, **Suzuki Y**, **Shimada S**, **Flores A**, **Lisznyai E**, **Collins K**, **Yoshida A**, **Rizzari M**, **Moonka D**, **Abouljoud MS**, and **Nagai S**. EFFECTS OF AGING AND ACUTE-ON-CHRONIC LIVER FAILURE ON LIVER TRANSPLANT WAITLIST MORTALITY. *Hepatology* 2020; 72:800A-801A.

[Kitajima, Toshihiro; Kuno, Yasutaka; Sukkarieh, Nicole; Suzuki, Yukiko; Shimada, Shingo; Flores, Alexander; Lisznyai, Eric; Rizzari, Michael] Henry Ford Hosp, Div Transplant & Hepatobiliary Surg, Detroit, MI 48202 USA. [Collins, Kelly] Henry Ford Hlth Syst, Transplant & Hepatobiliary Surg, Detroit, MI USA. [Yoshida, Atsushi] Henry Ford Hosp, Transplant Inst, Detroit, MI 48202 USA. [Moonka, Dilip] Henry Ford Hosp, Gastroenterol, Detroit, MI 48202 USA. [Abouljoud, Marwan S.; Nagai, Shunji] Henry Ford Hosp, Transplant & Hepatobiliary Surg, Detroit, MI 48202 USA.

Background: Acute-on-chronic liver failure (ACLF) is characterized by multiple organ failure with high short-term mortality. However, the effect of the severity of ACLF on waitlist outcomes in age groups has not been well elucidated. We hypothesized that the negative effect of ACLF may be different between age groups and older patients may increase the risk of waitlist mortality compared to younger population. The aim of this study is to investigate the effects of ACLF on waitlist mortality according to recipient age.

Methods: This study used data from the UNOS registry and evaluated adult patients listed for liver-only or liver-kidney transplant between 2014 and 2019. Patients listed as status 1A, multi- organ transplant, hepatocellular carcinoma, and re-transplant were excluded. We identified patients with ACLF using the European Association for the Study of the Liver-Chronic Liver Failure (EASL-CLIF) criteria. Ninety-day waitlist mortality was compared between ACLF grades 1, 2, and 3 in each age group at listing (age<50 [younger], 50-64 [mid], ≥65 [older]). The risks of 90-day waitlist mortality were analyzed in ACLF patients using Fine-Gray competing risk regression model. Risk was adjusted by recipient characteristics at listing. Results: Among the 30,486 patients eligible for the study, 6,316 (20.7%), 1,995 (6.5%) and 1,653 (5.4%) had ACLF 1,2 and 3, respectively. 7733 (25.3%) were in younger group, 17462 (57.3%) were in mid group, 5291 (17.4%) were in older group. In all age groups, ACLF 1, 2 and 3 groups showed significantly higher adjusted risk of 90-day waitlist mortality than those without ACLF (Figure). The adverse impact of ACLF on waitlist mortality was most significant in the older group. In patients with ACLF, higher grade of ACLF (ACLF- 2: adjusted hazard ratio [aHR] 1.33, P<0.001; ACLF-3: aHR 2.56, P<0.001; ref: ACLF-1) and older recipient age (mid: aHR 1.57, P<0.001: older: aHR 2.15, P<0.001; ref younger) independently increased the risk of 90-day waitlist mortality. Conclusion: While ACLF negatively affected 90-day mortality for patients of all age groups on waitlist, this effect was more prominent in the older populations. Given this fact and the higher risk of waitlist mortality for those with ACLF, increased priority in liver allocation to these patients should be considered.

Gastroenterology
Kuno Y, **Kitajima T**, **Moonka D**, **Sukkarieh N**, **Flores A**, **Lisznyai E**, **Shimada S**, **Suzuki Y**, **Collins K**, **Rizzari M**, **Yoshida A**, **Abouljoud MS**, and **Nagai S**. LIVER TRANSPLANTATION IN OLDER PATIENTS WITH ACUTE-ON-CHRONIC LIVER FAILURE: AN ANALYSIS OF UNOS REGISTRY. *Hepatology* 2020; 72:819A-820A.

[Kuno, Yasutaka; Kitajima, Toshihiro; Sukkarieh, Nicole; Flores, Alexander; Lisznyai, Eric; Shimada, Shingo; Suzuki, Yukiko; Rizzari, Michael] Henry Ford Hosp, Detroit, MI 48202 USA. [Moonka, Dilip] Henry Ford Hosp, Gastroenterol, Detroit, MI 48202 USA. [Collins, Kelly] Henry Ford Hlth Syst, Transplant & Hepatobiliary Surg, Detroit, MI USA. [Yoshida, Atsushi] Henry Ford Hosp, Transplant Inst, Detroit, MI 48202 USA. [Abouljoud, Marwan S.; Nagai, Shunji] Henry Ford Hosp, Transplant & Hepatobiliary Surg, Detroit, MI 48202 USA.

Background: Acute on chronic liver failure (ACLF) patients undergoing liver transplantation (LT) may require additional consideration in selection and management due to their severity of illness. We hypothesized that older recipient age might increase the risk of graft loss in ACLF patients. We aimed to identify risk factors for post-transplant mortality in patients with ACLF, focusing on recipient age. Methods: Using data from the UNOS registry, this study evaluated adult liver or liver and kidney transplant recipients between 2014 and 2019. Patients with status 1A, multi-organ, hepatocellular carcinoma, and re-transplant were excluded. We identified patients with ACLF using European Association for the Study of the Liver-Chronic Liver Failure (EASL-CLIF) criteria. One- year graft survival was compared between ACLF patients (ACLF grades 1, 2, 3) and those without ACLF for each age group (age<50 [younger], 50-64 [mid], ≥65 [older]). Risk factors for 1-year graft survival were analyzed in ACLF patients using Cox regression models. A subgroup analysis in older ACLF patients was performed based on identified risk factors. Risk was adjusted by donor and recipient characteristics at LT. Results: Among 17,148 patients eligible for the study, 3,836 (22.4%), 3,050 (17.8%) and 2,084 (12.2%) had ACLF 1,2 and 3. 2983 (17.4%) patients were in the older group. In all age groups, ACLF 1, 2 and 3 groups showed significantly higher risk of 1-year graft loss than those without ACLF (Figure). In patients with ACLF, older recipient (≥65 years, aHR 1.56, P<0.001, ref: <50 years) and ACLF-3 (aHR 1.57, P<0.001, ref: ACLF-1) were independent risk factors for one-year graft loss, along with black donor race (aHR 1.23, P=0.024, ref: white), DCD donor (aHR 2.00, P<0.001, ref: DBD), cold ischemia time (CIT)>8 hours (aHR 1.21, P=0.038), and older donor (>50 years: aHR 1.395, P<0.001, ref: ≤50 years). In older ACLF patients, risk of 1-year graft loss was decreased when graft was younger DBD donor with shorter CIT (<8hr) compared to those who did not meet all of these 3 [younger donor, DBD donor, and shorter CIT] factors (aHR 0.74, P=0.045). Conclusion: Liver transplant outcomes were significantly worse in patients with ACLF compared to those without ACLF regardless of recipient age. Donor selection and shortening cold ischemia time may mitigate risk of graft loss in older patients with ACLF.

Gastroenterology
Lu M, **Rupp LB**, Boscarino JA, Schmidt MA, Daida Y, **Zhou YR**, **Trudeau S**, **Li J**, and **Gordon SC**. IMPACT OF HISTORY OF CHRONIC VIRAL HEPATITIS AND LIVER FIBROSIS ON RISK OF HOSPITALIZATION AND DEATH AMONG PATIENTS WITH SARS-COV-2 INFECTION. *Hepatology* 2020; 72:280A-281A.

[Lu, Mei; Zhou, Yueren; Trudeau, Sheri; Li, Jia] Henry Ford Hlth Syst, Dept Publ Hlth Sci, Detroit, MI USA. [Rupp, Loralee B.] Henry Ford Hlth Syst, Ctr Hlth Policy & Hlth Serv Res, Detroit, MI USA. [Boscarino, Joseph A.] Geisinger Med Clin, Dept Populat Hlth Sci, Danville, PA USA. [Schmidt, Mark A.] Kaiser Permanente Northwest, Ctr Hlth Res, Washington, DC USA. [Daida, Yihe] Kaiser Permanente Hawaii, Ctr Integrated Hlth Care Res, Honolulu, HI USA. [Gordon, Stuart C.] Henry Ford Hlth Syst, Div Gastroenterol & Hepatol, Detroit, MI USA. [Gordon, Stuart C.] Wayne State Univ, Med, Sch Med, Detroit, MI 48202 USA.

Background: We investigated factors associated with Covid-19 related hospitalization and death among patients with and without a history of chronic viral hepatitis B or C (CHB/CHC) in a single large, integrated health system located in metropolitan Detroit, Michigan, an area that experienced a significant outbreak of SARS-Cov-2 in Spring 2020. Methods: Baseline data were collected before date of first positive SARS-CoV-2 test or Covid-related hospitalization, whichever was earlier. Risk of hospitalization was analyzed with logistic regression; risk of death with Cox regression. Variables with p-values <0.05 were retained in the final multivariable models. Results: Of 6661 patients that tested SARS-CoV-2 positive from March 12–April 26, 2020, 94 (1.4%) had a history of CHB or CHC. A total of 2604 were hospitalized due to Covid-19, 55 (58.5%) with CHB or CHC and 2549 (38.8%) without CHB/CHC. Among hospitalized patients, 10 (18.2%) CHB/CHC patients and 426 (16.7%) non-hepatitis patients died. In multivariable analyses, viral hepatitis was not a risk factor for hospitalization, but approached significance for death (adjusted Hazard Ratio [aHR] 1.82, 95% Confidence Interval [CI] 0.96–3.46). In addition to recognized risk factors for Covid-19 severity such as increasing age, obesity, type 2 diabetes, and multiple co-morbidities, we found that increasing Fibrosis-4 (FIB4) score (a biomarker for liver fibrosis and cirrhosis) was associated with risk of hospitalization (adjusted Odds Ratio [aOR] 95%CI 1.32, 1.16–1.51). African American and male patients were also at higher risk of hospitalization. Notably, a number of risk factors for hospitalization were not associated with or were associated with reduced risk of death among hospitalized patients; African American patients and those with BMI ≥30 had lower mortality than White patients and those with BMI <25 (aHR 0.73, 95%CI 0.60–0.89; and aHR 0.69, 95%CI 0.54–0.88) respectively. Conclusion: Increasing baseline FIB4 index is associated with higher risk of hospitalization among patients with Covid-19. History of CHB or CHC trended toward increased risk of Covid-related mortality; future studies in larger samples of patients with chronic viral hepatitis are warranted.

Gastroenterology
Naffouj S, **Selim R**, **Shamaa O**, **Ahmed A**, **Zhou YR**, **Rupp LB**, **Jafri SM**, **Gordon SC**, and **Gonzalez HC**. LIVER TRANSPLANT EVALUATION IN THE PETH ERA. *Hepatology* 2020; 72:176A-176A.

[Naffouj, Sandra; Shamaa, Omar] Henry Ford Hlth Syst, Internal Med, Detroit, MI USA. [Selim, Ranya; Jafri, Syed-Mohammed; Gordon, Stuart C.; Gonzalez, Humberto C.] Henry Ford Hlth Syst, Gastroenterol & Hepatol, Detroit, MI USA. [Ahmed, Abdelwahab; Jafri, Syed-Mohammed; Gordon, Stuart C.; Gonzalez, Humberto C.] Wayne State Univ, Sch Med, Detroit, MI 48202 USA. [Zhou, Yueren] Henry Ford Hlth Syst, Dept Publ Hlth Sci, Detroit, MI USA. [Rupp, Loralee B.] Henry Ford Hlth Syst, Ctr Hlth Policy & Hlth Serv Res, Detroit, MI USA.

Background: Phosphatidylethanol (PEth) is a phospholipid formed in the presence of ethanol with a high sensitivity, specificity, and long half-life compared to other alcohol detection tests. PEth has become a key biomarker in liver transplant (LT) evaluation since 2018. We aimed to determine the impact of PEth on the transplant evaluation process and LT waitlist in alcoholic liver disease. Methods: Candidates referred for LT evaluation 1/1/2017 to 11/12/2019 were captured using Organ Transplant Tracking Record at Henry Ford Hospital, Detroit, MI. 2018 evaluations were excluded (testing transition period). Only

patients with alcoholic liver disease were included. Patients were divided into pre-PEth (2017) and PEth (2019) eras. Demographics, use of PEth and non-PEth (serum ethanol or urine ethyl glucoronide) testing, Child Pugh/MELD scores, insurance and evaluation termination/delisting reasons were captured. PEth+ was defined as a level >10 ng/dL. Rates of terminations/de-listings were compared between groups using Chi-square. Logistic regression was used to identify factors associated with terminations/de-listings (as a composite outcome). Results: There were 375 evaluations for alcoholic liver disease; 157 in pre-PEth era, 210 in PEth era, and 8 excluded due to loss of follow-up. Patient characteristics are shown in Table 1. There were 72(46%) vs 85(41%) terminations (p=0.321) and 11(7%) vs 2(1%) de-listings in pre-PEth vs PEth eras (p=0.002), respectively. Of the terminations/de-listings, there were 5(7%) due to non-PEth+ in 2017 vs 16(19%) due to PEth+ in 2019 (p=0.069). Odds ratios of terminations/delistings due to alcohol use were 0.36 for black vs white race, 0.43 for employed vs unemployed, 0.52 for Medicare vs Medicaid and 1.37 for commercial insurance vs Medicaid (p=0.069, 0.126, and 0.063 for race, employment status, and insurance, respectively). Conclusion: Our results demonstrate that black race, employment, and commercial or Medicare insurance was associated with lower risk of termination/delisting. There were fewer de-listings in the PEth era. Despite the increased detection of surreptitious alcohol use due to PEth, the rates of termination/delisting for alcohol use were similar. We speculate that our results reflect the use of PEth test as a screening tool prior to transplant referral. Additionally, a recent shift toward a more liberal consideration of a) shorter period of sobriety and/or b) select alcoholic hepatitis patients may explain these findings.

Gastroenterology

Naffouj S, **Siddiqui MB**, **Shaikh A**, Shabbir N, Shabbir A, and **Salgia RJ**. THE IMPLICATIONS OF CHRONIC OPIOID USE ON POST-TRANSPLANT CLINICAL OUTCOMES: A SYSTEMATIC REVIEW AND META-ANALYSIS. *Hepatology* 2020; 72:852A-852A.

[Naffouj, Sandra] Henry Ford Hlth Syst, Internal Med, Detroit, MI USA. [Siddiqui, Mohammad B.; Salgia, Reena J.] Henry Ford Hlth Syst, Gastroenterol & Hepatol, Detroit, MI USA. [Shaikh, Amna] Henry Ford Hlth Syst, Anesthesiol, Detroit, MI USA. [Shabbir, Nawal; Shabbir, Aimun] Karachi Med & Dent Coll, Karachi, Pakistan.

Background: Based on current literature, pre-transplant chronic opioid use (COU) for analgesia is highly prevalent among patients awaiting solid-organ transplant. However, there are very few large-scale studies on the effect of COU on post-transplant outcomes. We conducted a systematic review and meta-analysis to evaluate the impact of pre-transplant COU on solid-organ transplantation clinical outcomes. Methods: A comprehensive literature review was conducted by searching the PubMed, Ovid Medline, Embase, Web of Science, and Cochrane databases from inception to April 2020 to identify all studies that evaluated the impact of pre-transplant COU on post-transplant clinical outcomes. COU was defined as >3 months of consecutive opioid use entering transplant listing. The search included studies regarding heart, lung, kidney, and liver transplantation. Our primary outcome was all-cause mortality, and secondary outcomes were graft failure and the one-year readmission rate. A random-effect model was used to estimate the pooled hazard ratios (HR) or odds ratios (OR) of our outcomes. Results: Nine retrospective studies involving 166,765 patients were included in the primary meta- analysis. The all-cause post-transplant mortality rate was significantly higher in patients who were on chronic opioids preceding transplant compared to those who were not (HR 1.42; 95% CI 1.34-1.50). The included studies demonstrated low heterogeneity (Figure 1, part A). Additionally, COU patients had an increased risk of graft failure compared to non-COU patients (HR 1.26; 95% CI (1.13-1.40) (Figure 1, part B). With regards to the one-year readmission rates, and noting that only three studies included data on readmission rates, there was no statistically significant difference in the readmission rate between the two groups (HR 1.78; 95% CI (0.87-3.63). The studies had high heterogeneity (Figure 1, part C). Conclusion: This study demonstrates that pre-transplant COU in solid-organ transplant patients is associated with an increased risk of all-cause mortality and graft failure. Pre- transplant COU may be a surrogate for comorbidities causing chronic pain or psychosocial traits that can contribute to non- compliance post-transplant. These potential risk factors may explain the increased risk of poor outcomes post-transplant. Therefore, a careful evaluation of opioid use patterns and consideration of alternative analgesic strategies is warranted in this population to lessen the reliance on opioid use and associated adverse outcomes.

Gastroenterology

Nagai S, **Nallabasannagari AR**, **Moonka D**, **Reddiboina M**, **Nanna M**, **Chau LC**, **Yeddula S**, **Kitajima T**, **Bajjoka-Francis I**, and **Abouljoud MS**. USE OF NEURAL NETWORK MODELS TO PREDICT MORTALITY/ SURVIVAL AMONG PATIENTS ON THE LIVER TRANSPLANT WAITLIST. *Hepatology* 2020; 72:2A-3A.

[Nagai, Shunji; Chau, Lucy Ching; Yeddula, Sirisha; Kitajima, Toshihiro; Abouljoud, Marwan S.] Henry Ford Hosp, Transplant & Hepatobiliary Surg, Detroit, MI 48202 USA. [Nallabasannagari, Anubhav Reddy; Reddiboina, Madhu; Nanna, Michael] Henry Ford Hosp, Rediminds, Detroit, MI 48202 USA. [Moonka, Dilip] Henry Ford Hosp, Gastroenterol, Detroit, MI 48202 USA. [Bajjoka-Francis, Iman] Henry Ford Transplant Inst, Detroit, MI USA.

Background: While use of the MELD-Na scores have shown success in predicting waitlist mortality in liver transplant (LT), questions remain whether there are more efficacious models. The objective of this study is to develop Neural Network (NN) models that more accurately predict waitlist mortality. NNs are a type of Machine Learning algorithm. The fundamental building blocks of a NN are layers which are composed of units of calculation called neurons. NN performs calculations on input data and extracts meaningful patterns for the problem. Methods: This study used data from the OPTN/UNOS registry, which includes data for 194,299 patients listed for LT between Feb 27, 2002 and Dec 31, 2018. Subsets of the data were used for the creation of 4 separate NN models. These models were constructed to predict mortality at different timeframes at 30, 90, 180, and 365 days. We excluded patients who received LTs before the outcome timeline, patients with liver cancer, patients who received MELD exceptions, and patients who were listed for combined organ transplants other than kidney. The Liver Data and the Liver Wait List History files in the OPTN/UNOS registry were combined and a total of 44 variables were selected, including recipient characteristics, trend of liver and kidney function during waiting time, UNOS regions, and registration year. Age, ethnicity, and gender were not included in the NN model to avoid assigning waitlist priority based on these factors. For each model, the data were split using random sampling into training, validation, and test dataset in a 60:20:20 ratio. The performance of the models was assessed using Area Under Receiver Operating Curve (AUC-ROC) and Area Under Precision-Recall curve (PR-AUC). Results: According to NN prediction models, the AUC- ROC for 30-Day, 90-Day, 180-Day, and 365-Day Mortality was 0.949, 0.928, 0.915, and 0.899 and the PR-AUC was 0.689, 0.730, 0.769, and 0.823, respectively. The 90-Day Mortality NN model outperformed MELD score for both AUC-ROC and PR-AUC. It also outperformed MELD score for Recall (Sensitivity), Negative Predictive Value (NPV), and F-1 score. The 90-Day Mortality model specifically identified more waitlist deaths with a higher Recall (Sensitivity) of 0.833 vs 0.308 ($P<0.001$). MELD score performed better for Specificity and Precision. (Figure) The performance metrics were compared by breaking the test dataset into multiple subsets based on Ethnicity, Gender, Region, Age, Diagnosis Group, and Year of listing. The 90-Day Mortality NN model significantly outperformed MELD scores across all subsets of the data for predicting waitlist mortality. Conclusion: Prediction models using NN more accurately identified waitlist mortality which outperformed MELD score. Using NN will improve predictive ability for waitlist mortality and lead to developing a more accurate and equitable allocation system with the ultimate goal of reducing LT waitlist mortality.

Gastroenterology

Siddiqui MB, **Suresh S**, **Abu Ghanimeh M**, **Karrick M**, **Nimri F**, **Musleh M**, **Mendiratta V**, **Al-Shammari M**, **Simmer S**, **Jou J**, **Russell SM**, **Dang DY**, **Salgia RJ**, and **Zuchelli T**. LIVER INJURY IS ASSOCIATED WITH INCREASED MORBIDITY AND MORTALITY IN COVID-19 PATIENTS. *Hepatology* 2020; 72:287A-287A.

[Siddiqui, Mohammad B.; Suresh, Suraj; Abu Ghanimeh, Mouhanna; Mendiratta, Vivek; Al-Shammari, Mustafa; Simmer, Stephen; Jou, Jessica; Russell, Sarah M.; Dang, Duyen; Salgia, Reena J.; Zuchelli, Tobias] Henry Ford Hosp, Gastroenterol, Detroit, MI 48202 USA. [Karrick, Megan; Nimri, Faisal; Musleh, Maher] Henry Ford Hosp, Internal Med, Detroit, MI 48202 USA.

Background: Based on current literature there appears to be a high prevalence of liver injury (LI) in patients with COVID-19. However, there are limited large scale studies on risk factors, morbidity, and

mortality associated with LI in these patients. We aim to determine risk factors and outcomes of patients hospitalized with COVID-19 and LI. Methods: We performed a retrospective single-center study at a large tertiary care hospital. All index admissions of adult patients with confirmed COVID19 between 3/1 to 4/30/2020 were included. Data on baseline characteristics and clinical outcomes was collected during manual chart review. Mild elevation in LFTs (MEL), defined as peak levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and total bilirubin (TB) above upper limit of normal (ULN) but lower than the threshold for LI. LI was defined as peak ALT/AST three times ULN and/or peak ALP/TB two times ULN. ULN threshold values of ALT 52, AST 35, TB 1.2, ALP 140 were used. Both cohorts were compared with our control group, who had normal LFTs at presentation and throughout the hospitalization. SAS 9.4 was used for analysis. Results: A total of 1935 patients were included of which 507 (26.2%) had normal LFTs, 1030 (53.2%) had MEL, and 397 (20.5%) had LI. Males were more commonly found in the MEL (p=0.0004) and LI groups compared to control (p<.0001). Patients in the MEL cohort were older (p=0.0005). African Americans were more likely to develop LI (p=0.0318). There was no difference in comorbidities between all groups. Among patients with LI, 241 (61%) had a hepatocellular pattern, 20 (5%) had a cholestatic pattern, and 135 (34%) had a mixed pattern. Patients with LI had an increased risk of mortality (RR 4.26 [95% CI 3.12, 5.81; p<.0001]), ICU admission (RR 5.52 [95% CI 4.07, 7.49; p<.0001]), intubation (RR 11.01 [95% CI 6.97, 17.34]); p<.0001) and 30-day readmission (1.81 [95% CI 1.17, 2.80; p<.0076]) (Table 2, Figure 1) compared to the control group. Conclusion: Our study demonstrates that patients with COVID-19 who present with LI have a significantly increased risk of mortality, mechanical ventilation, ICU admission, and 30-day re-admission compared to patients with MEL and normal LFTs. This information is important to appropriately manage COVID-19 patients. Further research looking at risk prediction models and pooling multi-center data should include liver injury as a key variable.

Gastroenterology
Suresh S, **Siddiqui MB**, **Abu Ghanimeh M**, **Nimri F**, **Karrick M**, **Musleh M**, **Mendiratta V**, **Russell SM**, **Jou J**, **Simmer S**, **Al-Shammari M**, **Dang D**, and **Zuchelli T**. CLINICAL OUTCOMES IN HOSPITALIZED COVID-19 PATIENTS WITH CHRONIC LIVER DISEASE AND CIRRHOSIS. *Hepatology* 2020; 72:263A-263A.

[Suresh, Suraj; Siddiqui, Mohammad B.; Abu Ghanimeh, Mouhanna; Mendiratta, Vivek; Russell, Sarah M.; Jou, Jessica; Simmer, Stephen; Al-Shammari, Mustafa; Dang, Duyen; Zuchelli, Tobias] Henry Ford Hosp, Gastroenterol, Detroit, MI 48202 USA. [Nimri, Faisal; Karrick, Megan; Musleh, Maher] Henry Ford Hosp, Internal Med, Detroit, MI 48202 USA.

Background: There is increasing evidence suggesting that liver dysfunction is a risk factor for severe COVID-19 illness. However, due to the low prevalence of liver disease and cirrhosis in the general population, larger studies looking at the impact of these conditions have utilized data from international registries which do not necessarily reflect the US population. Our study aims to assess the association between chronic liver disease and COVID-19 clinical outcomes across a single large inpatient cohort. Methods: We performed a retrospective single-center study at a large tertiary care hospital. All index admissions of adult patients with confirmed COVID-19 between 3/1/2020 and 4/30/2020 were included. A manual chart review was performed to collect data on baseline patient characteristics, medical comorbidities, and clinical outcomes. Patients with chronic liver disease (CLD) and cirrhosis were compared to the control group, who had no known underlying liver disease. SAS 9.4 was used for analysis. Results: A total of 1935 patients met our inclusion criteria of which 1869 (96.6%) had no underlying liver disease, 66 (3.4%) had CLD, and 21 (1.1%) had cirrhosis. Table 1 shows baseline patient characteristics. There were a higher proportion of males in the CLD and cirrhosis cohorts compared to the control group (67% and 76% vs 50%; p=0.0105). Patients with cirrhosis and chronic liver disease also had a significantly lower average BMI compared to the control group (25.8 and 27.3 vs. 31.8; p=0.002). There was no difference in comorbidities between all three cohorts. Patients with cirrhosis had a significantly higher mortality (RR 2.1 [95% CI 1.33-3.62; p=0.0022]) compared to non-cirrhotics. There was also a trend towards increased 30-day readmission in the cirrhotic cohort (RR 2.35 [95% CI 0.86-6.42]; p=0.0950) however no difference in rate of ICU admission or intubation. Patients with CLD did not have an increase in mortality, ICU admission, intubation, or 30-day re-admission compared to the control group. Conclusion: Our study demonstrates that cirrhosis is associated with increased mortality in

COVID-19 while chronic liver disease in the absence of cirrhosis does not confer the same degree of clinical risk. Future studies performed on a larger scale should evaluate how decompensated disease and MELD score may impact this risk profile.

Hematology-Oncology

Gartrelle KJ, **Schaff EM**, **Kirsch C**, **Kwon D**, **Ajlouni M**, **Khan G**, **Shah R**, **Dobrosotskaya I**, **Parikh PJ**, and **Siddiqui F**. Racial Disparities Among Pancreatic Adenocarcinoma Patients: A Retrospective Survival Analysis of Non-Metastatic Pancreatic Cancer Patients. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):e431.

Purpose/Objective(s): It is predicted that in 2020, approximately 57,600 individuals will be diagnosed with pancreatic cancer (PaC). Based on SEER database analysis, there are conflicting opinions in literature about the overall treatment and outcomes in African-American patients with PaC. The purpose of this study was to determine if there was a racial disparity in overall survival rates between African Americans (AAs) and non-African Americans (non-AAs) diagnosed with PaC who received neoadjuvant radiation therapy (RT) in a tertiary-care cancer center with an established multi-disciplinary PaC tumor board and clinic. Materials/Methods: An IRB-approved retrospective chart analysis was completed on 100 patients who were diagnosed with pancreatic adenocarcinoma and treated with neoadjuvant RT between 2017-2019. Patients who were deemed resectable, borderline resectable (BR), or locally advanced/unresectable (LA) at initial diagnosis were included in the analysis. The following baseline characteristics were collected for each patient: staging, gender, age and ECOG score at initial diagnosis, tumor site and size, clinical T and N stage, CA19-9, and treatment variables (i.e., surgery, chemotherapy, and RT type). Overall survival was calculated from the RT start date. In order to identify any baseline differences among the AA group and the non-AA group, a two-sample t-test and Chi-square were employed. A log-rank test and Kaplan-Meier were used to determine any differences in overall survival among the two groups. Results: Of the 100 patients included in the analysis, 25 were AA and 58 were female. There were 17 (68%) BR and 8 (32%) LA patients in the AA group. In the non-AA group, there were 2 (3%) resectable, 47 (63%) BR, and 26 (35%) LA patients. There were no statistically significant differences detected in any of the baseline characteristics except a trend for increased CA19-9 values of 399.8 U/mL for AAs and 229 U/mL for non-AAs. There was no statistically significant difference in receipt of chemotherapy and RT between the two groups. The estimated median survival rates were 11.5 months for non-AAs and 8.4 months for AAs. One-year overall survival was 45% for AAs versus 48% for non-AAs ($p = 0.57$). Conclusion: There was no difference in overall survival among AAs and non-AAs who received neoadjuvant RT+/- chemotherapy for PaC at our institution between 2017-2019. Contrary to previous publications based on large SEER database analysis, there does not appear to be any difference in overall survival based on race if patients receive treatment in a comprehensive multi-disciplinary collaborative center.

Hematology-Oncology

Schaff EM, **Gartrelle KJ**, **Kirsch C**, **Siddiqui F**, **Ajlouni M**, **Dragovic J**, **Aref I**, **Shah MM**, **Kwon D**, **Dobrosotskaya I**, **Shah R**, **Khan G**, and **Parikh PJ**. Magnetic Resonance Guided Stereotactic Ablative Radiation Therapy Versus External Beam RT with Chemotherapy For Pancreatic Cancer: Single Institution Toxicity Analysis Of Patients Treated In An Urban Academic Center. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):e582-e583.

Purpose/Objective(s): Several academic institutions have investigated stereotactic MR guided adaptive radiation therapy (SMART) to safely dose escalate for locally advanced and borderline resectable pancreatic cancer with initial favorable toxicity and survival outcomes. However, it is not clear that this treatment is safe or effective in more challenging populations, such as in an urban academic center. The purpose of this abstract was to review outcomes immediately before and after implementing dose escalated MR guided adaptive radiation therapy for pancreatic cancer. Materials/Methods: In this IRB approved analysis, we retrospectively reviewed 57 consecutive patients from 2017-2019 with locally advanced or borderline resectable pancreatic cancer who were treated with neoadjuvant radiation therapy. Initially all patients received standard fractionated chemoradiation (chemoRT) to a dose of 50.4 Gy in 28 fractions. In September 2018 our institutional treatment guidelines were changed to recommend

SMART (50Gy in 5 fractions) for these patients. Toxicity outcomes evaluated were grade 3+ GI toxicity based on CTCAE v5.0 as well as unplanned hospital admissions, both at 90 and 180 days. Treatment differences were analyzed using two sample t-test and chi-square test. Overall survival was evaluated at 180 days, and by Kaplan-Meier and log-rank test and was calculated from first day of radiation therapy. Results: 29 patients received chemoRT and 28 received SMART. Median follow up for the chemoRT group was 294 days and for SMART was 185 days. Groups did not have significant differences in age, performance status, stage, gender, CA 19-9, or neoadjuvant chemotherapy. Grade 3+ GI toxicity at 90 days was seen in 28% and 11% (p = 0.11) in the chemoRT and SMART groups, respectively. Types of toxicity were overall comparable with most being abdominal pain and duodenal bleeds. Hospital admissions at 90 days occurred in 38% and 21% of patients (p = 0.17) and at 180 days in 33% and 44% (p = 0.48). Surgical resection was achieved in 24% of chemoRT and 36% of SMART patients (p = 0.34). When evaluated using Kaplan-Meier and log-rank test there was a trend to overall survival benefit in the SMART group (p = 0.07). There was also a statistically significant 180-day survival improvement in SMART patients of 94% vs 70% in chemoRT patients (p = 0.046). Conclusion: Dose escalated SMART for locally advanced and borderline pancreatic cancer does not cause significant increase in GI grade 3+ GI toxicity at 90 days or hospitalization at 90 or 180 days as compared to chemoRT. Dose escalated SMART appears to be both safe and effective in our urban population. OS in the chemoRT group was comparable to previous trials such as LAP07. There is a trend to OS improvement on Kaplan-Meier analysis in the SBRT group (p = 0.07), as well as statistically significant improvement in 180-day survival; which supports the ongoing multi-institutional SMART study (NCT03621644). Updated results to be presented at the meeting.

Hematology-Oncology

Simone CB, **Movsas B**, Gore EM, Mohindra P, Vujaskovic Z, **Wang D**, **Ajlouni M**, Menon S, Thompson J, **Brown SL**, Kurman M, Dykstra JC, Rillo L, Ingram M, Serebrenik A, and Kaytor MD. A Phase 1b/2a Study Evaluating the Pharmacokinetics, Safety, and Efficacy of Nanogenistein in Combination with Chemoradiotherapy for Non-small Cell Lung Cancer. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):S103.

Purpose/Objective(s): Radiation therapy (RT) remains a critical component of locally advanced (LA) and limited metastatic non-small cell lung cancer (NSCLC) but is associated with significant risks of pneumonitis, esophagitis, and major cardiac events. Nanogenistein (NG) is a radioprotectant that promotes DNA repair, cell cycle arrest and anti-inflammatory signaling to mitigate RT-associated toxicities. The objective of this phase 1b/2a trial is to evaluate the safety, pharmacokinetics (PK), and efficacy of NG in combination with concurrent chemoradiotherapy for NSCLC. Materials/Methods: Patients with newly diagnosed stage II, III or IV (oligometastatic) NSCLC planned for 60-70/1.8-2.0 Gy RT and concurrent weekly paclitaxel/carboplatin were eligible. Patients were treated daily with a self-administered, oral suspension of NG at one of three dose levels (500, 1000, or 1500 mg) starting prior to and continuing during the entire course of chemoradiotherapy (up to 8 weeks). Three cohorts (n = 7/cohort) were enrolled sequentially. PK analysis was completed for NG, paclitaxel and carboplatin. Tumor response was defined per RECIST 1.1 criteria. CT scans were obtained during chemoradiotherapy, consolidation, and every 2-3 months following RT completion. Adverse events (AEs) were reported using the NCI CTCAEv4 and used to monitor dose-limiting toxicities (DLTs). Quality of life measurements included UCSD-SOBQ, FACT-L TOI and a swallowing diary. Results: Enrolled patients (n = 21) were a median of 69 years (range 50-84), predominantly Caucasian (n = 19) and female (n = 11), and had stage II (n = 5), III (n = 14) or IV (n = 2) disease. NG was well tolerated and no DLTs were identified. NG PK did not interfere with chemotherapeutic PK. AEs were not dose dependent and those possibly (n = 10), probably (n = 1) or definitely (n = 0) attributable to NG treatment were mild GI events (n = 8, all grade 1), fatigue (n = 1, grade 2), anorexia (n = 1, grade 2), and dysgeusia (n = 1, grade 1). Overall, 1 major cardiac event, 1 grade 3 esophagitis, and 2 cases of grade ≥2 pneumonitis occurred. Patient weight loss was ≤ 5%, pulmonary function (0, 9- and 13-months post-RT), and FACT-L TOI (0, 3, 6- and 13-months post-RT) remained stable across all cohorts (all p>0.05). Tumor response rate was 70%, with a complete response rate of 15%. The median progression-free survival across cohorts was 15.6 months, and the median overall survival was not reached at a median of 15.9 months follow-up. Conclusion: In this study, NG was found to be safe and well tolerated, with an incidence of Grade ≥2 hematological and normal tissue toxicities both less than that observed in RTOG 0617. These

encouraging safety and efficacy data support advancing the drug to an adequately powered, randomized, double-blind, placebo-controlled phase 2b study that is planned in LA-NSCLC patients.

Hematology-Oncology

Vaishampayan UN, Elliott T, Omlin AG, Graff JN, Hoimes CJ, Tagawa ST, **Hwang C**, Kilari D, Tije AJT, McDermott RS, Gerritsen WR, Wu H, Kim J, Schloss C, de Bono JS, and Antonarakis ES. Phase II study of pembrolizumab (pembro) plus enzalutamide for enzalutamide (enza)-resistant metastatic castration-resistant prostate cancer (mCRPC): Cohorts (C) 4 and 5 update from KEYNOTE-199. *Annals of Oncology* 2020; 31:S1330.

Background: Chemotherapy-naive patients (pts) with mCRPC who had disease progression with enza were enrolled in C4 and C5 of the multicohort phase II KEYNOTE-199 study (NCT02787005). Methods: Pts who did or did not previously take abiraterone acetate were eligible if they developed resistance to enza after prior response. Cohorts were composed of pts who had RECIST-measurable (C4) or bone-predominant nonmeasurable (C5) disease. Pts received pembro 200 mg Q3W for up to 35 cycles + enza QD until progression, toxicity, or withdrawal. The primary end point was ORR per RECIST v1.1 by blinded independent central review in C4; DOR was also analyzed. Secondary end points (both cohorts) were DCR, rPFS, OS, time to cytotoxic chemotherapy, time to new anticancer therapy, and safety. Results: A total of 126 pts (C4, 81; C5, 45) were treated. Median (range) time from enrollment to data cutoff was 15 mo (7-21) and 19 mo (7-21) in C4 and C5, respectively. In C4, ORR (95% CI) was 12% (6-22) (2 CRs, 8 PRs) and median (range) DOR was 6.3 mo (2.5+ to 13.4); 4 responders (73% by Kaplan-Meier estimation) had a response ≥6 mo (Table). Median time to cytotoxic chemotherapy was 11.1 and 11.3 mo in C4 and C5, and time to PSA progression was 4.2 mo in both cohorts (Table). A total of 26% and 24% of pts in C4 and C5, respectively, experienced grade ≥3 treatment-related adverse events (TRAEs). Two pts in C4 died of immune-related AEs (Miller Fisher syndrome and myasthenia gravis). Incidence of any-grade/grade 3 or 4 rash (33%/6%), regardless of treatment relatedness, was higher than previously reported for individual agents but manageable with standard-of-care treatments. [Formula presented] Conclusions: After enza resistance, pembro + enza showed antitumor activity and manageable safety for RECIST-measurable and bone-predominant mCRPC. Pembro + enza is being evaluated in the ongoing phase III KEYNOTE-641 trial (NCT03834493). Clinical trial identification: NCT02787005, June 1, 2016.

Infectious Diseases

Ashraf T, **Mendiratta V**, **Musleh M**, **Parraga T**, **Alangaden G**, **Brown KA**, and **Jafri SM**. PRIMARY CARE VISITS ARE THE KEY FACTOR IN ENSURING HIGHER VACCINATION RATES IN POST-LIVER TRANSPLANT PATIENTS. A SINGLE CENTER STUDY. *Hepatology* 2020; 72:836A-836A.

[Ashraf, Taha; Musleh, Maher] Henry Ford Hosp, Internal Med, Detroit, MI 48202 USA. [Mendiratta, Vivek] Henry Ford Hosp, Gastroenterol, Detroit, MI 48202 USA. [Parraga, Tommy; Alangaden, George] Henry Ford Hosp, Infect Dis, Detroit, MI 48202 USA. [Brown, Kimberly Ann; Jafri, Syed-Mohammed] Henry Ford Hosp, Gastroenterol & Hepatol, Detroit, MI 48202 USA.

Background: Liver transplant recipients are at an increased risk for life threatening vaccine preventable disease. If vaccines are not given pre-transplant, major societal guidelines recommend they are given in the post-transplant period. This retrospective study evaluates vaccination rates in our institution and potential areas for improvement. Methods: A retrospective study of patients transplanted between 1/2015-1/2018 at our institution was performed. Relevant data collected included patient demographics, travel distance to transplant center, primary care provider (PCP) location and PCP and transplant clinic visits. Vaccination status and eligibility for influenza (IV), pneumococcus (PV), Hepatitis-A (HAV) and B (HBV), Tdap and Td vaccines (TdV) were obtained through our electronic medical records and the Michigan Care Improvement Registry. Statistics were calculated using analysis of variance (ANOVA), chi-square, Fisher's exact test and Wilcoxon Rank Sum Test. Results: 406 patients met our inclusion criteria with 83.0% (336) Caucasians, 10.8% (44) African-Americans, 3.7% (15) Hispanics with overall mean age of 59. PCP visitation post-transplant was significantly associated with vaccination of IV (62.9% vs 47.2% p=0.007), HAV (66.7% vs 45.5% p= 0.003), HBV (60.0% vs 50.1% p=0.391), PV (64.6% vs 39.6% p<0.001) and Tdap (75.0% vs 36.4% p<0.001). However with the exception of PV (92.7% vs 88.5% p =0.314) the same was not seen with transplant clinic visits. Patients who were vaccinated were more

likely to have their PCP at their transplant center for PV (46.8% vs 27.8% p=0.005), TdAp (67.5% vs 24.7% p<0.001), IV (35.8% vs 33.6% p =0.689) , HAV (43.1% vs 31.7% p=0.093) and HBV (36.8% vs 33.7% p=0.780). Those who received IV post-transplant were significantly younger than those who did not (56.3 ± 9.7 vs 59.9 ± 9.8 p< 0.001). PV uptake trended towards an older age (60.1 ± 8.4 vs 56.9 ± 10.6 p=0.023), there was no association with age for the remaining vaccines. Notably, post-transplant hospital admissions was not significantly associated with uptake and at times trended towards a negative association. Conclusion: Our data highlights multiple areas for improvement in vaccination in the post-transplant period. Physicians should encourage patients to see their PCP and ideally at their transplant institution. Furthermore, transplant clinics should more attentively prescribe and administer vaccines during visits. The age disparity seen in PV, suggest guidelines for non- immunocompromized patients are erroneously being followed and could be corrected by appropriate education. Finally, our data demonstrates that hospital admissions post-transplant are a missed opportunity to vaccinate eligible patients.

Infectious Diseases

Tsang O, **Brar I**, Spinner C, Robinson P, Roestenberg M, Calmy A, Malvy D, Elboudwarej E, Tian Y, McDonald C, Tan S, Suri V, Hyland R, SenGupta D, Chokkalingam AP, Gaggar A, Osinusi AO, Brainard DM, Kim SW, Cooke G, Shan-Chwen SC, Nicastri E, Castano M, and Chai LYA. IMPACT OF BASELINE ALANINE AMINOTRANSFERASE LEVELS ON THE SAFETY AND EFFICACY OF REMDESIVIR IN MODERATE COVID-19 PATIENTS. *Hepatology* 2020; 72:88A-89A.

[Tsang, Owen] Princess Margaret Hosp, Kwai Chung, 2-10 Princess Margaret Hosp Rd, Hong Kong, Peoples R China. [Brar, Indrira] Henry Ford Hlth Syst, Detroit, MI USA. [Spinner, Christoph] Univ Hosp Klinikum Rechts Isar, Dept Med 2, Munich, Germany. [Robinson, Philip] Hoag Hosp Newport Beach, Newport Beach, CA USA. [Roestenberg, Meta] Leids Univ, Med Ctr, Leiden, Netherlands. [Calmy, Alexandra] Hop Univ Geneve, Geneva, Switzerland. [Malvy, Denis] CHU Pellegrin, Bordeaux, France. [Elboudwarej, Emon; Tian, Yuan; McDonald, Circe; Tan, Susanna; Suri, Vithika; Hyland, Robert; SenGupta, Devi; Chokkalingam, Anand P.; Gaggar, Anuj; Osinusi, Anu O.; Brainard, Diana M.] Gilead Sci Inc, 353 Lakeside Dr, Foster City, CA 94404 USA. [Kim, Shin-Woo] Kyungpook Natl Univ Hosp, Daegu, South Korea. [Cooke, Graham] Imperial Coll Healthcare NHS Trust, London, England. [Shan-Chwen, Shan-Chwen] Natl Taiwan Univ Hosp, Taipei, Taiwan. [Nicastri, Emanuele] Ist Nazl Malattie Infett, Uoc Malattie Infett Ad Alta Intens Cure, Milan, Italy. [Castano, Manuel] Hosp Reg Univ Malaga, Malaga, Spain. [Chai, Louis Yi Ann] Natl Univ Hlth Syst, Natl Univ Hosp, Singapore, Singapore.

Background: Several studies have reported hepatic impairment, in particular abnormal liver function tests in patients with mild to severe COVID-19. Remdesivir (RDV), a nucleotide analogue prodrug that inhibits viral RNA polymerases, has demonstrated favorable clinical efficacy and tolerability in moderate and severe COVID-19 patients. Here, we examined the safety and clinical outcomes in moderate COVID-19 patients with or without elevated baseline (BL) alanine aminotransferase (ALT) levels after RDV treatment. Methods: We conducted an open-label, phase 3 trial of hospitalized patients with confirmed SARS-CoV-2 infection, oxygen saturation of >94% on room air, and radiological evidence of pneumonia. We randomized participants 1:1:1 to receive 5d or 10d of intravenous RDV once daily plus standard of care (SoC), or SoC only. Patients with ALT or AST> 5x the upper limit of normal (ULN) were excluded. Within this posthoc analysis, we grouped patient using AASLD criteria (ALT 35 U/L for males, 25 U/L for females) into low ALT group (BL ALT ≤ULN) and high ALT group (BL ALT >ULN). Within these ALT groups, we compared those who received RDV vs SoC. Covariates for adjustment included BL demographics (age, sex, race, region and obesity) and disease characteristics (symptom duration, oxygen support status). 2-point clinical improvement and recovery were evaluated using Cox proportional hazards. Clinical outcomes and adverse events (AEs) were assessed through day 28. Results: Of 584 patients treated with RDV or SoC, 279 (48%) were in the high BL ALT group (183 [66%] RDV, 96 [34%] SoC). BL characteristics were similar for RDV vs SoC arms within high and low ALT groups, except for duration of symptoms before dosing (median RDV 7d vs SoC 9d, p=0.004) in low ALT group. AE profiles were generally similar for RDV vs SoC within high and low ALT groups (Table1). Hepatobiliary adverse events, particularly transaminase elevations, were not common but numerically higher with RDV in both high and low ALT groups. Clinical outcomes, including time to clinical recovery and 2-point clinical improvement were similar for RDV vs SoC within each of the high and low ALT

groups. Conclusion: In moderate COVID-19 patients, the adverse event profile and clinical outcomes of RDV vs SoC was generally similar for those with BL normal ALT and those with elevated ALT (1-5x ULN).

Internal Medicine

Ashraf T, **Mendiratta V**, **Gill S**, **Ahmed A**, and **Jafri SM**. LONG TERM USE OF URSODIOL IN POST-LIVER TRANSPLANT PATIENTS INCREASES BILIARY COMPLICATIONS. *Hepatology* 2020; 72:821A-822A.

[Ashraf, Taha; Gill, Sonika] Henry Ford Hosp, Internal Med, Detroit, MI 48202 USA. [Mendiratta, Vivek] Henry Ford Hosp, Gastroenterol, Detroit, MI USA. [Ahmed, Abdelwahab] Wayne State Univ, Detroit, MI 48202 USA. [Jafri, Syed-Mohammed] Henry Ford Hosp, Gastroenterol & Hepatol, Detroit, MI 48202 USA.

Background: Studies suggest ursodiol has beneficial effects in reducing liver enzymes during the first 4 weeks after liver transplantation (LT) as well as incidence of biliary casts and sludge in the first year. Hepatologists often continue ursodiol indefinitely despite evidence of improvement in long-term outcomes. This retrospective study evaluates ursodiol and its effect on LT outcomes over a 3-year period. Methods: A retrospective study of LT candidates transplanted between 5/2014- 10/2016 at our institution was performed. Patients with primary biliary cirrhosis, primary sclerosing cholangitis and autoimmune hepatitis were excluded and a total of 284 patients were recorded. Relevant data collected included: patient demographics, reason for transplantation, cold ischemic time, ursodiol use and dosage, presence and severity of rejection, number of hospitalizations, occurrences of biliary complications and mortality. Biliary complications were defined as strictures or leaks. Statistics were calculated using analysis of variance (ANOVA), chi-square, Fisher's exact test and Wilcoxon Rank Sum Test. Results: 284 liver transplants were performed in 180 males and 104 females with a mean age of 57.5. Ursodiol use was 62% at 6 months, 55% at 12 months, 45.4% at 2 years and 26.8% at 3 years. Univariate analysis showed that in spite of ursodiol use there remained a significant increase in biliary complications when compared to no use at 6 months (28.4% vs 10.3% p = <0.001) and between 6-12 months (10.3% vs 1.9% p= 0.010). This was again seen at 1-2 years (9.2% vs 3.3% p=0.053) and at 2-3 years (10.4% vs 2.8% p=0.055). There was no significant difference in mortality associated with use at 6 months (10.2% vs 8.3% p = 0.597) or 12 months (8.4% vs 8.3% p=0.982). There was consistently no significant difference in the number of hospitalizations, moderate or severe rejections at any time point (Table 1). This was true when analyzing all rejections at 6 months, 12 months, 2 years and 3 years as well (p=0.248, p=0.333, p=0.275 and p=0.100). Conclusion: Our data shows no long-term benefit of ursodiol use on mortality, re-admission rate, or number of rejections at 3 years post-transplant. Ursodiol does not reduce incidence of biliary complications in patients where medication was used for this purpose and instead increases number of biliary complications at 6 and 12 months. This suggests that ursodiol does not have long term protective effects and should be weaned off in the vast majority of patients.

Internal Medicine

Ashraf T, **Mendiratta V**, **Musleh M**, **Parraga T**, **Alangaden G**, **Brown KA**, and **Jafri SM**. PRIMARY CARE VISITS ARE THE KEY FACTOR IN ENSURING HIGHER VACCINATION RATES IN POST-LIVER TRANSPLANT PATIENTS. A SINGLE CENTER STUDY. *Hepatology* 2020; 72:836A-836A.

[Ashraf, Taha; Musleh, Maher] Henry Ford Hosp, Internal Med, Detroit, MI 48202 USA. [Mendiratta, Vivek] Henry Ford Hosp, Gastroenterol, Detroit, MI 48202 USA. [Parraga, Tommy; Alangaden, George] Henry Ford Hosp, Infect Dis, Detroit, MI 48202 USA. [Brown, Kimberly Ann; Jafri, Syed-Mohammed] Henry Ford Hosp, Gastroenterol & Hepatol, Detroit, MI 48202 USA.

Background: Liver transplant recipients are at an increased risk for life threatening vaccine preventable disease. If vaccines are not given pre-transplant, major societal guidelines recommend they are given in the post-transplant period. This retrospective study evaluates vaccination rates in our institution and potential areas for improvement. Methods: A retrospective study of patients transplanted between 1/2015-1/2018 at our institution was performed. Relevant data collected included patient demographics, travel distance to transplant center, primary care provider (PCP) location and PCP and transplant clinic visits. Vaccination status and eligibility for influenza (IV), pneumococcus (PV), Hepatitis-A (HAV) and B (HBV), Tdap and Td vaccines (TdV) were obtained through our electronic medical records and the Michigan

Care Improvement Registry. Statistics were calculated using analysis of variance (ANOVA), chi-square, Fisher's exact test and Wilcoxon Rank Sum Test. Results: 406 patients met our inclusion criteria with 83.0% (336) Caucasians, 10.8% (44) African-Americans, 3.7% (15) Hispanics with overall mean age of 59. PCP visitation post-transplant was significantly associated with vaccination of IV (62.9% vs 47.2% p=0.007), HAV (66.7% vs 45.5% p= 0.003), HBV (60.0% vs 50.1% p=0.391), PV (64.6% vs 39.6% p<0.001) and Tdap (75.0% vs 36.4% p<0.001). However with the exception of PV (92.7% vs 88.5% p =0.314) the same was not seen with transplant clinic visits. Patients who were vaccinated were more likely to have their PCP at their transplant center for PV (46.8% vs 27.8% p=0.005), TdAp (67.5% vs 24.7% p<0.001), IV (35.8% vs 33.6% p =0.689) , HAV (43.1% vs 31.7% p=0.093) and HBV (36.8% vs 33.7% p=0.780). Those who received IV post-transplant were significantly younger than those who did not (56.3 ± 9.7 vs 59.9 ± 9.8 p< 0.001). PV uptake trended towards an older age (60.1 ± 8.4 vs 56.9 ± 10.6 p=0.023), there was no association with age for the remaining vaccines. Notably, post-transplant hospital admissions was not significantly associated with uptake and at times trended towards a negative association. Conclusion: Our data highlights multiple areas for improvement in vaccination in the post-transplant period. Physicians should encourage patients to see their PCP and ideally at their transplant institution. Furthermore, transplant clinics should more attentively prescribe and administer vaccines during visits. The age disparity seen in PV, suggest guidelines for non- immunocompromized patients are erroneously being followed and could be corrected by appropriate education. Finally, our data demonstrates that hospital admissions post-transplant are a missed opportunity to vaccinate eligible patients.

Internal Medicine

Ashraf T, **Siddiqui MB**, **Khorfan K**, and **Moonka D**. LONG-TERM SAFETY OF SIROLIMUS IN LIVER TRANSPLANT RECIPIENTS. *Hepatology* 2020; 72:823A-824A.

[Ashraf, Taha; Khorfan, Kamal] Henry Ford Hosp, Internal Med, Detroit, MI 48202 USA. [Siddiqui, Mohammad B.; Moonka, Dilip] Henry Ford Hosp, Gastroenterol, Detroit, MI 48202 USA.

Background: Sirolimus (SRL) has been used as an alternative to calcineurin inhibitors (CI) to help spare renal function in liver transplant (LT) recipients. SRL received a black-box warning in LT because of concerns about hepatic artery thrombosis (HAT). Prior to this, our center initiated a large number of LT patients on SRL. This study assesses the long-term safety of SRL in LT recipients. Methods: This is a retrospective, single-center study of all LT recipients who initiated SRL from 2001-2006. A group that remained on SRL was compared to a group that discontinued SRL (CNI group) for adverse events. Groups were compared for LT outcomes. Kaplan-Meier analyses with Cox regression models were done to determine risk factors (RF), including SRL use, for death or end-stage renal disease (ESRD). Results: 159 patients were included. 109 (68.5%) remained on SRL and 50 (31.4%) discontinued (CNI). There were no differences between groups in age at transplant, gender, race, etiology of liver disease or time after LT to SRL initiation. The mean and median follow up time for the SRL group was 703.87 and 739.71 weeks respectively and was 703.58 and 757.15 weeks for the CNI group. In comparing SRL to CNI groups, there were no differences in HAT (2.8 vs. 2.0%), CAD (6.4 vs. 10%) or CVA (5.7% vs. 11.9%). Fewer patients on SRL died (47.7% vs. 58.0%) or developed ESRD (19.3 vs. 32.0%) though neither difference was significant (P=0.228: P=0.078). No significant differences were noted in GFR between the two groups up to 10 years after LT. In the evaluation of risk factors to time to ESRD, CNI (SRL discontinuation) had a small trend towards earlier onset ESRD on univariate analysis (HR:1.56, CI:0.78, 3.23, p=0.207 but even less so on multivariate analysis (HR:1.366, CI:0.675-2.763) (Figure 1). In the evaluation of RF for time to death, CNI was associated with greater mortality from time of transplant (HR:1.46, CI: 1.06-2.03, p=0.023) and from time of SRL initiation (HR:1.64, CI:1.06- 2.55, p=0.026) (Figure 1). However, when including age, diabetes and GFR at LT in multivariate analyses, the effect of CNI was no longer significant. Conclusion: The results describe one of the longest follow-up periods for SRL use in LT patients, with mean follow up extending over a decade. The results demonstrate that patients receiving SRL after LT did not have an increased risk of developing diabetes, CAD, CVA or HAT. Furthermore, SRL was at least equivalent to CNI in terms of ESRD and mortality. This suggests that SRL, in appropriate LT patients, is safe and that LT patients currently receiving SRL can continue to do so.

Internal Medicine

Caines A, **Mishra K**, **Stanley S**, **Sturza S**, **Abouljoud MS**, and **Salgia RJ**. THE IMPACT OF HCC LOCOREGIONAL THERAPY ON PERI-OPERATIVE AND POST-TRANSPLANT COMPLICATIONS. *Hepatology* 2020; 72:850A-851A.

[Caines, Allyce] Henry Ford Hlth Syst, Detroit, MI USA. [Caines, Allyce] Henry Ford Hlth Syst, Gastroenterol & Hepatol, Detroit, MI USA. [Mishra, Kajali; Stanley, Sara] Henry Ford Hlth Syst, Internal Med, Detroit, MI USA. [Sturza, Scott] Henry Ford Hlth Syst, Intervent & Diagnost Radiol, Detroit, MI USA. [Abouljoud, Marwan S.] Henry Ford Hosp, Transplant & Hepatobiliary Surg, Detroit, MI 48202 USA. [Salgia, Reena J.] Henry Ford Hlth Syst, Hepatol, Detroit, MI USA.

Background: Transplant candidacy in the setting of HCC is largely dependent on a patient falling within Milan criteria. For those who fall outside of Milan criteria or in regions where liver transplant (LT) waiting times are prolonged, locoregional therapies (LRT) are used to decrease tumor burden as a bridge to LT. There is limited amount of data available regarding the effects of LRT on peri-operative LT complications and outcomes. The aim of this study was to examine the effects of LRT for treatment of HCC on peri-operative LT outcomes. Methods: We conducted a retrospective review of patients who underwent LT from 2012 - 2018. Patients with cirrhosis and HCC who were transplanted within the study period and received LRT (drug eluting bead chemoembolization, thermal ablation, SBRT or yttrium-90 glass sphere radioembolization) for HCC prior to LT were compared to a control group of patients who did not receive LRT. Demographic variables and peri-operative data were collected for both groups. Univariate two-group comparisons were performed using 2-sample t-tests and wilcoxon rank sum tests. Results: 160 LRT patients were compared to 200 controls. Patients who received LRT prior to LT were older than the control group (60.95 vs. 56.47; p< 0.001). HCV was more common in the LRT group than controls (69% vs. 26%; p <.001). 11% of the LRT group and 21% of controls had cirrhosis due to alcohol (p<.001). Mean native MELD at time of LT was 23.57 and 25.56 (p = 0.005) for the LRT patients and control groups respectively. The control group had significantly greater intra- operative transfusion requirements and longer hospital stays than the LRT group. There were no significant differences in the occurrence of bile leak, anastomotic biliary stricture or hepatic artery stenosis, post-LT nor total operative time, need for take back to OR or overall post LT mortality between the LRT and control groups. On subgroup analysis we did not find an increase in complications based on type of LRT or number of LRT treatments received. However, the long-term post LT mortality rate was higher among those who received TARE compared to those who did not receive TARE (33% vs. 12%; p=0.015). Conclusion: We found that the occurrence of LRT for HCC prior to LT did not lead to increased intra-operative transfusion requirements, longer post-LT hospital stay, higher post-LT complications, longer operative times, increased rates of return to the OR or increased overall mortality compared to patients who did not undergo LRT prior to LT.

Internal Medicine

Naffouj S, **Selim R**, **Shamaa O**, **Ahmed A**, **Zhou YR**, **Rupp LB**, **Jafri SM**, **Gordon SC**, and **Gonzalez HC**. LIVER TRANSPLANT EVALUATION IN THE PETH ERA. *Hepatology* 2020; 72:176A-176A.

[Naffouj, Sandra; Shamaa, Omar] Henry Ford Hlth Syst, Internal Med, Detroit, MI USA. [Selim, Ranya; Jafri, Syed-Mohammed; Gordon, Stuart C.; Gonzalez, Humberto C.] Henry Ford Hlth Syst, Gastroenterol & Hepatol, Detroit, MI USA. [Ahmed, Abdelwahab; Jafri, Syed-Mohammed; Gordon, Stuart C.; Gonzalez, Humberto C.] Wayne State Univ, Sch Med, Detroit, MI 48202 USA. [Zhou, Yueren] Henry Ford Hlth Syst, Dept Publ Hlth Sci, Detroit, MI USA. [Rupp, Loralee B.] Henry Ford Hlth Syst, Ctr Hlth Policy & Hlth Serv Res, Detroit, MI USA.

Background: Phosphatidylethanol (PEth) is a phospholipid formed in the presence of ethanol with a high sensitivity, specificity, and long half-life compared to other alcohol detection tests. PEth has become a key biomarker in liver transplant (LT) evaluation since 2018. We aimed to determine the impact of PEth on the transplant evaluation process and LT waitlist in alcoholic liver disease. Methods: Candidates referred for LT evaluation 1/1/2017 to 11/12/2019 were captured using Organ Transplant Tracking Record at Henry Ford Hospital, Detroit, MI. 2018 evaluations were excluded (testing transition period). Only patients with alcoholic liver disease were included. Patients were divided into pre-PEth (2017) and PEth

(2019) eras. Demographics, use of PEth and non-PEth (serum ethanol or urine ethyl glucoronide) testing, Child Pugh/MELD scores, insurance and evaluation termination/delisting reasons were captured. PEth+ was defined as a level >10 ng/dL. Rates of terminations/de-listings were compared between groups using Chi-square. Logistic regression was used to identify factors associated with terminations/de-listings (as a composite outcome). Results: There were 375 evaluations for alcoholic liver disease; 157 in pre-PEth era, 210 in PEth era, and 8 excluded due to loss of follow-up. Patient characteristics are shown in Table 1. There were 72(46%) vs 85(41%) terminations (p=0.321) and 11(7%) vs 2(1%) de-listings in pre-PEth vs PEth eras (p=0.002), respectively. Of the terminations/de-listings, there were 5(7%) due to non-PEth+ in 2017 vs 16(19%) due to PEth+ in 2019 (p=0.069). Odds ratios of terminations/delistings due to alcohol use were 0.36 for black vs white race, 0.43 for employed vs unemployed, 0.52 for Medicare vs Medicaid and 1.37 for commercial insurance vs Medicaid (p=0.069, 0.126, and 0.063 for race, employment status, and insurance, respectively). Conclusion: Our results demonstrate that black race, employment, and commercial or Medicare insurance was associated with lower risk of termination/delisting. There were fewer de-listings in the PEth era. Despite the increased detection of surreptitious alcohol use due to PEth, the rates of termination/delisting for alcohol use were similar. We speculate that our results reflect the use of PEth test as a screening tool prior to transplant referral. Additionally, a recent shift toward a more liberal consideration of a) shorter period of sobriety and/or b) select alcoholic hepatitis patients may explain these findings.

Internal Medicine

Naffouj S, **Siddiqui MB**, **Shaikh A**, Shabbir N, Shabbir A, and **Salgia RJ**. THE IMPLICATIONS OF CHRONIC OPIOID USE ON POST-TRANSPLANT CLINICAL OUTCOMES: A SYSTEMATIC REVIEW AND META-ANALYSIS. *Hepatology* 2020; 72:852A-852A.

[Naffouj, Sandra] Henry Ford Hlth Syst, Internal Med, Detroit, MI USA. [Siddiqui, Mohammad B.; Salgia, Reena J.] Henry Ford Hlth Syst, Gastroenterol & Hepatol, Detroit, MI USA. [Shaikh, Amna] Henry Ford Hlth Syst, Anesthesiol, Detroit, MI USA. [Shabbir, Nawal; Shabbir, Aimun] Karachi Med & Dent Coll, Karachi, Pakistan.

Background: Based on current literature, pre-transplant chronic opioid use (COU) for analgesia is highly prevalent among patients awaiting solid-organ transplant. However, there are very few large-scale studies on the effect of COU on post-transplant outcomes. We conducted a systematic review and meta-analysis to evaluate the impact of pre-transplant COU on solid-organ transplantation clinical outcomes. Methods: A comprehensive literature review was conducted by searching the PubMed, Ovid Medline, Embase, Web of Science, and Cochrane databases from inception to April 2020 to identify all studies that evaluated the impact of pre-transplant COU on post-transplant clinical outcomes. COU was defined as >3 months of consecutive opioid use entering transplant listing. The search included studies regarding heart, lung, kidney, and liver transplantation. Our primary outcome was all-cause mortality, and secondary outcomes were graft failure and the one-year readmission rate. A random-effect model was used to estimate the pooled hazard ratios (HR) or odds ratios (OR) of our outcomes. Results: Nine retrospective studies involving 166,765 patients were included in the primary meta- analysis. The all-cause post-transplant mortality rate was significantly higher in patients who were on chronic opioids preceding transplant compared to those who were not (HR 1.42; 95% CI 1.34-1.50). The included studies demonstrated low heterogeneity (Figure 1, part A). Additionally, COU patients had an increased risk of graft failure compared to non-COU patients (HR 1.26; 95% CI (1.13-1.40) (Figure 1, part B). With regards to the one-year readmission rates, and noting that only three studies included data on readmission rates, there was no statistically significant difference in the readmission rate between the two groups (HR 1.78; 95% CI (0.87-3.63). The studies had high heterogeneity (Figure 1, part C). Conclusion: This study demonstrates that pre-transplant COU in solid-organ transplant patients is associated with an increased risk of all-cause mortality and graft failure. Pre- transplant COU may be a surrogate for comorbidities causing chronic pain or psychosocial traits that can contribute to non- compliance post-transplant. These potential risk factors may explain the increased risk of poor outcomes post-transplant. Therefore, a careful evaluation of opioid use patterns and consideration of alternative analgesic strategies is warranted in this population to lessen the reliance on opioid use and associated adverse outcomes.

Internal Medicine

Siddiqui MB, **Suresh S**, **Abu Ghanimeh M**, **Karrick M**, **Nimri F**, **Musleh M**, **Mendiratta V**, **Al-Shammari M**, **Simmer S**, **Jou J**, **Russell SM**, **Dang DY**, **Salgia RJ**, and **Zuchelli T**. LIVER INJURY IS ASSOCIATED WITH INCREASED MORBIDITY AND MORTALITY IN COVID-19 PATIENTS. *Hepatology* 2020; 72:287A-287A.

[Siddiqui, Mohammad B.; Suresh, Suraj; Abu Ghanimeh, Mouhanna; Mendiratta, Vivek; Al-Shammari, Mustafa; Simmer, Stephen; Jou, Jessica; Russell, Sarah M.; Dang, Duyen; Salgia, Reena J.; Zuchelli, Tobias] Henry Ford Hosp, Gastroenterol, Detroit, MI 48202 USA. [Karrick, Megan; Nimri, Faisal; Musleh, Maher] Henry Ford Hosp, Internal Med, Detroit, MI 48202 USA.

Background: Based on current literature there appears to be a high prevalence of liver injury (LI) in patients with COVID-19. However, there are limited large scale studies on risk factors, morbidity, and mortality associated with LI in these patients. We aim to determine risk factors and outcomes of patients hospitalized with COVID-19 and LI. Methods: We performed a retrospective single-center study at a large tertiary care hospital. All index admissions of adult patients with confirmed COVID19 between 3/1 to 4/30/2020 were included. Data on baseline characteristics and clinical outcomes was collected during manual chart review. Mild elevation in LFTs (MEL), defined as peak levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and total bilirubin (TB) above upper limit of normal (ULN) but lower than the threshold for LI. LI was defined as peak ALT/AST three times ULN and/or peak ALP/TB two times ULN. ULN threshold values of ALT 52, AST 35, TB 1.2, ALP 140 were used. Both cohorts were compared with our control group, who had normal LFTs at presentation and throughout the hospitalization. SAS 9.4 was used for analysis. Results: A total of 1935 patients were included of which 507 (26.2%) had normal LFTs, 1030 (53.2%) had MEL, and 397 (20.5%) had LI. Males were more commonly found in the MEL (p=0.0004) and LI groups compared to control (p<.0001). Patients in the MEL cohort were older (p=0.0005). African Americans were more likely to develop LI (p=0.0318). There was no difference in comorbidities between all groups. Among patients with LI, 241 (61%) had a hepatocellular pattern, 20 (5%) had a cholestatic pattern, and 135 (34%) had a mixed pattern. Patients with LI had an increased risk of mortality (RR 4.26 [95% CI 3.12, 5.81; p<.0001]), ICU admission (RR 5.52 [95% CI 4.07, 7.49; p<.0001]), intubation (RR 11.01 [95% CI 6.97, 17.34]); p<.0001) and 30-day readmission (1.81 [95% CI 1.17, 2.80; p<.0076]) (Table 2, Figure 1) compared to the control group. Conclusion: Our study demonstrates that patients with COVID-19 who present with LI have a significantly increased risk of mortality, mechanical ventilation, ICU admission, and 30-day re-admission compared to patients with MEL and normal LFTs. This information is important to appropriately manage COVID-19 patients. Further research looking at risk prediction models and pooling multi-center data should include liver injury as a key variable.

Internal Medicine

Suresh S, **Siddiqui MB**, **Abu Ghanimeh M**, **Nimri F**, **Karrick M**, **Musleh M**, **Mendiratta V**, **Russell SM**, **Jou J**, **Simmer S**, **Al-Shammari M**, **Dang D**, and **Zuchelli T**. CLINICAL OUTCOMES IN HOSPITALIZED COVID-19 PATIENTS WITH CHRONIC LIVER DISEASE AND CIRRHOSIS. *Hepatology* 2020; 72:263A-263A.

[Suresh, Suraj; Siddiqui, Mohammad B.; Abu Ghanimeh, Mouhanna; Mendiratta, Vivek; Russell, Sarah M.; Jou, Jessica; Simmer, Stephen; Al-Shammari, Mustafa; Dang, Duyen; Zuchelli, Tobias] Henry Ford Hosp, Gastroenterol, Detroit, MI 48202 USA. [Nimri, Faisal; Karrick, Megan; Musleh, Maher] Henry Ford Hosp, Internal Med, Detroit, MI 48202 USA.

Background: There is increasing evidence suggesting that liver dysfunction is a risk factor for severe COVID-19 illness. However, due to the low prevalence of liver disease and cirrhosis in the general population, larger studies looking at the impact of these conditions have utilized data from international registries which do not necessarily reflect the US population. Our study aims to assess the association between chronic liver disease and COVID-19 clinical outcomes across a single large inpatient cohort. Methods: We performed a retrospective single-center study at a large tertiary care hospital. All index admissions of adult patients with confirmed COVID-19 between 3/1/2020 and 4/30/2020 were included. A

manual chart review was performed to collect data on baseline patient characteristics, medical comorbidities, and clinical outcomes. Patients with chronic liver disease (CLD) and cirrhosis were compared to the control group, who had no known underlying liver disease. SAS 9.4 was used for analysis. Results: A total of 1935 patients met our inclusion criteria of which 1869 (96.6%) had no underlying liver disease, 66 (3.4%) had CLD, and 21 (1.1%) had cirrhosis. Table 1 shows baseline patient characteristics. There were a higher proportion of males in the CLD and cirrhosis cohorts compared to the control group (67% and 76% vs 50%; p=0.0105). Patients with cirrhosis and chronic liver disease also had a significantly lower average BMI compared to the control group (25.8 and 27.3 vs. 31.8; p=0.002). There was no difference in comorbidities between all three cohorts. Patients with cirrhosis had a significantly higher mortality (RR 2.1 [95% CI 1.33-3.62; p=0.0022]) compared to non-cirrhotics. There was also a trend towards increased 30-day readmission in the cirrhotic cohort (RR 2.35 [95% CI 0.86-6.42]; p=0.0950) however no difference in rate of ICU admission or intubation. Patients with CLD did not have an increase in mortality, ICU admission, intubation, or 30-day re-admission compared to the control group. Conclusion: Our study demonstrates that cirrhosis is associated with increased mortality in COVID-19 while chronic liver disease in the absence of cirrhosis does not confer the same degree of clinical risk. Future studies performed on a larger scale should evaluate how decompensated disease and MELD score may impact this risk profile.

Nursing

Gartrelle KJ, **Schaff EM**, **Kirsch C**, **Kwon D**, **Ajlouni M**, **Khan G**, **Shah R**, **Dobrosotskaya I**, **Parikh PJ**, and **Siddiqui F**. Racial Disparities Among Pancreatic Adenocarcinoma Patients: A Retrospective Survival Analysis of Non-Metastatic Pancreatic Cancer Patients. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):e431.

Purpose/Objective(s): It is predicted that in 2020, approximately 57,600 individuals will be diagnosed with pancreatic cancer (PaC). Based on SEER database analysis, there are conflicting opinions in literature about the overall treatment and outcomes in African-American patients with PaC. The purpose of this study was to determine if there was a racial disparity in overall survival rates between African Americans (AAs) and non-African Americans (non-AAs) diagnosed with PaC who received neoadjuvant radiation therapy (RT) in a tertiary-care cancer center with an established multi-disciplinary PaC tumor board and clinic. Materials/Methods: An IRB-approved retrospective chart analysis was completed on 100 patients who were diagnosed with pancreatic adenocarcinoma and treated with neoadjuvant RT between 2017-2019. Patients who were deemed resectable, borderline resectable (BR), or locally advanced/unresectable (LA) at initial diagnosis were included in the analysis. The following baseline characteristics were collected for each patient: staging, gender, age and ECOG score at initial diagnosis, tumor site and size, clinical T and N stage, CA19-9, and treatment variables (i.e., surgery, chemotherapy, and RT type). Overall survival was calculated from the RT start date. In order to identify any baseline differences among the AA group and the non-AA group, a two-sample t-test and Chi-square were employed. A log-rank test and Kaplan-Meier were used to determine any differences in overall survival among the two groups. Results: Of the 100 patients included in the analysis, 25 were AA and 58 were female. There were 17 (68%) BR and 8 (32%) LA patients in the AA group. In the non-AA group, there were 2 (3%) resectable, 47 (63%) BR, and 26 (35%) LA patients. There were no statistically significant differences detected in any of the baseline characteristics except a trend for increased CA19-9 values of 399.8 U/mL for AAs and 229 U/mL for non-AAs. There was no statistically significant difference in receipt of chemotherapy and RT between the two groups. The estimated median survival rates were 11.5 months for non-AAs and 8.4 months for AAs. One-year overall survival was 45% for AAs versus 48% for non-AAs ($p = 0.57$). Conclusion: There was no difference in overall survival among AAs and non-AAs who received neoadjuvant RT+/- chemotherapy for PaC at our institution between 2017-2019. Contrary to previous publications based on large SEER database analysis, there does not appear to be any difference in overall survival based on race if patients receive treatment in a comprehensive multi-disciplinary collaborative center.

Obstetrics, Gynecology and Women's Health Services

Chan CW, **Eisenstein DI**, **Abood J**, **Chavali N**, **Arun J**, and Gonte M. Effectiveness of Hysteroscopic Morcellation of Endometrial Polyps Compared to Traditional Technique: A Comparison of Disease Recurrence. *Journal of Minimally Invasive Gynecology* 2020; 27(7):S142.

C.W. Chan, Henry Ford Health Systems, West Bloomfield, MI, United States

Study Objective: To compare the outcomes between hysteroscopic morcellation of endometrial polyps and traditional techniques such as hysteroscopic resection with monopolar or bipolar radiofrequency energy, scissors and graspers or mechanical resection with polyp forceps. Design: Retrospective chart review. Setting: Academic tertiary referral center. Patients or Participants: 193 patients who underwent operative hysteroscopic polypectomy between January 2015 and May 2016. Interventions: Hysteroscopic polypectomy with intrauterine morcellation, monopolar or bipolar radiofrequency energy, scissors and graspers or mechanical resection with polyp forceps with evaluation and/or treatment of recurrent abnormal uterine bleeding (AUB) after operative polypectomy. Measurements and Main Results: There were 9 patients who underwent hysteroscopic polypectomy with monopolar radiofrequency energy, 3 patients with bipolar radiofrequency energy, 91 patients with intrauterine morcellation, 67 patients with polyp forceps and 12 patients with scissors and graspers. The recurrence rate for AUB for monopolar was 1.89%, bipolar was 1.67%, intrauterine morcellation was 1.93%, polyp forceps was 1.84% and hysteroscopic scissors and/or graspers was 1.83%. Among the recurrences the average time until recurrence was 1162 days for monopolar, 207 days for bipolar, 749.5 days for intrauterine morcellation, 477.6 days for polyp forceps and 341.5 days for hysteroscopic scissors and graspers. Conclusion: There was no significant difference in terms of recurrence of AUB following the different modalities of operative hysteroscopy. Among the patients with recurrence in order of shortest time until recurrence: bipolar, hysteroscopic scissors and graspers, polyp forceps, intrauterine morcellation and monopolar.

Obstetrics, Gynecology and Women's Health Services

Cook AE, **Khalil R**, **Burmeister C**, **Dimitrova I**, and **Elshaikh MA**. The Impact of Different Adjuvant Management Strategies on Survival Endpoints in Women with Early Stage Uterine Serous Carcinoma. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):e481.

Purpose/Objective(s): To determine the impact of adjuvant chemotherapy, radiation treatment, combined modality treatment, and observation on survival and recurrence outcomes in women with early stage uterine serous carcinoma (USC). Materials/Methods: After IRB study approval, our prospectively-maintained database for women with endometrial carcinoma was queried for women with 2009 International Federation of Gynecology and Obstetrics (FIGO) stages I-II USC based on WHO pathologic definition who underwent adequate surgical staging between 1/1991 and 4/2017 followed by adjuvant management [observation, radiation therapy (RT), chemotherapy (CT), or combination treatment (CRT)]. Chi-squared tests were performed to compare differences in outcome by type of adjuvant management. Recurrence-free (RFS), disease-specific (DSS), and overall survival (OS) were assessed by Kaplan-Meier and log-rank tests. Univariate and multivariate analyses (MVA) were performed to identify statistically significant predictors of survival endpoints. Results: We identified 171 women who met our inclusion criteria. The median follow-up time was 70.5 months. 75% of the study cohort were with stage IA, 13% stage IB and 12% with stage II. All women underwent pelvic lymph node dissection with a median number of dissected lymph nodes of 14. Omentectomy was performed in 61% of patients. Adjuvant RT was utilized in 56% of women (65 with vaginal brachytherapy alone, 10 with pelvic RT and 21 with combination). Most commonly used chemotherapy was carboplatin and paclitaxel with a median number of cycles of 6 5-year RFS was 73% for those received CRT, 84% for RT alone, 68% who received CT alone and 55% for those who were observed ($p = 0.13$). 5-year DSS was 81%, 94%, 71% and 60%, respectively ($p = 0.02$). 5-year OS was 76%, 70%, 60% and 56%, respectively ($p = 0.11$). On MVA of OS and DSS, higher percentage of myometrial invasion, presence of lower uterine segment involvement, positive peritoneal cytology, and receiving chemotherapy alone/observation were independent predictors of worse outcomes. The independent predictor of worse RFS on MVA was the presence of positive peritoneal cytology. Conclusion: In this cohort of women with early stage uterine serous carcinoma who underwent surgical staging, adjuvant radiation treatment with or without chemotherapy is associated with improved survival and trended towards improved recurrence rates.

Obstetrics, Gynecology and Women's Health Services

Elshaikh MA, **Aref I**, **Ghanem AI**, **Khalil R**, **Burmeister C**, and **Hanna RK**. Quantification of Recurrence Risk Based on Number of Adverse Prognostic Factors in Women with Early Stage Uterine Endometrioid Carcinoma. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):e499-e500.

Purpose/Objective(s): We sought to quantify the risk of recurrence in women with International Federation of Gynecology and Obstetrics (FIGO) stage I endometrial carcinoma, solely of endometrioid based on the number of adverse prognostic factors Materials/Methods: We identified 1133 women at our institution who underwent a hysterectomy and did not receive any adjuvant therapy between 1/1990 and 12/2019. Cox proportional hazards model was used to identify independent predictors of recurrence. Prognostic groups were created based on the number of independent predictors of recurrence (0, 1 or 2 or 3 risk factors). Results: Median follow-up was 84 months. Independent prognostic factors of recurrence included age ≥ 60, grade 2/3 and the presence of lymphovascular space invasion (LVSI). Due to small number in groups with 2 or 3 risk factors, these were combined into one group (group 2). Isolated vaginal cuff recurrence was the most common site of recurrence in the study groups (81%, 58% and 70% for groups 0, 1 and 2, respectively). Five-year recurrence rates were 4%, 15%, and 43% for groups 0, 1, and 2 ($p<0.001$), respectively. Five-year disease-specific survival were 99%, 96% and 85% and 5-year overall survival were 94%, 85% and 63% ($p<0.001$), respectively. Conclusion: On the basis of 3 well-known prognostic factors, individualized recurrence rate can be predicted in women with stage I endometrial carcinoma. This simplified predictive tool may be helpful in estimating individualized risk of recurrence and guide counseling with regard to adjuvant treatment.

Obstetrics, Gynecology and Women's Health Services

Ghanem AI, **Aref I**, **Khalil R**, **Burmeister C**, **Hanna RK**, and **Elshaikh MA**. Does the Time to Adjuvant Radiotherapy Impact Outcomes in Women With Stage III Uterine Cancer? *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):e478.

Purpose/Objective(s): Adjuvant radiotherapy (ART) combined with chemotherapy (CT) is an effective adjuvant therapy in women with stage III uterine carcinoma (UC). However, there exists a sparse evidence for the optimal time to start ART. We evaluated the impact of time interval to ART initiation on survival endpoints for surgically staged patients with stage III EC receiving adjuvant multimodality therapy. Materials/Methods: We queried our prospectively- maintained database for women with FIGO stage III UC who underwent surgical staging at our institution between 12/1990 and 12/2019. All patients in the study received ART and CT with various sequences. CT consisted of 4-6 cycles of paclitaxel-carboplatin combined with ART (external beam RT (EBRT) ± vaginal brachytherapy (VB) boost). Time to RT initiation (TRTI) elapsing between surgical staging and 1st fraction of ART was calculated in weeks for each patient. We studied the influence of TRTI on relapse- free (RFS), disease- specific (DSS) and overall (OS) survival using log-rank test (continuous) and Kaplan-Meier curves to compare outcomes at weekly increments (8-12 weeks). Clinico-pathological and treatment characteristics were dichotomized at the 8 weeks' time-point and compared. Cox regression multivariate analyses (MVA) were performed to determine independent predictors for survival endpoints. Results: 137 patients were identified. Median age was 64 years (range, 38-85), 45% of patients had non-endometrioid histology. Median number of lymph nodes (LN) examined was 23 (range, 1-55) and median number of positive LN was 2 (range, 0-18). Stage IIIC constituted 78% of the study cohort followed by stage IIIA (20%). 51% of the patients received EBRT alone, while 49% received an additional VB boost. 72 cases (52.5%) received ART ≤8 weeks after hysterectomy, and 47.5% (n = 65) received ART > 8 weeks. After a median follow up of 58 months (CI: 42-66), longer TRTI > 8 weeks was associated with worse 5-year RFS (49% (CI:36-62) vs. 71% (CI:55-83); $p = 0.01$), which persisted at latter time points (9-12 weeks), $p<0.05$ for all; with a trend when assessed as a continuous variable ($p = 0.053$). TRTI was neither correlated with 5-year OS or DSS. On MVA for RFS, TRTI (> vs. ≤ 8 weeks) (HR 2.9 (CI:1.4-6.03); $p = 0.004$), lymphovascular space invasion (HR 4.05; $p = 0.009$) and advanced stage (HR 3.63; $p = 0.04$) were all independent prognostic factors. African American race was the only independently predictive for shorter OS (HR 2.44; $p = 0.002$) and DSS (HR 3.26; $p = 0.006$). Conclusion: Within the context of multimodality therapy, our study suggests that earlier start of ART within 8 weeks was independently associated with improved recurrence- free survival in women with advanced stage endometrial cancer. Multi-institutional research collaboration is needed to validate our results.

Obstetrics, Gynecology and Women's Health Services

Hathout L, Wang Y, **Elshaikh MA**, **Dimitrova I**, Damast S, Li JY, Fields EC, Beriwal S, Keller A, Kidd EA, Usoz M, Jolly S, Jaworski E, Leung EW, Donovan E, Taunk NK, Russo AL, Lea JS, Albuquerque KV, and Lee LJ. Does Sequencing of Adjuvant Therapy Influence Outcome for Stage IIIC Endometrial Carcinoma? A Multi-institutional Analysis. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):S50-S51.

Purpose/Objective(s): In GOG-258, patients who received upfront chemoradiotherapy had more distant relapses compared to those treated with systemic chemotherapy alone, although vaginal and nodal recurrence rates were lower with the addition of adjuvant radiotherapy (RT). Given the importance of both systemic and local therapies, this study evaluates clinical outcomes by the sequence and type of adjuvant therapy for patients with stage IIIC endometrial cancer (EC). Materials/Methods: In a multi-institutional retrospective cohort study, clinical and treatment data from 12 academic centers were collected for patients with stage IIIC EC treated with curative intent. All patients had surgical staging and received chemotherapy and radiation. Adjuvant treatment (AT) regimens were classified as: adjuvant chemotherapy followed by sequential radiation (ACTRT), concurrent chemoradiation followed by chemotherapy (CCTRT), systemic chemotherapy before and after RT (Sandwich), adjuvant RT followed by chemotherapy (ARTCT) or chemotherapy concurrent with vaginal cuff brachytherapy alone (CCTBT). Overall survival (OS) and recurrence-free survival (RFS) rates were estimated by Kaplan-Meier method and covariates were compared by log-rank test. Chi-square tests were used to compare categorical variables. Results: A total of 670 eligible patients were included (Table) with a median follow-up of 44.1 months. The estimated 5-year OS and RFS rates were 71.5% and 65.5%, respectively. On univariate analysis (UVA) for OS, older age, non-white race, non-endometrioid histology, grade 3 tumor, 2 or more positive nodes, adnexal involvement, cervical involvement, stage IIIC2 vs. IIIC1, and in-field recurrence were associated with worse OS (all $p<0.02$). On UVA for RFS, older age, non-endometrioid histology, grade 3 tumor, lymphovascular invasion, adnexal involvement, cervical involvement and stage IIIC2 were associated with recurrence. The sequence and type of adjuvant therapy was not correlated with OS or RFS ($p = 0.08$ and 0.8, respectively). The most common pattern of recurrence was distant metastasis only (66%). Site of first recurrence was significantly different by adjuvant treatment regimen ($p = 0.02$): ACTRT, CCTRT and Sandwich had a higher proportion of distant metastasis whereas ARTCT and CCTBT had more para-aortic nodal recurrences. Pelvic control was highest for ACTRT. Conclusion: The sequence and type of adjuvant therapy did not impact OS or RFS rates, which were comparable to those of the prospective GOG 258 and PORTEC-3 studies. Adjuvant radiotherapy resulted in excellent pelvic control. Most recurrences were distant despite upfront systemic chemotherapy given in most patients, highlighting the need for novel regimens. [Formula presented]

Obstetrics, Gynecology and Women's Health Services

Shah AA, and **Fisher JE**. Concomitant Use of Laparoscopic Radiofrequency Ablation with Hysteroscopic Myomectomy for Large, Multi-Fibroid Uterus. *Journal of Minimally Invasive Gynecology* 2020; 27(7):S99.

A.A. Shah, Obstetrics and Gynecology, William Beaumont Hospital, Royal Oak, MI, United States

Study Objective: To discuss the combination of minimally invasive myomectomy techniques for large multi-fibroid uteri to ensure resolution of all associated symptoms. Design: Case Study. Setting: Suburban hospital, Michigan. Patients or Participants: 37-year-old Caucasian G2P1011. Interventions: 1. Hysteroscopic resectoscope of submucosal fibroid (TruClear) 2. Ultrasound guided laparoscopic radiofrequency ablation (Acessa system) of intramural, subserosal, and broad ligament fibroids Measurements and Main Results: Patient presented with a longstanding history of a bulky, multi-fibroid uterus. Her symptoms included menorrhagia (resulting in anemia), lower abdominal pressure, cramping and back pain. Two prior gynecologists had recommended open hysterectomy given that she had completed childbearing, however she desired uterine conserving surgery. Physical exam revealed a BMI of 24 and a 20-week multi-fibroid uterus. Previous ultrasound noted a multi-fibroid uterus measuring 19 × 14.1 × 8.3 cm and pre-operative MRI demonstrated the largest intramural fibroid to measure 10.9 × 9.1 ×

9.2 cm in the posterior lower uterine segment. A pedunculated submucosal (type 0) fibroid was also identified with significant distortion of the endometrial cavity. She elected to proceed with laparoscopic radiofrequency ablation with ultrasound guidance for the type 4-8 fibroids with concurrent mechanical resection of her submucous fibroid. The procedure was performed without complication and the total operative time was less than 2.5 hours. She was discharged from recovery in good condition. At 6-month follow-up, she noted significant reduction in pain, pressure and cramping, with almost complete resolution of menorrhagia. Conclusion: Uterine sparing concomitant multi-modality surgery can be considered for patients presenting with large fibroids, including those with submucosal fibroids as a cause for their symptoms. Laparoscopic radiofrequency ablation combined with hysteroscopic resection, even for fibroids larger than 8 cm, can provide dramatic relief of menorrhagia, bulk and pain symptoms.

Obstetrics, Gynecology and Women's Health Services
Shah AA, and **Fisher JE**. Ultrasound Guided Laparoscopic Radiofrequency Ablation for Very Large Multi-Fibroid Uterus. *Journal of Minimally Invasive Gynecology* 2020; 27(7):S59-S60.

A.A. Shah, Obstetrics and Gynecology, William Beaumont Hospital, Royal Oak, MI, United States

Study Objective: This video describes the technique and advantages of laparoscopic radiofrequency ablation with ultrasound guidance for the treatment of very large multi-fibroid uteri. Design: N/A Setting: Large tertiary care hospital. Patients or Participants: 45-year-old gravida 2 para 0 female with menorrhagia, dysmenorrhea, and bulk symptoms secondary to a very large multi-fibroid uterus. She desired a minimally invasive and uterine conserving method to treat her symptoms. Interventions: We performed laparoscopic radiofrequency ablation under ultrasound guidance for the patients' multiple fibroids. The uterus was mapped ultrasonographically using the laparoscopic ultrasound transducer. Next, under laparoscopic visualization, the needle handpiece was inserted into the abdomen three centimeters away from the ultrasound transducer insertion point. With careful coordination between visualization on the ultrasound and the laparoscope, the handpiece was directed into specific myomas for ablation with deployment of the needle arrays. This allowed emission of radiofrequency energy to shrink the myoma tissue. The exact depth and total ablation time is calculated for each deployment prior to initiation of the ablation. It is important to note that larger myomas may require multiple overlapping treatments due to their size and density. The procedure was performed in an outpatient setting with an estimated blood loss of less than 10 milliliters. Measurements and Main Results: N/A Conclusion: Laparoscopic radiofrequency ablation for very large multi-fibroid uteri can be successfully performed under ultrasound guidance as a uterine conserving method to treat symptomatic fibroids. The technique has many advantages when compared to other surgical techniques used to treat fibroids, including minimal blood loss, decreased post-operative pain, shorter recovery time, and a potentially narrower learning curve given that advanced laparoscopic suturing skills are not required.

Obstetrics, Gynecology and Women's Health Services
Zhu S, **Khalil R**, **Altairy O**, **Burmeister C**, **Dimitrova I**, and **Elshaikh MA**. The Prognostic Impact of Time Interval Between Hysterectomy and Initiation of Adjuvant Radiation Treatment in Women With Early-Stage Endometrial Carcinoma. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):e472.

Purpose/Objective(s): Adjuvant radiation therapy (ART) is indicated for women with endometrial carcinoma (EC) who are at high risk for recurrence. However, due to various reasons, some patients do not receive ART in a timely manner. In this study, we evaluated the prognostic impact of the time interval (TI) between hysterectomy and starting date of ART. Materials/Methods: After institutional review board approval, we queried our prospectively-maintained institutional database for women with uterine endometrioid EC of 2009 FIGO stages I-II who received ART without chemotherapy after surgical staging. The patients were classified into two groups, based on whether they received ART ≤8 weeks (group A) or >8 weeks (group B) after hysterectomy. We then compared the two groups with regards to the following survival endpoints: recurrence-free survival (RFS), disease-specific survival (DSS) and overall survival (OS). Univariate and multivariate analyses were also performed. Results: A total of 460 patients were identified. Median follow-up duration was 70.5 months. The median age for the entire cohort was 66.0

years. The cohort consisted of 176 patients with FIGO stage IA (38%), 207 (45%) with stage IB and 77 (17%) with stage II. Group A consisted of 354 (77%) patients, and group B had 106 (23%). The median TIs from hysterectomy to ART were 6 weeks and 10 weeks for groups A and B, respectively. There was no statistically significant difference between the groups in terms of baseline demographic and disease characteristics including age, race, grade, FIGO stage, extent of myometrial invasion, presence of lymphovascular space invasion and radiation treatment modality. A total of 52 patients experienced recurrences. Patients in group A (vs. group B) experienced significantly less recurrences overall (9% vs. 18%; p = 0.01). Rate of vaginal recurrence was significantly lower in group A (9% vs. 42%, p = 0.01). Univariate analysis showed that having RT ≤8 weeks was associated with significantly improved 5-year RFS rate, which was 89% and 80% for groups A and B (p = 0.04), respectively. The rates of 5-year OS (86% vs. 85% for groups A and B, respectively) and 5-year DSS (93% vs. 93% for groups A and B, respectively) were similar. In addition, multivariate analysis showed a statistical trend for improved 5-year RFS when receiving RT ≤8 weeks (p = 0.07). Conclusion: Our study suggests that delaying adjuvant radiation treatment beyond 8 weeks post-hysterectomy is associated with significantly more cancer recurrences for women with early-stage endometrial cancer.

Plastic Surgery

Rama S, **Atisha D**, Evangelista M, **Cannella C**, **Barry R**, Ghosh S, **Luker J**, **Chen Y**, Zhu S, **Bensenhaver J**, **Levin KJ**, and **Walker EM**. The Effect of Oncoplastic Reduction on The Incidence of Post-Operative Lymphedema in Breast Cancer Patients Undergoing Lumpectomy. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):e45.

Purpose/Objective(s): In patients with macromastia, breast conservation surgery (BCS) followed by radiation therapy (RT) may be associated with increased radiation exposure and a different complication profile than those without macromastia. The oncoplastic reduction mammoplasty (ORM) procedure includes breast reduction at the time of BCS. The purpose of this study is to determine if women with macromastia who undergo ORM have a different complication profile compared to those who undergo BCS followed by RT. Materials/Methods: We performed a retrospective chart review on patients who underwent lumpectomy with RT from 2014 to 2017. Chronic breast lymphedema (CBL) was defined as swelling that persisted >1-year post-RT. Breast volumes (BV) were determined by contoured breast volumes or, if unavailable, estimated by the 95% isodose volumes from the RT treatment planning system. Univariate analysis was used to evaluate various patient factors and treatment outcomes in women with BV ≥1300 cc compared to <1300 cc. These same factors were compared in women who underwent ORM vs. BCS. Multivariate regression analysis was used to evaluate factors associated with ≥1 complication. Logistic regression was performed to identify factors associated with the development of CBL. Results: The total population included 785 patients, of which 28 (3.6%) underwent ORM and 757 (96.4%) underwent BCS. The total population was stratified into two groups, in which 289 (36.8%) patients had BV ≥1300 cc and 496 (63.2%) patients had a BV <1300 cc. Compared to patients with BV<1300 cc, those with BV ≥1300 cc had a higher percentage of African Americans (52.6% vs. 41.5%, P = 0.002), higher median BMI (34.96 vs. 27.87, P<0.001), higher incidence of diabetes (39.8% vs. 27.2%, P<0.001), higher incidence of hypertension (75.4% vs. 63.1%, P<0.001), and higher incidence of CBL (12.5% vs. 4.2%, P<0.001). Compared to BCS patients, ORM patients with BV ≥1300 cc had increased incidence of CBL (36.4% vs. 11.5%, P = 0.035). Logistic regression showed that the incidence of ≥1 complication was associated with BMI, presence of SLNB, and the number of lymph nodes removed in either SLNB or ALND. However, factors such as ORM and BV were not associated with an increased risk of ≥1 complication. Logistic regression demonstrated that having a BV ≥1300 cc was associated with 2.5 times increased odds of CBL compared to those with BV <1300 cc. Even though those who underwent ORM did not change the risk for CBL for the entire cohort, ORM patients with BV ≥1300 had a higher risk of CBL. Ultimately, logistic regression demonstrates that ORM does not increase the risk of CBL when adjusting for BV. Conclusion: In conclusion, axillary surgery contributed most significantly to the incidence of having ≥1 complication. However, BV was associated with an increased risk of CBL, regardless of the presence of ORM. Therefore, women with BV ≥1300 cc should be offered ORM at the time of lumpectomy in order to reduce their future risk of CBL.

Plastic Surgery

Zhu S, **Atisha D**, **Evangelistia M**, **Barry R**, **Rama S**, Ghosh S, **Cannella C**, **Chen Y**, **Bensenhaver J**, **Levin KJ**, and **Walker EM**. Factors Associated with Chronic Breast Lymphedema After Adjuvant Radiation in Women Undergoing Breast Conservation Therapy. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):e32.

Purpose/Objective(s): Unlike temporary breast edema caused by post-lumpectomy radiation therapy (RT), the edema that persists beyond one year is not well defined and difficult to treat. The aim of this study is to define the incidence and risk factors for the development of chronic breast lymphedema in women undergoing lumpectomy with RT at a large metropolitan cancer center. Materials/Methods: A retrospective chart review was performed on all patients who underwent lumpectomy from 2014 to 2017. Women who did not undergo RT at our institution and those with stage IV disease were excluded from the analysis. Patient demographics, comorbidities, operative data, RT data and postoperative complications were obtained. Chronic breast lymphedema (CBL) was defined as edema that persisted beyond one-year post completion of radiation therapy. Breast volumes were determined by contoured breast volumes or, if unavailable, estimated by the 95% isodose volumes from the RT treatment planning system. Using a density curve, the distribution of breast volumes was plotted for patients with and patients without CBL. Univariate analysis was used to evaluate factors associated with CBL. Multivariate regression analysis was used to evaluate factors associated with the risk of CBL while accounting for potential confounding variables as defined by the univariate analysis. Results: A total of 811 patients were included for analysis. Fifty-seven (7.0%) patients developed breast lymphedema beyond one year. For the entire cohort, mean age was 63.3 years old, mean BMI was 31.21 kg/m2, and mean breast volume was 1195 cc (SD = 643.25 cc). Compared to the cohort that did not develop CBL (n = 754), the CBL cohort (n = 57) had a higher BMI (33.10 kg/m2 vs. 29.84 kg/m2, p<0.001), higher percentage of black race (61.4% vs. 43.8%, P = 0.024), larger breast volume (1504 cc vs. 1081 cc, P<0.001), greater number of lymph nodes taken at time of surgery (3 vs. 1, P<0.001), higher percentage that had underwent ALND (12.3% vs. 5.2%, P = 0.036), and larger size of lumpectomy specimen (118.95 cm3 vs. 96.00 cm3, P = 0.016). The density curve determined that the optimal cutoff for breast volume was around 1300 cc. When accounting for potential confounding variables, multivariate regression analysis revealed that those whose breast volume > 1300 cc (vs. <1300 cc) were 2.5 times more likely to experience breast lymphedema after one year (OR = 2.53, p = 0.005). When volume was evaluated as a continuous variable, regression analysis revealed that for every 1cc increase in breast volume, the risk of breast lymphedema increases by 0.1% (OR = 1.001, P = 0.001). Conclusion: Chronic breast lymphedema presents a clinical concern for women undergoing lumpectomy with postoperative radiation, particularly women with larger breasts. Further studies should focus on preventative strategies, as well as the psychosocial and economic impact of this morbidity.

Public Health Sciences

Cook AE, **Khalil R**, **Burmeister C**, **Dimitrova I**, and **Elshaikh MA**. The Impact of Different Adjuvant Management Strategies on Survival Endpoints in Women with Early Stage Uterine Serous Carcinoma. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):e481.

Purpose/Objective(s): To determine the impact of adjuvant chemotherapy, radiation treatment, combined modality treatment, and observation on survival and recurrence outcomes in women with early stage uterine serous carcinoma (USC). Materials/Methods: After IRB study approval, our prospectively-maintained database for women with endometrial carcinoma was queried for women with 2009 International Federation of Gynecology and Obstetrics (FIGO) stages I-II USC based on WHO pathologic definition who underwent adequate surgical staging between 1/1991 and 4/2017 followed by adjuvant management [observation, radiation therapy (RT), chemotherapy (CT), or combination treatment (CRT)]. Chi-squared tests were performed to compare differences in outcome by type of adjuvant management. Recurrence-free (RFS), disease-specific (DSS), and overall survival (OS) were assessed by Kaplan-Meier and log-rank tests. Univariate and multivariate analyses (MVA) were performed to identify statistically significant predictors of survival endpoints. Results: We identified 171 women who met our inclusion criteria. The median follow-up time was 70.5 months. 75% of the study cohort were with stage IA, 13% stage IB and 12% with stage II. All women underwent pelvic lymph node dissection with a median number of dissected lymph nodes of 14. Omentectomy was performed in 61% of patients. Adjuvant RT was utilized in 56% of women (65 with vaginal brachytherapy alone, 10 with pelvic RT and

21 with combination). Most commonly used chemotherapy was carboplatin and paclitaxel with a median number of cycles of 6 5-year RFS was 73% for those received CRT, 84% for RT alone, 68% who received CT alone and 55% for those who were observed (p = 0.13). 5-year DSS was 81%, 94%, 71% and 60%, respectively (p = 0.02). 5-year OS was 76%, 70%, 60% and 56%, respectively (p = 0.11). On MVA of OS and DSS, higher percentage of myometrial invasion, presence of lower uterine segment involvement, positive peritoneal cytology, and receiving chemotherapy alone/observation were independent predictors of worse outcomes. The independent predictor of worse RFS on MVA was the presence of positive peritoneal cytology. Conclusion: In this cohort of women with early stage uterine serous carcinoma who underwent surgical staging, adjuvant radiation treatment with or without chemotherapy is associated with improved survival and trended towards improved recurrence rates.

Public Health Sciences

Elshaikh MA, **Aref I**, **Ghanem AI**, **Khalil R**, **Burmeister C**, and **Hanna RK**. Quantification of Recurrence Risk Based on Number of Adverse Prognostic Factors in Women with Early Stage Uterine Endometrioid Carcinoma. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):e499-e500.

Purpose/Objective(s): We sought to quantify the risk of recurrence in women with International Federation of Gynecology and Obstetrics (FIGO) stage I endometrial carcinoma, solely of endometrioid based on the number of adverse prognostic factors Materials/Methods: We identified 1133 women at our institution who underwent a hysterectomy and did not receive any adjuvant therapy between 1/1990 and 12/2019. Cox proportional hazards model was used to identify independent predictors of recurrence. Prognostic groups were created based on the number of independent predictors of recurrence (0, 1 or 2 or 3 risk factors). Results: Median follow-up was 84 months. Independent prognostic factors of recurrence included age ≥ 60, grade 2/3 and the presence of lymphovascular space invasion (LVSI). Due to small number in groups with 2 or 3 risk factors, these were combined into one group (group 2). Isolated vaginal cuff recurrence was the most common site of recurrence in the study groups (81%, 58% and 70% for groups 0, 1 and 2, respectively). Five-year recurrence rates were 4%, 15%, and 43% for groups 0, 1, and 2 ($p<0.001$), respectively. Five-year disease-specific survival were 99%, 96% and 85% and 5-year overall survival were 94%, 85% and 63% ($p<0.001$), respectively. Conclusion: On the basis of 3 well-known prognostic factors, individualized recurrence rate can be predicted in women with stage I endometrial carcinoma. This simplified predictive tool may be helpful in estimating individualized risk of recurrence and guide counseling with regard to adjuvant treatment.

Public Health Sciences

Ghanem AI, **Aref I**, **Khalil R**, **Burmeister C**, **Hanna RK**, and **Elshaikh MA**. Does the Time to Adjuvant Radiotherapy Impact Outcomes in Women With Stage III Uterine Cancer? *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):e478.

Purpose/Objective(s): Adjuvant radiotherapy (ART) combined with chemotherapy (CT) is an effective adjuvant therapy in women with stage III uterine carcinoma (UC). However, there exists a sparse evidence for the optimal time to start ART. We evaluated the impact of time interval to ART initiation on survival endpoints for surgically staged patients with stage III EC receiving adjuvant multimodality therapy. Materials/Methods: We queried our prospectively- maintained database for women with FIGO stage III UC who underwent surgical staging at our institution between 12/1990 and 12/2019. All patients in the study received ART and CT with various sequences. CT consisted of 4-6 cycles of paclitaxel-carboplatin combined with ART (external beam RT (EBRT) ± vaginal brachytherapy (VB) boost). Time to RT initiation (TRTI) elapsing between surgical staging and 1st fraction of ART was calculated in weeks for each patient. We studied the influence of TRTI on relapse- free (RFS), disease- specific (DSS) and overall (OS) survival using log-rank test (continuous) and Kaplan-Meier curves to compare outcomes at weekly increments (8-12 weeks). Clinico-pathological and treatment characteristics were dichotomized at the 8 weeks' time-point and compared. Cox regression multivariate analyses (MVA) were performed to determine independent predictors for survival endpoints. Results: 137 patients were identified. Median age was 64 years (range, 38-85), 45% of patients had non-endometrioid histology. Median number of lymph nodes (LN) examined was 23 (range, 1-55) and median number of positive LN was 2 (range, 0-18). Stage IIIC constituted 78% of the study cohort followed by stage IIIA (20%). 51% of the patients received EBRT alone, while 49% received an additional VB boost. 72 cases (52.5%) received ART ≤8 weeks after

hysterectomy, and 47.5% (n = 65) received ART > 8 weeks. After a median follow up of 58 months (CI: 42-66), longer TRTI > 8 weeks was associated with worse 5-year RFS (49% (CI:36-62) vs. 71% (CI:55-83); p = 0.01), which persisted at latter time points (9-12 weeks), p<0.05 for all; with a trend when assessed as a continuous variable (p = 0.053). TRTI was neither correlated with 5-year OS or DSS. On MVA for RFS, TRTI (> vs. ≤ 8 weeks) (HR 2.9 (CI:1.4-6.03); p = 0.004), lymphovascular space invasion (HR 4.05; p = 0.009) and advanced stage (HR 3.63; p = 0.04) were all independent prognostic factors. African American race was the only independently predictive for shorter OS (HR 2.44; p = 0.002) and DSS (HR 3.26; p = 0.006). Conclusion: Within the context of multimodality therapy, our study suggests that earlier start of ART within 8 weeks was independently associated with improved recurrence- free survival in women with advanced stage endometrial cancer. Multi-institutional research collaboration is needed to validate our results.

Public Health Sciences

Gordon SC, **Li J**, Moorman AC, Spradling PR, Teshale EH, Boscarino JA, Daida Y, Schmidt MA, **Zhou YR**, **Rupp LB**, **Trudeau S**, and **Lu M**. PATIENT CHARACTERISTICS AND EFFICACY OF PANGENOTYPIC DIRECT-ACTING ANTIVIRAL REGIMENS AMONG A COHORT OF CHRONIC HEPATITIS C PATIENTS RECEIVING ROUTINE CLINICAL CARE IN THE US. *Hepatology* 2020; 72:540A-541A.

[Gordon, Stuart C.] Henry Ford Hlth Syst, Gastroenterol & Hepatol, Detroit, MI USA. [Gordon, Stuart C.] Wayne State Univ, Sch Med, Med, Detroit, MI 48202 USA. [Li, Jia; Zhou, Yueren; Trudeau, Sheri; Lu, Mei] Henry Ford Hlth Syst, Dept Publ Hlth Sci, Detroit, MI USA. [Moorman, Anne C.; Spradling, Philip R.; Teshale, Eyasu H.] Ctr Dis Control & Prevent, Div Viral Hepatitis, Natl Ctr HIV Hepatitis STD & TB Prevent, Atlanta, GA USA. [Boscarino, Joseph A.] Geisinger Med Clin, Dept Populat Hlth Sci, Danville, PA USA. [Daida, Yihe] Kaiser Permanente Hawaii, Ctr Integrated Hlth Care Res, Honolulu, HI USA. [Schmidt, Mark A.] Kaiser Permanente Northwest, Ctr Integrated Hlth Care Res, Washington, DC USA. [Rupp, Loralee B.] Henry Ford Hlth Syst, Ctr Hlth Policy, Detroit, MI USA. [Rupp, Loralee B.] Henry Ford Hlth Syst, Hlth Serv Res, Detroit, MI USA.

Background: Using recent data from the Chronic Hepatitis Cohort study (CHeCS), we report patient characteristics and “real world” efficacy of three pangenotypic direct-acting antiviral (DAA) regimens used to treat chronic hepatitis C (CHC) patients with a range of HCV genotypes (GT 1-4 and 6) under routine care. Methods: CHeCS CHC patients were followed through mid-2019. Baseline patient characteristics and rates of sustained virological response 12 weeks after end of treatment (SVR12) were compared among the three pangenotypic regimens (SOF/VEL, SOF/VEL/VOX, and GLE/PIB). Results: A total of 1842 patients were included, of which 1019 were treated with SOF/VEL, 753 with GLE/ PIB, and 70 with SOF/VEL/VOX. There were statistically significant differences in patient characteristics among the three groups (p-values <0.05): (1) 46% and 54% of patients treated with SOF/VEL and GLE/PIB were aged 60 years and older, respectively, versus only 25% of those treated with SOF/VEL/VOX; (2) 7% of patients treated with SOF/VEL had decompensated cirrhosis (DCC) while almost none treated with the other regimens had DCC (≤1%); (3) 93% of the SOF/ VEL/VOX-treated group were DAA experienced, compared with only 2-4% in the other treated groups; (4) GT distribution varied among the three regimens (Table). Observed rates of SVR12 were 97%, 98% and 97% with SOF/VEL, GLE/PIB, and SOF/VEL/VOX, respectively, with no significant difference observed (p-values in the range of 0.50 to 0.62 from pairwise comparisons). Among the 48 patients that did not achieve SVR12: (1) 19% were DAA experienced (vs. 6% of those that achieved SVR12); (2) 10% had DCC (vs. 4% of those that achieved SVR12); (3) 21% experienced a toxicity (vs. 11% of those that achieved SVR12); (4) 31% had diabetes and 4% were on proton pump inhibitor therapy at time of DAA initiation (vs. 21% and 1%, respectively, of those that achieved SVR12). Conclusion: Observed rates of SVR12 were very high for all three pangenotypic regimens, with no significant difference between them. A sizeable majority of CHC patients treated with SOF/VEL/VOX and GLE/PIB had GT 1, while the largest proportion of patients treated with SOF/VEL had GT 2. Patients with DCC were mostly treated with SOF/VEL, as would be expected based on treatment guidelines. Patients who did not achieve SVR12 had higher rates of prior DAA experience, DCC, diabetes, and on-treatment toxicities.

Public Health Sciences

Gordon SC, **Rupp LB**, Boscarino JA, Daida Y, Schmidt MA, **Zhou YR**, **Trudeau S**, **Li J**, and **Lu M**. RISK FACTORS FOR SARS-COV-2 INFECTION AMONG PATIENTS WITH CHRONIC VIRAL HEPATITIS. *Hepatology* 2020; 72:299A-300A.

[Gordon, Stuart C.] Henry Ford Hlth Syst, Div Gastroenterol & Hepatol, Detroit, MI USA. [Gordon, Stuart C.] Wayne State Univ, Sch Med, Med, Detroit, MI 48202 USA. [Rupp, Loralee B.] Henry Ford Hlth Syst, Ctr Hlth Policy & Hlth Serv Res, Detroit, MI USA. [Boscarino, Joseph A.] Geisinger Med Clin, Dept Populat Hlth Sci, Detroit, MI USA. [Daida, Yihe] Kaiser Permanente Hawaii, Ctr Integrated Hlth Care Res, Honolulu, HI USA. [Schmidt, Mark A.] Kaiser Permanente Northwest, Ctr Hlth Res, Washington, DC USA. [Zhou, Yueren; Trudeau, Sheri; Li, Jia; Lu, Mei] Henry Ford Hlth Syst, Dept Publ Hlth Sci, Detroit, MI USA.

Background: We investigated factors associated with risk of SARS-CoV-2 infection among an established cohort of chronic hepatitis B and C (CHB/ CHC) patients at a large, vertically integrated health system located in southeastern Michigan (which includes Detroit), a racially-diverse area that experienced a significant outbreak of COVID-19 during March–May 2020. Methods: Patient characteristics and clinical conditions were collected for the period prior to date of first positive SARS-CoV-2 test, or March 11, 2020 for those who were not SARS-CoV-2 infected. Variables included: age; gender; race; insurance type; household income; BMI; CHC vs. CHB; AST; ALT; liver fibrosis status (as measured by APRI/ FIB4); diagnosis of liver cirrhosis; Charlson-Deyo comorbidity index; select individual comorbidities; and history of antiviral therapy. Patients coinfected with both CHB and CHC were excluded. Logistic regression, univariate followed by multivariable modeling, was performed. Variables with p-values <0.05 were retained in the final model. Results: A total of 13,556 patients with a history of chronic viral hepatitis were included; 94 had a positive SARS-CoV-2 result. In univariate comparisons, there was a significant difference between groups (p<0.05) with regard to type of hepatitis infection (C vs. B), age, race, BMI, insurance type, household income, comorbidity index, AST, ALT, APRI, presence of cirrhosis, type 2 diabetes, chronic heart disease, renal disease, peripheral vascular disease, history of receipt of antiviral therapy, and achievement of sustained viral response (CHC). In the final multivariable model, increased risk of SARS-CoV-2 infection was associated with CHC vs CHB (adjusted Odds Ratio [aOR])=4.00, 95% confidence interval [CI] 1.89–8.47), presence of cirrhosis (aOR=1.66, 95%CI 1.08–2.55), normal AST at baseline (aOR=2.50, 95%CI 1.46–4.27), higher comorbidity index (aOR=1.40, 95%CI 1.19–1.67), Black/ African American vs white race (aOR=18.0, CI 6.59–45.5), and BMI (BMI 25–30 vs <25: aOR=3.82, CI 1.95–7.49; BMI >30 vs <25: aOR=2.85, CI 1.46–5.56). Conclusion: In a cohort of chronic viral hepatitis patients drawn from a geographic area that experienced a significant COVID-19 outbreak, Black/ African American race, BMI>25, cirrhosis, CHC (active or post-SVR) vs. CHB, and higher comorbidity index were associated with higher risk of SARS-CoV-2 infection.

Public Health Sciences

Liang E, **Morris ED**, **Vono J**, **Bazan L**, **Lu M**, Modh A, and **Glide-Hurst C**. Coupling Continuous Positive Airway Pressure (CPAP) and MR-guided Radiation Therapy. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):S169.

Purpose/Objective(s): Continuous positive airway pressure (CPAP) is a cost effective and readily available device that increases lung volumes and has shown promise in conventional x-ray-based radiation therapy (RT). However, limited data are available to quantify the impact of CPAP on lung reproducibility due to the use of ionizing radiation during imaging. We propose a novel pilot study combining CPAP with the powerful soft tissue capabilities of MR-guided RT to reduce the amount of radiation exposure to organs at risk, with the overarching goals of quantifying the impact of CPAP on lung stability under free-breathing (FB) and deep inspiration breath-hold (DIBH) conditions and assessing feasibility. Materials/Methods: An MR-safe configuration was devised by affixing several CPAP breathing circuits and verifying pressure maintenance using a manometer. Six healthy volunteers (median age 38, range: 28-54) underwent MRIs of the thorax (25 second TrueFISP, 1.5×1.5×3 mm3 resolution) using a 0.35T MR-Linac. FB and 2 verbally coached DIBH acquisitions were performed at CPAP of 0, 6, 10, 12, and 15 cm H20. To define a mutual coordinate system between successive datasets, automated rigid registration was performed (translations only) based on bony anatomy to the reference condition (FB, CPAP 0 cm H20). To quantify the linear relationship between lung volume and pressure under FB conditions, R2 was estimated for each subject. To study positioning reproducibility that may depend on

increased pressures in the setting of DIBH, a Spearman correlation coefficient was calculated based on the centroid differences in lung volume. A paired t-test was used to compare the difference between pressures of 0, 6, 10, 12, and 15 cm H20. Image quality with and without CPAP under FB conditions were assessed. Surveys about volunteer perceptions of CPAP were administered after initial CPAP tolerability screening and following the imaging session based on a ten-point scale (10 = least tolerable). Results: FB lung volumes increased as CPAP increased ($R2 = 0.85 \pm 0.13$, range: 0.57 to 0.99) with visible reductions in motion artifacts. A significant negative correlation was observed between CPAP and the lung anterior/posterior centroid differences under DIBH, indicating a reduced difference on repeated measures (i.e., increased lung stability) as pressure increased. Paired t-tests showed significantly better reproducibility in lung volumes at pressures of 6, 10, 12, and 15 cm H20, as compared to 0 cm H20. Patient-reported difficulty tolerating CPAP was perceived to be lower after the study session (mean 2.0, range 1-4) than before (mean 2.83, range 1-5). Conclusion: This study confirms that integrating CPAP into MR-guided RT is feasible and well-tolerated. CPAP not only increases lung volumes under FB conditions, but also improves reproducibility of DIBH, offering potential for reducing treatment-related side effects regardless of treatment delivery platform.

Public Health Sciences

Lu M, **Rupp LB**, Boscarino JA, Schmidt MA, Daida Y, **Zhou YR**, **Trudeau S**, **Li J**, and **Gordon SC**. IMPACT OF HISTORY OF CHRONIC VIRAL HEPATITIS AND LIVER FIBROSIS ON RISK OF HOSPITALIZATION AND DEATH AMONG PATIENTS WITH SARS-COV-2 INFECTION. *Hepatology* 2020; 72:280A-281A.

[Lu, Mei; Zhou, Yueren; Trudeau, Sheri; Li, Jia] Henry Ford Hlth Syst, Dept Publ Hlth Sci, Detroit, MI USA. [Rupp, Loralee B.] Henry Ford Hlth Syst, Ctr Hlth Policy & Hlth Serv Res, Detroit, MI USA. [Boscarino, Joseph A.] Geisinger Med Clin, Dept Populat Hlth Sci, Danville, PA USA. [Schmidt, Mark A.] Kaiser Permanente Northwest, Ctr Hlth Res, Washington, DC USA. [Daida, Yihe] Kaiser Permanente Hawaii, Ctr Integrated Hlth Care Res, Honolulu, HI USA. [Gordon, Stuart C.] Henry Ford Hlth Syst, Div Gastroenterol & Hepatol, Detroit, MI USA. [Gordon, Stuart C.] Wayne State Univ, Med, Sch Med, Detroit, MI 48202 USA.

Background: We investigated factors associated with Covid-19 related hospitalization and death among patients with and without a history of chronic viral hepatitis B or C (CHB/CHC) in a single large, integrated health system located in metropolitan Detroit, Michigan, an area that experienced a significant outbreak of SARS-Cov-2 in Spring 2020. Methods: Baseline data were collected before date of first positive SARS-CoV-2 test or Covid-related hospitalization, whichever was earlier. Risk of hospitalization was analyzed with logistic regression; risk of death with Cox regression. Variables with p-values <0.05 were retained in the final multivariable models. Results: Of 6661 patients that tested SARS-CoV-2 positive from March 12–April 26, 2020, 94 (1.4%) had a history of CHB or CHC. A total of 2604 were hospitalized due to Covid-19, 55 (58.5%) with CHB or CHC and 2549 (38.8%) without CHB/CHC. Among hospitalized patients, 10 (18.2%) CHB/CHC patients and 426 (16.7%) non-hepatitis patients died. In multivariable analyses, viral hepatitis was not a risk factor for hospitalization, but approached significance for death (adjusted Hazard Ratio [aHR] 1.82, 95% Confidence Interval [CI] 0.96–3.46). In addition to recognized risk factors for Covid-19 severity such as increasing age, obesity, type 2 diabetes, and multiple co-morbidities, we found that increasing Fibrosis-4 (FIB4) score (a biomarker for liver fibrosis and cirrhosis) was associated with risk of hospitalization (adjusted Odds Ratio [aOR] 95%CI 1.32, 1.16–1.51). African American and male patients were also at higher risk of hospitalization. Notably, a number of risk factors for hospitalization were not associated with or were associated with reduced risk of death among hospitalized patients; African American patients and those with BMI ≥30 had lower mortality than White patients and those with BMI <25 (aHR 0.73, 95%CI 0.60–0.89; and aHR 0.69, 95%CI 0.54–0.88) respectively. Conclusion: Increasing baseline FIB4 index is associated with higher risk of hospitalization among patients with Covid-19. History of CHB or CHC trended toward increased risk of Covid-related mortality; future studies in larger samples of patients with chronic viral hepatitis are warranted.

Public Health Sciences

Naffouj S, **Selim R**, **Shamaa O**, **Ahmed A**, **Zhou YR**, **Rupp LB**, **Jafri SM**, **Gordon SC**, and **Gonzalez HC**. LIVER TRANSPLANT EVALUATION IN THE PETH ERA. *Hepatology* 2020; 72:176A-176A.

[Naffouj, Sandra; Shamaa, Omar] Henry Ford Hlth Syst, Internal Med, Detroit, MI USA. [Selim, Ranya; Jafri, Syed-Mohammed; Gordon, Stuart C.; Gonzalez, Humberto C.] Henry Ford Hlth Syst, Gastroenterol & Hepatol, Detroit, MI USA. [Ahmed, Abdelwahab; Jafri, Syed-Mohammed; Gordon, Stuart C.; Gonzalez, Humberto C.] Wayne State Univ, Sch Med, Detroit, MI 48202 USA. [Zhou, Yueren] Henry Ford Hlth Syst, Dept Publ Hlth Sci, Detroit, MI USA. [Rupp, Loralee B.] Henry Ford Hlth Syst, Ctr Hlth Policy & Hlth Serv Res, Detroit, MI USA.

Background: Phosphatidylethanol (PEth) is a phospholipid formed in the presence of ethanol with a high sensitivity, specificity, and long half-life compared to other alcohol detection tests. PEth has become a key biomarker in liver transplant (LT) evaluation since 2018. We aimed to determine the impact of PEth on the transplant evaluation process and LT waitlist in alcoholic liver disease. Methods: Candidates referred for LT evaluation 1/1/2017 to 11/12/2019 were captured using Organ Transplant Tracking Record at Henry Ford Hospital, Detroit, MI. 2018 evaluations were excluded (testing transition period). Only patients with alcoholic liver disease were included. Patients were divided into pre-PEth (2017) and PEth (2019) eras. Demographics, use of PEth and non-PEth (serum ethanol or urine ethyl glucoronide) testing, Child Pugh/MELD scores, insurance and evaluation termination/delisting reasons were captured. PEth+ was defined as a level >10 ng/dL. Rates of terminations/de-listings were compared between groups using Chi-square. Logistic regression was used to identify factors associated with terminations/de-listings (as a composite outcome). Results: There were 375 evaluations for alcoholic liver disease; 157 in pre-PEth era, 210 in PEth era, and 8 excluded due to loss of follow-up. Patient characteristics are shown in Table 1. There were 72(46%) vs 85(41%) terminations (p=0.321) and 11(7%) vs 2(1%) de-listings in pre-PEth vs PEth eras (p=0.002), respectively. Of the terminations/de-listings, there were 5(7%) due to non-PEth+ in 2017 vs 16(19%) due to PEth+ in 2019 (p=0.069). Odds ratios of terminations/delistings due to alcohol use were 0.36 for black vs white race, 0.43 for employed vs unemployed, 0.52 for Medicare vs Medicaid and 1.37 for commercial insurance vs Medicaid (p=0.069, 0.126, and 0.063 for race, employment status, and insurance, respectively). Conclusion: Our results demonstrate that black race, employment, and commercial or Medicare insurance was associated with lower risk of termination/delisting. There were fewer de-listings in the PEth era. Despite the increased detection of surreptitious alcohol use due to PEth, the rates of termination/delisting for alcohol use were similar. We speculate that our results reflect the use of PEth test as a screening tool prior to transplant referral. Additionally, a recent shift toward a more liberal consideration of a) shorter period of sobriety and/or b) select alcoholic hepatitis patients may explain these findings.

Public Health Sciences

Rama S, **Atisha D**, Evangelista M, **Cannella C**, **Barry R**, Ghosh S, **Luker J**, **Chen Y**, Zhu S, **Bensenhaver J**, **Levin KJ**, and **Walker EM**. The Effect of Oncoplastic Reduction on The Incidence of Post-Operative Lymphedema in Breast Cancer Patients Undergoing Lumpectomy. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):e45.

Purpose/Objective(s): In patients with macromastia, breast conservation surgery (BCS) followed by radiation therapy (RT) may be associated with increased radiation exposure and a different complication profile than those without macromastia. The oncoplastic reduction mammoplasty (ORM) procedure includes breast reduction at the time of BCS. The purpose of this study is to determine if women with macromastia who undergo ORM have a different complication profile compared to those who undergo BCS followed by RT. Materials/Methods: We performed a retrospective chart review on patients who underwent lumpectomy with RT from 2014 to 2017. Chronic breast lymphedema (CBL) was defined as swelling that persisted >1-year post-RT. Breast volumes (BV) were determined by contoured breast volumes or, if unavailable, estimated by the 95% isodose volumes from the RT treatment planning system. Univariate analysis was used to evaluate various patient factors and treatment outcomes in women with BV ≥1300 cc compared to <1300 cc. These same factors were compared in women who underwent ORM vs. BCS. Multivariate regression analysis was used to evaluate factors associated with ≥1 complication. Logistic regression was performed to identify factors associated with the development of CBL. Results: The total population included 785 patients, of which 28 (3.6%) underwent ORM and 757 (96.4%) underwent BCS. The total population was stratified into two groups, in which 289 (36.8%) patients had BV ≥1300 cc and 496 (63.2%) patients had a BV <1300 cc. Compared to patients with

BV<1300 cc, those with BV ≥1300 cc had a higher percentage of African Americans (52.6% vs. 41.5%, P = 0.002), higher median BMI (34.96 vs. 27.87, P<0.001), higher incidence of diabetes (39.8% vs. 27.2%, P<0.001), higher incidence of hypertension (75.4% vs. 63.1%, P<0.001), and higher incidence of CBL (12.5% vs. 4.2%, P<0.001). Compared to BCS patients, ORM patients with BV ≥1300 cc had increased incidence of CBL (36.4% vs. 11.5%, P = 0.035). Logistic regression showed that the incidence of ≥1 complication was associated with BMI, presence of SLNB, and the number of lymph nodes removed in either SLNB or ALND. However, factors such as ORM and BV were not associated with an increased risk of ≥1 complication. Logistic regression demonstrated that having a BV ≥1300 cc was associated with 2.5 times increased odds of CBL compared to those with BV <1300 cc. Even though those who underwent ORM did not change the risk for CBL for the entire cohort, ORM patients with BV ≥1300 had a higher risk of CBL. Ultimately, logistic regression demonstrates that ORM does not increase the risk of CBL when adjusting for BV. Conclusion: In conclusion, axillary surgery contributed most significantly to the incidence of having ≥1 complication. However, BV was associated with an increased risk of CBL, regardless of the presence of ORM. Therefore, women with BV ≥1300 cc should be offered ORM at the time of lumpectomy in order to reduce their future risk of CBL.

Public Health Sciences

Zhu S, **Atisha D**, **Evangelistia M**, **Barry R**, **Rama S**, Ghosh S, **Cannella C**, **Chen Y**, **Bensenhaver J**, **Levin KJ**, and **Walker EM**. Factors Associated with Chronic Breast Lymphedema After Adjuvant Radiation in Women Undergoing Breast Conservation Therapy. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):e32.

Purpose/Objective(s): Unlike temporary breast edema caused by post-lumpectomy radiation therapy (RT), the edema that persists beyond one year is not well defined and difficult to treat. The aim of this study is to define the incidence and risk factors for the development of chronic breast lymphedema in women undergoing lumpectomy with RT at a large metropolitan cancer center. Materials/Methods: A retrospective chart review was performed on all patients who underwent lumpectomy from 2014 to 2017. Women who did not undergo RT at our institution and those with stage IV disease were excluded from the analysis. Patient demographics, comorbidities, operative data, RT data and postoperative complications were obtained. Chronic breast lymphedema (CBL) was defined as edema that persisted beyond one-year post completion of radiation therapy. Breast volumes were determined by contoured breast volumes or, if unavailable, estimated by the 95% isodose volumes from the RT treatment planning system. Using a density curve, the distribution of breast volumes was plotted for patients with and patients without CBL. Univariate analysis was used to evaluate factors associated with CBL. Multivariate regression analysis was used to evaluate factors associated with the risk of CBL while accounting for potential confounding variables as defined by the univariate analysis. Results: A total of 811 patients were included for analysis. Fifty-seven (7.0%) patients developed breast lymphedema beyond one year. For the entire cohort, mean age was 63.3 years old, mean BMI was 31.21 kg/m2, and mean breast volume was 1195 cc (SD = 643.25 cc). Compared to the cohort that did not develop CBL (n = 754), the CBL cohort (n = 57) had a higher BMI (33.10 kg/m2 vs. 29.84 kg/m2, p<0.001), higher percentage of black race (61.4% vs. 43.8%, P = 0.024), larger breast volume (1504 cc vs. 1081 cc, P<0.001), greater number of lymph nodes taken at time of surgery (3 vs. 1, P<0.001), higher percentage that had underwent ALND (12.3% vs. 5.2%, P = 0.036), and larger size of lumpectomy specimen (118.95 cm3 vs. 96.00 cm3, P = 0.016). The density curve determined that the optimal cutoff for breast volume was around 1300 cc. When accounting for potential confounding variables, multivariate regression analysis revealed that those whose breast volume > 1300 cc (vs. <1300 cc) were 2.5 times more likely to experience breast lymphedema after one year (OR = 2.53, p = 0.005). When volume was evaluated as a continuous variable, regression analysis revealed that for every 1cc increase in breast volume, the risk of breast lymphedema increases by 0.1% (OR = 1.001, P = 0.001). Conclusion: Chronic breast lymphedema presents a clinical concern for women undergoing lumpectomy with postoperative radiation, particularly women with larger breasts. Further studies should focus on preventative strategies, as well as the psychosocial and economic impact of this morbidity.

Public Health Sciences

Zhu S, **Khalil R**, **Altairy O**, **Burmeister C**, **Dimitrova I**, and **Elshaikh MA**. The Prognostic Impact of Time Interval Between Hysterectomy and Initiation of Adjuvant Radiation Treatment in Women With

Early-Stage Endometrial Carcinoma. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):e472.

Purpose/Objective(s): Adjuvant radiation therapy (ART) is indicated for women with endometrial carcinoma (EC) who are at high risk for recurrence. However, due to various reasons, some patients do not receive ART in a timely manner. In this study, we evaluated the prognostic impact of the time interval (TI) between hysterectomy and starting date of ART. Materials/Methods: After institutional review board approval, we queried our prospectively-maintained institutional database for women with uterine endometrioid EC of 2009 FIGO stages I-II who received ART without chemotherapy after surgical staging. The patients were classified into two groups, based on whether they received ART ≤8 weeks (group A) or >8 weeks (group B) after hysterectomy. We then compared the two groups with regards to the following survival endpoints: recurrence-free survival (RFS), disease-specific survival (DSS) and overall survival (OS). Univariate and multivariate analyses were also performed. Results: A total of 460 patients were identified. Median follow-up duration was 70.5 months. The median age for the entire cohort was 66.0 years. The cohort consisted of 176 patients with FIGO stage IA (38%), 207 (45%) with stage IB and 77 (17%) with stage II. Group A consisted of 354 (77%) patients, and group B had 106 (23%). The median TIs from hysterectomy to ART were 6 weeks and 10 weeks for groups A and B, respectively. There was no statistically significant difference between the groups in terms of baseline demographic and disease characteristics including age, race, grade, FIGO stage, extent of myometrial invasion, presence of lymphovascular space invasion and radiation treatment modality. A total of 52 patients experienced recurrences. Patients in group A (vs. group B) experienced significantly less recurrences overall (9% vs. 18%; p = 0.01). Rate of vaginal recurrence was significantly lower in group A (9% vs. 42%, p = 0.01). Univariate analysis showed that having RT ≤8 weeks was associated with significantly improved 5-year RFS rate, which was 89% and 80% for groups A and B (p = 0.04), respectively. The rates of 5-year OS (86% vs. 85% for groups A and B, respectively) and 5-year DSS (93% vs. 93% for groups A and B, respectively) were similar. In addition, multivariate analysis showed a statistical trend for improved 5-year RFS when receiving RT ≤8 weeks (p = 0.07). Conclusion: Our study suggests that delaying adjuvant radiation treatment beyond 8 weeks post-hysterectomy is associated with significantly more cancer recurrences for women with early-stage endometrial cancer.

Pulmonary and Critical Care Medicine

Liang E, **Morris ED**, **Vono J**, **Bazan L**, **Lu M**, Modh A, and **Glide-Hurst C**. Coupling Continuous Positive Airway Pressure (CPAP) and MR-guided Radiation Therapy. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):S169.

Purpose/Objective(s): Continuous positive airway pressure (CPAP) is a cost effective and readily available device that increases lung volumes and has shown promise in conventional x-ray-based radiation therapy (RT). However, limited data are available to quantify the impact of CPAP on lung reproducibility due to the use of ionizing radiation during imaging. We propose a novel pilot study combining CPAP with the powerful soft tissue capabilities of MR-guided RT to reduce the amount of radiation exposure to organs at risk, with the overarching goals of quantifying the impact of CPAP on lung stability under free-breathing (FB) and deep inspiration breath-hold (DIBH) conditions and assessing feasibility. Materials/Methods: An MR-safe configuration was devised by affixing several CPAP breathing circuits and verifying pressure maintenance using a manometer. Six healthy volunteers (median age 38, range: 28-54) underwent MRIs of the thorax (25 second TrueFISP, 1.5×1.5×3 mm3 resolution) using a 0.35T MR-Linac. FB and 2 verbally coached DIBH acquisitions were performed at CPAP of 0, 6, 10, 12, and 15 cm H20. To define a mutual coordinate system between successive datasets, automated rigid registration was performed (translations only) based on bony anatomy to the reference condition (FB, CPAP 0 cm H20). To quantify the linear relationship between lung volume and pressure under FB conditions, R2 was estimated for each subject. To study positioning reproducibility that may depend on increased pressures in the setting of DIBH, a Spearman correlation coefficient was calculated based on the centroid differences in lung volume. A paired t-test was used to compare the difference between pressures of 0, 6, 10, 12, and 15 cm H20. Image quality with and without CPAP under FB conditions were assessed. Surveys about volunteer perceptions of CPAP were administered after initial CPAP tolerability screening and following the imaging session based on a ten-point scale (10 = least tolerable). Results: FB lung volumes increased as CPAP increased (R2 = 0.85 ± 0.13, range: 0.57 to 0.99) with visible reductions

in motion artifacts. A significant negative correlation was observed between CPAP and the lung anterior/posterior centroid differences under DIBH, indicating a reduced difference on repeated measures (i.e., increased lung stability) as pressure increased. Paired t-tests showed significantly better reproducibility in lung volumes at pressures of 6, 10, 12, and 15 cm H20, as compared to 0 cm H20. Patient-reported difficulty tolerating CPAP was perceived to be lower after the study session (mean 2.0, range 1-4) than before (mean 2.83, range 1-5). Conclusion: This study confirms that integrating CPAP into MR-guided RT is feasible and well-tolerated. CPAP not only increases lung volumes under FB conditions, but also improves reproducibility of DIBH, offering potential for reducing treatment-related side effects regardless of treatment delivery platform.

Radiation Oncology
Boike TP, Hochstedler K, **Movsas B**, Stevens CW, Kestin LL, Devisetty K, Dominello MM, Grills IS, Laucis AM, Matuszak MM, Hayman JA, Paximadis P, Schipper M, and Jolly S. Predictors of Early Death or Hospice in Curative Inoperable Lung Cancer Patients. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):e120.

Purpose/Objective(s): The current treatment approach for inoperable stage II-III non-small cell lung cancer (NSCLC) involves aggressive chemo/radiotherapy (CRT). While outcomes have improved with immunotherapy, some patients transition to hospice or die early into their treatment. To help identify these patients and tailor treatment interventions, we developed a predictive model for early poor outcomes in this population. Materials/Methods: We included patients who received definitive CRT for stage II-III lung cancer from April 2012 - November 2019. Patient information was collected prospectively as part of a statewide consortium involving 27 sites. We defined an early poor outcome as termination of treatment due to hospice enrollment or death within 5 months of initiating radiation therapy. Potential predictors included patient and disease characteristics, patient reported outcomes (PROs), and treatment variables. Generalized linear models were used to describe the relationships between single predictors and outcomes of interest. Due to missing data, we imputed 25 datasets to fit multivariable models. We used Lasso regression on all 25 datasets to select variables of interest. Using these selected variables, we fit generalized linear models on all 25 imputed data sets and present pooled results. Results: A total of 2127 patients met criteria, of which 96 patients discontinued treatment early due to hospice enrollment or death. Of the 96 patients, 59% received concurrent chemotherapy and the mean age was 71 years old. When modeled individually, age, ECOG performance status, PTV volume, distance to critical structures, mean heart dose, insurance status, functional and physical well-being scale, and lung cancer symptom scale were all significant predictors of early hospice or death. Additionally, specific PRO questions, including “I have a lack of energy”, “I have been coughing”, and “I have been short of breath” were significant univariable predictors. Gender, marital status, baseline FEV1, treatment center, lung radiation dose (V5, V20, mean), and esophageal dose (D2cc) were not significant univariable predictors. Our Lasso procedure selected the following predictors for multivariable analysis: age, ECOG performance status, PTV volume, patient reported lack of energy, patient reported cough, mean heart dose, and patient insurance status. The pooled estimate of AUC for this multivariable model was 0.71. Conclusion: Our models identified a combination of initial patient, disease and treatment characteristics, and PROs that may help identify individuals undergoing curative CRT who are at high risk of early hospice enrollment or death. Further research to determine if interventions for this group (e.g. treatment modifications, supportive care) may help improve patients’ outcomes.

Radiation Oncology
Cook AE, **Khalil R**, **Burmeister C**, **Dimitrova I**, and **Elshaikh MA**. The Impact of Different Adjuvant Management Strategies on Survival Endpoints in Women with Early Stage Uterine Serous Carcinoma. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):e481.

Purpose/Objective(s): To determine the impact of adjuvant chemotherapy, radiation treatment, combined modality treatment, and observation on survival and recurrence outcomes in women with early stage uterine serous carcinoma (USC). Materials/Methods: After IRB study approval, our prospectively-maintained database for women with endometrial carcinoma was queried for women with 2009 International Federation of Gynecology and Obstetrics (FIGO) stages I-II USC based on WHO pathologic definition who underwent adequate surgical staging between 1/1991 and 4/2017 followed by adjuvant

management [observation, radiation therapy (RT), chemotherapy (CT), or combination treatment (CRT)]. Chi-squared tests were performed to compare differences in outcome by type of adjuvant management. Recurrence-free (RFS), disease-specific (DSS), and overall survival (OS) were assessed by Kaplan-Meier and log-rank tests. Univariate and multivariate analyses (MVA) were performed to identify statistically significant predictors of survival endpoints. Results: We identified 171 women who met our inclusion criteria. The median follow-up time was 70.5 months. 75% of the study cohort were with stage IA, 13% stage IB and 12% with stage II. All women underwent pelvic lymph node dissection with a median number of dissected lymph nodes of 14. Omentectomy was performed in 61% of patients. Adjuvant RT was utilized in 56% of women (65 with vaginal brachytherapy alone, 10 with pelvic RT and 21 with combination). Most commonly used chemotherapy was carboplatin and paclitaxel with a median number of cycles of 6 5-year RFS was 73% for those received CRT, 84% for RT alone, 68% who received CT alone and 55% for those who were observed ($p = 0.13$). 5-year DSS was 81%, 94%, 71% and 60%, respectively ($p = 0.02$). 5-year OS was 76%, 70%, 60% and 56%, respectively ($p = 0.11$). On MVA of OS and DSS, higher percentage of myometrial invasion, presence of lower uterine segment involvement, positive peritoneal cytology, and receiving chemotherapy alone/observation were independent predictors of worse outcomes. The independent predictor of worse RFS on MVA was the presence of positive peritoneal cytology. Conclusion: In this cohort of women with early stage uterine serous carcinoma who underwent surgical staging, adjuvant radiation treatment with or without chemotherapy is associated with improved survival and trended towards improved recurrence rates.

Radiation Oncology

Devisetty K, Griffith K, Boike TP, Moran JM, Radawski J, Nettleton JL, Dilworth JT, **Walker EM**, Hayman JA, Jagsi R, Pierce LJ, and Vicini FA. Trends in Close Margin Status and Radiation Therapy Boost in Early Stage Breast Cancer Treated with Breast Conserving Therapy. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):e37-e38.

Purpose/Objective(s): The Society of Surgical Oncology and American Society for Radiation Oncology released a consensus statement in 2014 (later endorsed by Choosing Wisely in 2016) recommending “no tumor on ink” as an adequate margin for breast cancer treated with lumpectomy. This guideline targeted patients with close margins (CM, i.e. 2 mm or less) in order to decrease rates of re-excision, improve cosmetic outcomes, and decrease costs. We hypothesize that a consequence of this policy would be an increased rate of CM and corresponding increase in radiation therapy boost (RTB) utilization to compensate. Materials/Methods: A statewide, multi-institutional consortium of up to 26 academic and community clinics prospectively collected patient level data from 2012 – 2019 of breast cancer patients treated with breast conserving therapy. For this analysis, inclusion criteria included T0-3 disease, lumpectomy for initial surgical management, pathologic margin of 2 mm or less, and use of adjuvant radiation therapy (either conventional [CFX] or accelerated [AFX] fractionation with or without boost). Chi-square testing was used to compare time periods. Results: A total of 12,499 pts were in the database from which CM was identified in 383/2480 DCIS pts (15.4%) and 1110/10019 carcinoma pts (11.1%). Comparing pre- and post- Choosing Wisely endorsement (2012-2016 vs. 2017-2019), rates of CM decreased for both DCIS and carcinoma (13.9% vs. 9.5%, $p<0.0001$) as did overall rates of RTB (84.1% vs. 79.8%, $p<0.0001$). However, trends in RTB differed based on fractionation: CFX was stable (94.1% vs. 94.2%, $p = 0.0862$) whereas AFX had increased (69.2% vs. 74.2%, $p<0.0001$). RTB for the CM subset (CFX and AFX) were steady over these time periods. Conclusion: Despite a loosening of margin requirements through consensus guidelines and campaigns, there has actually been a decrease in both rates of CM and overall RTB. Trends in RTB differed by fractionation (CFX stable, AFX increase) which were independent of rates of CM. [Formula presented]

Radiation Oncology

Elshaikh MA, **Aref I**, **Ghanem AI**, **Khalil R**, **Burmeister C**, and **Hanna RK**. Quantification of Recurrence Risk Based on Number of Adverse Prognostic Factors in Women with Early Stage Uterine Endometrioid Carcinoma. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):e499-e500.

Purpose/Objective(s): We sought to quantify the risk of recurrence in women with International Federation of Gynecology and Obstetrics (FIGO) stage I endometrial carcinoma, solely of endometrioid based on the number of adverse prognostic factors Materials/Methods: We identified 1133 women at our institution who

underwent a hysterectomy and did not receive any adjuvant therapy between 1/1990 and 12/2019. Cox proportional hazards model was used to identify independent predictors of recurrence. Prognostic groups were created based on the number of independent predictors of recurrence (0, 1 or 2 or 3 risk factors). Results: Median follow-up was 84 months. Independent prognostic factors of recurrence included age ≥ 60, grade 2/3 and the presence of lymphovascular space invasion (LVSI). Due to small number in groups with 2 or 3 risk factors, these were combined into one group (group 2). Isolated vaginal cuff recurrence was the most common site of recurrence in the study groups (81%, 58% and 70% for groups 0, 1 and 2, respectively). Five-year recurrence rates were 4%, 15%, and 43% for groups 0, 1, and 2 ($p<0.001$), respectively. Five-year disease-specific survival were 99%, 96% and 85% and 5-year overall survival were 94%, 85% and 63% ($p<0.001$), respectively. Conclusion: On the basis of 3 well-known prognostic factors, individualized recurrence rate can be predicted in women with stage I endometrial carcinoma. This simplified predictive tool may be helpful in estimating individualized risk of recurrence and guide counseling with regard to adjuvant treatment.

Radiation Oncology

Feldman AM, **Dai Z**, **Zong W**, **Pantelic M**, **Elshaikh MA**, and **Wen N**. Utilizing Semi-Supervised Learning and Image Matting in Combination With Mask R-CNN for Accurate Dominant Intraprostatic Lesion Identification and Segmentation on Multiparametric-MRI. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):e257.

Purpose/Objective(s): Identification of the dominant intraprostatic lesion (DIL) using multiparametric-MRI (mp-MRI) can aid clinicians in the diagnosis, risk stratification, staging and therapeutic options in men with prostate cancer. Deep-learning based segmentation models such as Mask R-CNN are an emerging modality capable of identification and auto-segmentation of these lesions. However, model generation is limited by relatively sparse annotated data and anatomic challenges such as the ambiguous transition zone between the DIL and normal prostate tissue. Here we used a Mask R-CNN backbone in combination with semi-supervised training and image matting in an effort to overcome these limitations and achieve accurate segmentation of the DIL. Materials/Methods: A total of 244 patients, split into 2 cohorts, with biopsy proven prostate adenocarcinoma and mp-MRI imaging, were reviewed. Cohort 1 included 202 patients from the SPIE-AAPM-NCI Prostate MR Gleason Grade Group Challenge (PROSTATEx-2 Challenge). Cohort 2 included 42 patients from our institution. All patients in cohort 2 and 96 patients in cohort 1 had the DIL annotated by two experienced clinicians from our institution on T2-weighted imaging (T2WI) to establish the ground truth. Apparent diffusion coefficient mapping was rigidly registered to T2WI. A base Mask R-CNN model was trained in a supervised fashion using 84 annotated patients gathered from both cohorts. The base model with the most confident label was then used to predict 106 cohort 1 patients without annotations. The 84 annotated patients and 106 self-annotated patients were then used as the training set to train a semi-supervised model. Finally, image matting was applied as a post-processing approach to refine the boundaries of detected lesions. Ten annotated cohort 1 patients were used as the validation set and 23 and 21 cohort 1 and cohort 2 patients, respectively, were used as the testing set. Dice similarity coefficient (DSC) and the 95th percentile Hausdorff distance (95 HD) were used as evaluation metrics. We defined agreement as the degree to which a model's predictions concurred with the ground truth annotations. Results: The DSC, 95HD (mm) and agreement for the validation on the base model were 0.659 ± 0.105, 3.75 ± 1.40, and 90.0%, respectively. For the testing set on the base model, these results were 0.564 ± 0.153, 4.52 ± 2.16 and 78.6%, respectively. When applying the semi-supervised model, the DSC, 95HD (mm) and agreement were 0.635 ± 0.142, 4.31 ± 1.34 and 100.0% for the validation set and 0.585 ± 0.146, 4.83 ± 2.53 and 76.8% on the testing set. Using image mapping, these values were increased to 0.725 ± 0.116, 3.70 ± 1.09, 100%; and 0.672 ± 0.123, 4.18 ± 1.97, 76.8% on validation and testing sets, respectively. Conclusion: Semi-supervised learning offered limited improvements when applied to the Mask R-CNN backbone model. However, image matting proved to be a powerful tool in improving the segmentation of the DIL.

Radiation Oncology

Gartrelle KJ, **Schaff EM**, **Kirsch C**, **Kwon D**, **Ajlouni M**, **Khan G**, **Shah R**, **Dobrosotskaya I**, **Parikh PJ**, and **Siddiqui F**. Racial Disparities Among Pancreatic Adenocarcinoma Patients: A Retrospective Survival Analysis of Non-Metastatic Pancreatic Cancer Patients. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):e431.

Purpose/Objective(s): It is predicted that in 2020, approximately 57,600 individuals will be diagnosed with pancreatic cancer (PaC). Based on SEER database analysis, there are conflicting opinions in literature about the overall treatment and outcomes in African-American patients with PaC. The purpose of this study was to determine if there was a racial disparity in overall survival rates between African Americans (AAs) and non-African Americans (non-AAs) diagnosed with PaC who received neoadjuvant radiation therapy (RT) in a tertiary-care cancer center with an established multi-disciplinary PaC tumor board and clinic. Materials/Methods: An IRB-approved retrospective chart analysis was completed on 100 patients who were diagnosed with pancreatic adenocarcinoma and treated with neoadjuvant RT between 2017-2019. Patients who were deemed resectable, borderline resectable (BR), or locally advanced/unresectable (LA) at initial diagnosis were included in the analysis. The following baseline characteristics were collected for each patient: staging, gender, age and ECOG score at initial diagnosis, tumor site and size, clinical T and N stage, CA19-9, and treatment variables (i.e., surgery, chemotherapy, and RT type). Overall survival was calculated from the RT start date. In order to identify any baseline differences among the AA group and the non-AA group, a two-sample t-test and Chi-square were employed. A log-rank test and Kaplan-Meier were used to determine any differences in overall survival among the two groups. Results: Of the 100 patients included in the analysis, 25 were AA and 58 were female. There were 17 (68%) BR and 8 (32%) LA patients in the AA group. In the non-AA group, there were 2 (3%) resectable, 47 (63%) BR, and 26 (35%) LA patients. There were no statistically significant differences detected in any of the baseline characteristics except a trend for increased CA19-9 values of 399.8 U/mL for AAs and 229 U/mL for non-AAs. There was no statistically significant difference in receipt of chemotherapy and RT between the two groups. The estimated median survival rates were 11.5 months for non-AAs and 8.4 months for AAs. One-year overall survival was 45% for AAs versus 48% for non-AAs ($p = 0.57$). Conclusion: There was no difference in overall survival among AAs and non-AAs who received neoadjuvant RT+/- chemotherapy for PaC at our institution between 2017-2019. Contrary to previous publications based on large SEER database analysis, there does not appear to be any difference in overall survival based on race if patients receive treatment in a comprehensive multi-disciplinary collaborative center.

Radiation Oncology

Ghanem AI, **Aref I**, **Khalil R**, **Burmeister C**, **Hanna RK**, and **Elshaikh MA**. Does the Time to Adjuvant Radiotherapy Impact Outcomes in Women With Stage III Uterine Cancer? *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):e478.

Purpose/Objective(s): Adjuvant radiotherapy (ART) combined with chemotherapy (CT) is an effective adjuvant therapy in women with stage III uterine carcinoma (UC). However, there exists a sparse evidence for the optimal time to start ART. We evaluated the impact of time interval to ART initiation on survival endpoints for surgically staged patients with stage III EC receiving adjuvant multimodality therapy. Materials/Methods: We queried our prospectively- maintained database for women with FIGO stage III UC who underwent surgical staging at our institution between 12/1990 and 12/2019. All patients in the study received ART and CT with various sequences. CT consisted of 4-6 cycles of paclitaxel-carboplatin combined with ART (external beam RT (EBRT) ± vaginal brachytherapy (VB) boost). Time to RT initiation (TRTI) elapsing between surgical staging and 1st fraction of ART was calculated in weeks for each patient. We studied the influence of TRTI on relapse- free (RFS), disease- specific (DSS) and overall (OS) survival using log-rank test (continuous) and Kaplan-Meier curves to compare outcomes at weekly increments (8-12 weeks). Clinico-pathological and treatment characteristics were dichotomized at the 8 weeks' time-point and compared. Cox regression multivariate analyses (MVA) were performed to determine independent predictors for survival endpoints. Results: 137 patients were identified. Median age was 64 years (range, 38-85), 45% of patients had non-endometrioid histology. Median number of lymph nodes (LN) examined was 23 (range, 1-55) and median number of positive LN was 2 (range, 0-18). Stage IIIC constituted 78% of the study cohort followed by stage IIIA (20%). 51% of the patients received EBRT alone, while 49% received an additional VB boost. 72 cases (52.5%) received ART ≤8 weeks after hysterectomy, and 47.5% ($n = 65$) received ART > 8 weeks. After a median follow up of 58 months (CI: 42-66), longer TRTI > 8 weeks was associated with worse 5-year RFS (49% (CI:36-62) vs. 71% (CI:55-83); $p = 0.01$), which persisted at latter time points (9-12 weeks), $p<0.05$ for all; with a trend when assessed as a continuous variable ($p = 0.053$). TRTI was neither correlated with 5-year OS or DSS. On

MVA for RFS, TRTI (> vs. ≤ 8 weeks) (HR 2.9 (CI:1.4-6.03); p = 0.004), lymphovascular space invasion (HR 4.05; p = 0.009) and advanced stage (HR 3.63; p = 0.04) were all independent prognostic factors. African American race was the only independently predictive for shorter OS (HR 2.44; p = 0.002) and DSS (HR 3.26; p = 0.006). Conclusion: Within the context of multimodality therapy, our study suggests that earlier start of ART within 8 weeks was independently associated with improved recurrence- free survival in women with advanced stage endometrial cancer. Multi-institutional research collaboration is needed to validate our results.

Radiation Oncology

Hathout L, Wang Y, **Elshaikh MA**, **Dimitrova I**, Damast S, Li JY, Fields EC, Beriwal S, Keller A, Kidd EA, Usoz M, Jolly S, Jaworski E, Leung EW, Donovan E, Taunk NK, Russo AL, Lea JS, Albuquerque KV, and Lee LJ. Does Sequencing of Adjuvant Therapy Influence Outcome for Stage IIIC Endometrial Carcinoma? A Multi-institutional Analysis. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):S50-S51.

Purpose/Objective(s): In GOG-258, patients who received upfront chemoradiotherapy had more distant relapses compared to those treated with systemic chemotherapy alone, although vaginal and nodal recurrence rates were lower with the addition of adjuvant radiotherapy (RT). Given the importance of both systemic and local therapies, this study evaluates clinical outcomes by the sequence and type of adjuvant therapy for patients with stage IIIC endometrial cancer (EC). Materials/Methods: In a multi-institutional retrospective cohort study, clinical and treatment data from 12 academic centers were collected for patients with stage IIIC EC treated with curative intent. All patients had surgical staging and received chemotherapy and radiation. Adjuvant treatment (AT) regimens were classified as: adjuvant chemotherapy followed by sequential radiation (ACTRT), concurrent chemoradiation followed by chemotherapy (CCTRT), systemic chemotherapy before and after RT (Sandwich), adjuvant RT followed by chemotherapy (ARTCT) or chemotherapy concurrent with vaginal cuff brachytherapy alone (CCTBT). Overall survival (OS) and recurrence-free survival (RFS) rates were estimated by Kaplan-Meier method and covariates were compared by log-rank test. Chi-square tests were used to compare categorical variables. Results: A total of 670 eligible patients were included (Table) with a median follow-up of 44.1 months. The estimated 5-year OS and RFS rates were 71.5% and 65.5%, respectively. On univariate analysis (UVA) for OS, older age, non-white race, non-endometrioid histology, grade 3 tumor, 2 or more positive nodes, adnexal involvement, cervical involvement, stage IIIC2 vs. IIIC1, and in-field recurrence were associated with worse OS (all p<0.02). On UVA for RFS, older age, non-endometrioid histology, grade 3 tumor, lymphovascular invasion, adnexal involvement, cervical involvement and stage IIIC2 were associated with recurrence. The sequence and type of adjuvant therapy was not correlated with OS or RFS (p = 0.08 and 0.8, respectively). The most common pattern of recurrence was distant metastasis only (66%). Site of first recurrence was significantly different by adjuvant treatment regimen (p = 0.02): ACTRT, CCTRT and Sandwich had a higher proportion of distant metastasis whereas ARTCT and CCTBT had more para-aortic nodal recurrences. Pelvic control was highest for ACTRT. Conclusion: The sequence and type of adjuvant therapy did not impact OS or RFS rates, which were comparable to those of the prospective GOG 258 and PORTEC-3 studies. Adjuvant radiotherapy resulted in excellent pelvic control. Most recurrences were distant despite upfront systemic chemotherapy given in most patients, highlighting the need for novel regimens. [Formula presented]

Radiation Oncology

Janic B, Neff R, **Brown SL**, Liu F, Mao G, **Chetty IJ**, **Movsas B**, and **Wen N**. Radiation and Gold Nanoparticle Immunomodulation in MDA MB 231 Mouse Breast Cancer Model. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):e545-e546.

Purpose/Objective(s): In recent years, radiation therapy (RT) has been evidenced to stimulate immune tumor rejection through immunomodulation of the tumor microenvironment (TME). One of the RT immunomodulation mechanisms include immunogenic cell death (ICD) that plays a major role in stimulating host anti-cancer immune response and can determine the success of cancer RT. The main feature of ICD is the release of immunogenic molecules by dying cells, termed damage associated molecular patterns (DAMPs) that act on innate and adaptive immune components to induce long-lasting antitumor immunity. Calreticulin (CRT) is a DAMPs molecule involved in phagocytosis and dendritic cell

antigen presentation. In breast cancer (BC) calreticulin pronounced expression was associated with tumor metastatic potential and size. Therefore, DAMPs are being studied for their therapeutic and prognostic potential. As RT, either alone or in combination, is often part of standard BC therapies, the effect of RT and radiosensitizers (such as gold nanoparticles (AuNP)) on DAMPs expression must be considered when designing new protocols, especially if combining RT with an adjuvant mode such as immunotherapy. The goal of this study was to measure the effect of radiation on CRT expression and associated macrophage infiltration in the presence and absence of a novel AuNP radiosensitizer in MDA MB 231 BC mouse models. We hypothesize that AuNP modulates RT induced immunological changes such as increase in CRT expression and infiltration by F4/80 positive macrophages. Materials/Methods: Female nude mice bearing MDA MB 231 tumors received intratumoral injections of 4nm or 14 nm AuNPs. After 24h mice were irradiated with 15 Gy dose using 160 kV photons. Mice were euthanized, histological sections prepared, stained with anti CRT and anti F4/80 antibodies and analyzed by light microscopy. Results: In animals receiving RT or 14 nm AuNP only, CRT and F4/80 expression exhibited trend in increase relative to control but did not reach the significance. However, after the combined RT and AuNP (4nm or 14nm) treatment, CRT expression was further increased and reached the significance, compared to controls. However, F4/80 expression was significantly increased only in animals receiving the combination of RT and 14 nm AuNP, compared to controls (Table 1). Conclusion: In BC patients, induction of ICD may play a critical role in improving clinical outcomes. Here we show that AuNP enhanced the immunogenic effect of a single RT dose in BC mouse model. This effect was measured by an increase in the expression of CRT and F4/80, an indicator of macrophage infiltration. These findings support the role of immunological mechanisms in BC depends and provide a platform for designing multimodal BC RT formulations with novel radiosensitizers or immunotherapy. [Formula presented]

Radiation Oncology

Kim J, Bassetti MF, Raldow A, Low D, Lee P, Green OL, Chuong MD, and **Parikh PJ**. Focus On Adaptive Treatments For The First Multi-Institutional Online Adaptive Radiation Therapy Trial (SMART) in Pancreas Cancer. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):e575-e576.

Purpose/Objective(s): Early clinical data suggest that Stereotactic MR-guided adaptive radiation therapy (SMART) can safely deliver ablative doses to pancreatic cancer (PCa) patients and potentially improve overall survival in this patient population. A multi-institutional prospective, phase II SMART study for PCa patients has been initiated. This study presents unique quality assurance challenges as each patient will be treated with up to 5 different plans. Of specific concern is that the tumor not be significantly underdosed when adapting to meet normal tissue constraints. We report initial results for the adaptation of PCa patients enrolled in the SMART trial. Materials/Methods: The 25 reported patients enrolled at 3 institutions had a mean age of 65.4 years. Tumors were mainly located in the pancreatic head or neck (N = 20) rather than the body/tail (N = 5). Gross tumor volume (GTV), duodenum, small bowel, colon, and stomach were delineated on MR simulation images. The planning target volume (PTV) was generated by expanding the GTV by 3mm, and a PTVopt structure was created by subtracting the OARs from the PTV. Mean GTV and PTV volumes were 91.4 cc (36.6 to 174.9 cc) and 148.0 cc (70.4 to 259.8 cc), respectively. Dose was prescribed up to 50 Gy in 5 fractions as limited by protocol-specified OAR constraints. Motion management was required and performed using end exhale (N = 22) or end inhale (N = 3) breath hold. An MRI was acquired daily and used to recontour all OARs within 3cm of the PTV. The original plan was recalculated using the day's anatomy and estimated over 5 fractions. The plan was adapted if >1cc of any contoured OARs was within the 33Gy isodose or if target coverage was insufficient. Real-time tumor tracking in a sagittal plane was acquired through treatment. Results: Over the 125 fractions treated, 109 (87.2%) required adaptation. Of these, 107 (98.2%) were adapted due to violating OAR constraints. The duodenum was the OAR most often exceeding dose limits (N = 76) where the mean volume >33Gy without adaptation (V33) would have been 4.5cc. Results for the stomach (N = 63, V33 = 5.1cc), small bowel (N = 47, V33 = 4.1cc), and colon (N = 24, V33 = 5.0cc) were similar. Adapted plans achieved V33 of < 0.5cc for all OARs. An average of 15.9cc of the PTV overlapped with OARs leading to a mean D95% of 33.9 Gy for the adapted fractions. However, for the PTVopt structure that excluded overlapping OARs, coverage was maintained at a mean D98% of 41.0Gy. This resulted in a mean CTV D95% of 42.4 Gy (85% of Rx dose). Conclusion: On-line ART was performed using MR-guided treatment devices for an initial set of PCa patients enrolled in the SMART trial. Patients received an escalated SBRT dose regimen while maintaining the isotoxicity of surrounding OARs. Further work will

evaluate patient characteristics and optimization parameters that produced the best quality plans as well as toxicity relative to delivered dose.

Radiation Oncology
Kumarasiri AD, **Brown SL**, **Elshaikh MA**, **Movsas B**, and **Chetty IJ**. A Prospective Study of the Dosimetric Impact and Quality of Life from Margin Reduction for Patients with Localized Prostate Cancer. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):e925.

Purpose/Objective(s): To investigate the impact of reducing CTV to PTV margins on dosimetry and patient reported Quality of Life (QOL) for patients with localized prostate cancer. Materials/Methods: Twenty patients were included in a single institution IRB-approved prospective study. Nine were planned using reduced margins (5 mm uniformly except 4 mm at prostate/rectum boundary), and 11 were control patients with standard margins (10/6 mm). Cumulative delivered dose was calculated using deformable dose accumulation. Each daily CBCT dataset was deformed to the planning CT (pCT), dose was computed, and accumulated on the resampled pCT using a parameter-optimized, B-spline algorithm (Elastix, ITK/VTK). EPIC-26 based patient reported QOL data was collected pre-treatment, post-treatment, and at 2, 6, 12, 18, 24, 36, 48 and 60 months follow-up. Post-radiation therapy (RT) QOL scores were baseline corrected and standardized to a [0-100] scale using EPIC-26 methodology. QOL comparisons between the margin-reduced and the standard cohorts including the averages within each arm and the overall mean QOL differences between the groups (QOLM-R-QOLcontrol) were made at each time point. Results: The median QOL follow-up length for the 20 patients was 48 months. Cumulative delivered dose and planned dose did not reach statistical significance ($p>0.1$) for targets and organs at risk, for both mean and maximum dose. At 4 years after RT, standardized and baseline-corrected mean QOLM-R-QOLcontrol were improved for “Urinary Incontinence”, “Urinary Irritative/Obstructive”, “Bowel”, and “Sexual” EPIC domains by 3.5, 14.8, 10.2, and 16.1, respectively (higher value is better). The control group showed larger PTV/rectum and PTV/bladder intersection volumes (7.2±5.8, 18.2±8.1 cc) than the margin-reduced group (2.6±1.8, 12.5±8.3 cc), though the dose to these intersection volumes did not reach statistical significance ($p>0.1$) between the groups. PTV/rectum intersection volume showed a moderate correlation ($R = -0.6$) to “Bowel” EPIC domain. Conclusion: Margin-reduced group exhibited clinically meaningful improvement of QOL without compromising the target dose coverage. [Formula presented]

Radiation Oncology
Liang E, **Morris ED**, **Vono J**, **Bazan L**, **Lu M**, Modh A, and **Glide-Hurst C**. Coupling Continuous Positive Airway Pressure (CPAP) and MR-guided Radiation Therapy. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):S169.

Purpose/Objective(s): Continuous positive airway pressure (CPAP) is a cost effective and readily available device that increases lung volumes and has shown promise in conventional x-ray-based radiation therapy (RT). However, limited data are available to quantify the impact of CPAP on lung reproducibility due to the use of ionizing radiation during imaging. We propose a novel pilot study combining CPAP with the powerful soft tissue capabilities of MR-guided RT to reduce the amount of radiation exposure to organs at risk, with the overarching goals of quantifying the impact of CPAP on lung stability under free-breathing (FB) and deep inspiration breath-hold (DIBH) conditions and assessing feasibility. Materials/Methods: An MR-safe configuration was devised by affixing several CPAP breathing circuits and verifying pressure maintenance using a manometer. Six healthy volunteers (median age 38, range: 28-54) underwent MRIs of the thorax (25 second TrueFISP, 1.5×1.5×3 mm3 resolution) using a 0.35T MR-Linac. FB and 2 verbally coached DIBH acquisitions were performed at CPAP of 0, 6, 10, 12, and 15 cm H20. To define a mutual coordinate system between successive datasets, automated rigid registration was performed (translations only) based on bony anatomy to the reference condition (FB, CPAP 0 cm H20). To quantify the linear relationship between lung volume and pressure under FB conditions, R2 was estimated for each subject. To study positioning reproducibility that may depend on increased pressures in the setting of DIBH, a Spearman correlation coefficient was calculated based on the centroid differences in lung volume. A paired t-test was used to compare the difference between pressures of 0, 6, 10, 12, and 15 cm H20. Image quality with and without CPAP under FB conditions were assessed. Surveys about volunteer perceptions of CPAP were administered after initial CPAP tolerability

screening and following the imaging session based on a ten-point scale (10 = least tolerable). Results: FB lung volumes increased as CPAP increased (R2 = 0.85 ± 0.13, range: 0.57 to 0.99) with visible reductions in motion artifacts. A significant negative correlation was observed between CPAP and the lung anterior/posterior centroid differences under DIBH, indicating a reduced difference on repeated measures (i.e., increased lung stability) as pressure increased. Paired t-tests showed significantly better reproducibility in lung volumes at pressures of 6, 10, 12, and 15 cm H20, as compared to 0 cm H20. Patient-reported difficulty tolerating CPAP was perceived to be lower after the study session (mean 2.0, range 1-4) than before (mean 2.83, range 1-5). Conclusion: This study confirms that integrating CPAP into MR-guided RT is feasible and well-tolerated. CPAP not only increases lung volumes under FB conditions, but also improves reproducibility of DIBH, offering potential for reducing treatment-related side effects regardless of treatment delivery platform.

Radiation Oncology

McFarlane M, Hochstedler K, Laucis AM, Sun Y, Chowdhury A, Matuszak MM, Hayman JA, Bergsma DP, Boike TP, Kestin LL, **Movsas B**, Grills IS, Dominello MM, Dess RT, Schonewolf CA, Spratt DE, Pierce LJ, Paximadis P, Jolly S, and Schipper M. Predictors of Pneumonitis after Lung Cancer Radiotherapy. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):S139.

Purpose/Objective(s): Multiple factors influence the risk of developing pneumonitis after radiotherapy for lung cancer, but few resources exist to guide clinicians in predicting risk in an individual patient using modern techniques. We analyzed toxicity data from a state-wide consortium to develop an integrated pneumonitis risk model. Materials/Methods: All patients received radiation therapy for stage II-III NSCLC between April 2012 and July 2019. Data were prospectively collected from 24 academic and community clinics participating in a state-wide quality consortium. Pneumonitis within 6 months of treatment was graded by local practitioners (no centralized review). Weighted, univariate regression models were used to describe the risk of pneumonitis toxicity as a function of dosimetric and clinical covariates. Pneumonitis was modeled as either G ≥ 2 versus G ≤ 1 or as G ≥ 3 versus G ≤ 2. We used a stepwise modeling procedure to build a multivariable model. AUC values were calculated for each model to quantify the ability of each covariate to discriminate between patients who did or did not experience toxicity. Results: Our analysis included 1302 patients, equally divided between male and female, with a median age of 67 years. Median comorbidity count was 1 and over 48% of patients had ≥ 2 comorbidities. 68% of patients had an ECOG performance status of 0-1. The overall rate of pneumonitis in the 6 months following RT was 16% (215 cases). 6% (92 cases) were G2+ and 1% (13 cases) were G3+. Adjusting for incomplete follow-up, estimated rates for G2+ and G3+ were 32% and 2%, respectively. In univariate analyses, V5, V10, V20, V30, and Mean Lung Dose (MLD) were positively associated with G2+ pneumonitis risk (OR 1.34, 1.34, 1.79, 1.48 per 10% increase, and 1.11 per 1 Gy increase respectively), while current smoking status was associated with lower odds of pneumonitis (OR 0.311). G2+ pneumonitis risk of > = 22% was independently predicted by MLD of > = 20 Gy, V20 of > = 35%, and V5 of > = 75% which correspond to commonly-used planning constraints. In multivariate analyses, the lung V5 metric remained a significant predictor of G2+ pneumonitis even when controlling for MLD, despite being closely correlated (coefficient 0.743). For G3+ pneumonitis, MLD (OR 1.25 per Gy) and V20 (OR 2.59 per 10% increase) were statistically significant predictors. Number of comorbidities was an independent predictor of G3+, but not G2+ pneumonitis (OR 1.61 per comorbidity). Conclusion: We present a large, prospectively-collected dataset evaluating pneumonitis risk after definitive radiation therapy for lung cancer. We incorporate comorbidity burden, smoking status, and dosimetric parameters in an integrated risk model. Low-grade pneumonitis is associated with MLD, V5, and V20, and negatively associated with smoking. High-grade pneumonitis is positively associated with MLD, V20, and comorbidity burden. These data may guide clinicians in assessing pneumonitis risk in individual patients.

Radiation Oncology

Rama S, **Atisha D**, Evangelista M, **Cannella C**, **Barry R**, Ghosh S, **Luker J**, **Chen Y**, Zhu S, **Bensenhaver J**, **Levin KJ**, and **Walker EM**. The Effect of Oncoplastic Reduction on The Incidence of Post-Operative Lymphedema in Breast Cancer Patients Undergoing Lumpectomy. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):e45.

Purpose/Objective(s): In patients with macromastia, breast conservation surgery (BCS) followed by radiation therapy (RT) may be associated with increased radiation exposure and a different complication profile than those without macromastia. The oncoplastic reduction mammoplasty (ORM) procedure includes breast reduction at the time of BCS. The purpose of this study is to determine if women with macromastia who undergo ORM have a different complication profile compared to those who undergo BCS followed by RT. Materials/Methods: We performed a retrospective chart review on patients who underwent lumpectomy with RT from 2014 to 2017. Chronic breast lymphedema (CBL) was defined as swelling that persisted >1-year post-RT. Breast volumes (BV) were determined by contoured breast volumes or, if unavailable, estimated by the 95% isodose volumes from the RT treatment planning system. Univariate analysis was used to evaluate various patient factors and treatment outcomes in women with BV ≥1300 cc compared to <1300 cc. These same factors were compared in women who underwent ORM vs. BCS. Multivariate regression analysis was used to evaluate factors associated with ≥1 complication. Logistic regression was performed to identify factors associated with the development of CBL. Results: The total population included 785 patients, of which 28 (3.6%) underwent ORM and 757 (96.4%) underwent BCS. The total population was stratified into two groups, in which 289 (36.8%) patients had BV ≥1300 cc and 496 (63.2%) patients had a BV <1300 cc. Compared to patients with BV<1300 cc, those with BV ≥1300 cc had a higher percentage of African Americans (52.6% vs. 41.5%, P = 0.002), higher median BMI (34.96 vs. 27.87, P<0.001), higher incidence of diabetes (39.8% vs. 27.2%, P<0.001), higher incidence of hypertension (75.4% vs. 63.1%, P<0.001), and higher incidence of CBL (12.5% vs. 4.2%, P<0.001). Compared to BCS patients, ORM patients with BV ≥1300 cc had increased incidence of CBL (36.4% vs. 11.5%, P = 0.035). Logistic regression showed that the incidence of ≥1 complication was associated with BMI, presence of SLNB, and the number of lymph nodes removed in either SLNB or ALND. However, factors such as ORM and BV were not associated with an increased risk of ≥1 complication. Logistic regression demonstrated that having a BV ≥1300 cc was associated with 2.5 times increased odds of CBL compared to those with BV <1300 cc. Even though those who underwent ORM did not change the risk for CBL for the entire cohort, ORM patients with BV ≥1300 had a higher risk of CBL. Ultimately, logistic regression demonstrates that ORM does not increase the risk of CBL when adjusting for BV. Conclusion: In conclusion, axillary surgery contributed most significantly to the incidence of having ≥1 complication. However, BV was associated with an increased risk of CBL, regardless of the presence of ORM. Therefore, women with BV ≥1300 cc should be offered ORM at the time of lumpectomy in order to reduce their future risk of CBL.

Radiation Oncology

Schaff EM, **Gartrelle KJ**, **Kirsch C**, **Siddiqui F**, **Ajlouni M**, **Dragovic J**, **Aref I**, **Shah MM**, **Kwon D**, **Dobrosotskaya I**, **Shah R**, **Khan G**, and **Parikh PJ**. Magnetic Resonance Guided Stereotactic Ablative Radiation Therapy Versus External Beam RT with Chemotherapy For Pancreatic Cancer: Single Institution Toxicity Analysis Of Patients Treated In An Urban Academic Center. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):e582-e583.

Purpose/Objective(s): Several academic institutions have investigated stereotactic MR guided adaptive radiation therapy (SMART) to safely dose escalate for locally advanced and borderline resectable pancreatic cancer with initial favorable toxicity and survival outcomes. However, it is not clear that this treatment is safe or effective in more challenging populations, such as in an urban academic center. The purpose of this abstract was to review outcomes immediately before and after implementing dose escalated MR guided adaptive radiation therapy for pancreatic cancer. Materials/Methods: In this IRB approved analysis, we retrospectively reviewed 57 consecutive patients from 2017-2019 with locally advanced or borderline resectable pancreatic cancer who were treated with neoadjuvant radiation therapy. Initially all patients received standard fractionated chemoradiation (chemoRT) to a dose of 50.4 Gy in 28 fractions. In September 2018 our institutional treatment guidelines were changed to recommend SMART (50Gy in 5 fractions) for these patients. Toxicity outcomes evaluated were grade 3+ GI toxicity based on CTCAE v5.0 as well as unplanned hospital admissions, both at 90 and 180 days. Treatment differences were analyzed using two sample t-test and chi-square test. Overall survival was evaluated at 180 days, and by Kaplan-Meier and log-rank test and was calculated from first day of radiation therapy. Results: 29 patients received chemoRT and 28 received SMART. Median follow up for the chemoRT group was 294 days and for SMART was 185 days. Groups did not have significant differences in age, performance status, stage, gender, CA 19-9, or neoadjuvant chemotherapy. Grade 3+ GI toxicity at 90

days was seen in 28% and 11% (p = 0.11) in the chemoRT and SMART groups, respectively. Types of toxicity were overall comparable with most being abdominal pain and duodenal bleeds. Hospital admissions at 90 days occurred in 38% and 21% of patients (p = 0.17) and at 180 days in 33% and 44% (p = 0.48). Surgical resection was achieved in 24% of chemoRT and 36% of SMART patients (p = 0.34). When evaluated using Kaplan-Meier and log-rank test there was a trend to overall survival benefit in the SMART group (p = 0.07). There was also a statistically significant 180-day survival improvement in SMART patients of 94% vs 70% in chemoRT patients (p = 0.046). Conclusion: Dose escalated SMART for locally advanced and borderline pancreatic cancer does not cause significant increase in GI grade 3+ GI toxicity at 90 days or hospitalization at 90 or 180 days as compared to chemoRT. Dose escalated SMART appears to be both safe and effective in our urban population. OS in the chemoRT group was comparable to previous trials such as LAP07. There is a trend to OS improvement on Kaplan-Meier analysis in the SBRT group (p = 0.07), as well as statistically significant improvement in 180-day survival; which supports the ongoing multi-institutional SMART study (NCT03621644). Updated results to be presented at the meeting.

Radiation Oncology

Simone CB, **Movsas B**, Gore EM, Mohindra P, Vujaskovic Z, **Wang D**, **Ajlouni M**, Menon S, Thompson J, **Brown SL**, Kurman M, Dykstra JC, Rillo L, Ingram M, Serebrenik A, and Kaytor MD. A Phase 1b/2a Study Evaluating the Pharmacokinetics, Safety, and Efficacy of Nanogenistein in Combination with Chemoradiotherapy for Non-small Cell Lung Cancer. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):S103.

Purpose/Objective(s): Radiation therapy (RT) remains a critical component of locally advanced (LA) and limited metastatic non-small cell lung cancer (NSCLC) but is associated with significant risks of pneumonitis, esophagitis, and major cardiac events. Nanogenistein (NG) is a radioprotectant that promotes DNA repair, cell cycle arrest and anti-inflammatory signaling to mitigate RT-associated toxicities. The objective of this phase 1b/2a trial is to evaluate the safety, pharmacokinetics (PK), and efficacy of NG in combination with concurrent chemoradiotherapy for NSCLC. Materials/Methods: Patients with newly diagnosed stage II, III or IV (oligometastatic) NSCLC planned for 60-70/1.8-2.0 Gy RT and concurrent weekly paclitaxel/carboplatin were eligible. Patients were treated daily with a self-administered, oral suspension of NG at one of three dose levels (500, 1000, or 1500 mg) starting prior to and continuing during the entire course of chemoradiotherapy (up to 8 weeks). Three cohorts (n = 7/cohort) were enrolled sequentially. PK analysis was completed for NG, paclitaxel and carboplatin. Tumor response was defined per RECIST 1.1 criteria. CT scans were obtained during chemoradiotherapy, consolidation, and every 2-3 months following RT completion. Adverse events (AEs) were reported using the NCI CTCAEv4 and used to monitor dose-limiting toxicities (DLTs). Quality of life measurements included UCSD-SOBQ, FACT-L TOI and a swallowing diary. Results: Enrolled patients (n = 21) were a median of 69 years (range 50-84), predominantly Caucasian (n = 19) and female (n = 11), and had stage II (n = 5), III (n = 14) or IV (n = 2) disease. NG was well tolerated and no DLTs were identified. NG PK did not interfere with chemotherapeutic PK. AEs were not dose dependent and those possibly (n = 10), probably (n = 1) or definitely (n = 0) attributable to NG treatment were mild GI events (n = 8, all grade 1), fatigue (n = 1, grade 2), anorexia (n = 1, grade 2), and dysgeusia (n = 1, grade 1). Overall, 1 major cardiac event, 1 grade 3 esophagitis, and 2 cases of grade ≥2 pneumonitis occurred. Patient weight loss was ≤ 5%, pulmonary function (0, 9- and 13-months post-RT), and FACT-L TOI (0, 3, 6- and 13-months post-RT) remained stable across all cohorts (all p>0.05). Tumor response rate was 70%, with a complete response rate of 15%. The median progression-free survival across cohorts was 15.6 months, and the median overall survival was not reached at a median of 15.9 months follow-up. Conclusion: In this study, NG was found to be safe and well tolerated, with an incidence of Grade ≥2 hematological and normal tissue toxicities both less than that observed in RTOG 0617. These encouraging safety and efficacy data support advancing the drug to an adequately powered, randomized, double-blind, placebo-controlled phase 2b study that is planned in LA-NSCLC patients.

Radiation Oncology

Zhu S, **Atisha D**, **Evangelistia M**, **Barry R**, **Rama S**, Ghosh S, **Cannella C**, **Chen Y**, **Bensenhaver J**, **Levin KJ**, and **Walker EM**. Factors Associated with Chronic Breast Lymphedema After Adjuvant

Radiation in Women Undergoing Breast Conservation Therapy. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):e32.

Purpose/Objective(s): Unlike temporary breast edema caused by post-lumpectomy radiation therapy (RT), the edema that persists beyond one year is not well defined and difficult to treat. The aim of this study is to define the incidence and risk factors for the development of chronic breast lymphedema in women undergoing lumpectomy with RT at a large metropolitan cancer center. Materials/Methods: A retrospective chart review was performed on all patients who underwent lumpectomy from 2014 to 2017. Women who did not undergo RT at our institution and those with stage IV disease were excluded from the analysis. Patient demographics, comorbidities, operative data, RT data and postoperative complications were obtained. Chronic breast lymphedema (CBL) was defined as edema that persisted beyond one-year post completion of radiation therapy. Breast volumes were determined by contoured breast volumes or, if unavailable, estimated by the 95% isodose volumes from the RT treatment planning system. Using a density curve, the distribution of breast volumes was plotted for patients with and patients without CBL. Univariate analysis was used to evaluate factors associated with CBL. Multivariate regression analysis was used to evaluate factors associated with the risk of CBL while accounting for potential confounding variables as defined by the univariate analysis. Results: A total of 811 patients were included for analysis. Fifty-seven (7.0%) patients developed breast lymphedema beyond one year. For the entire cohort, mean age was 63.3 years old, mean BMI was 31.21 kg/m2, and mean breast volume was 1195 cc (SD = 643.25 cc). Compared to the cohort that did not develop CBL (n = 754), the CBL cohort (n = 57) had a higher BMI (33.10 kg/m2 vs. 29.84 kg/m2, p<0.001), higher percentage of black race (61.4% vs. 43.8%, P = 0.024), larger breast volume (1504 cc vs. 1081 cc, P<0.001), greater number of lymph nodes taken at time of surgery (3 vs. 1, P<0.001), higher percentage that had underwent ALND (12.3% vs. 5.2%, P = 0.036), and larger size of lumpectomy specimen (118.95 cm3 vs. 96.00 cm3, P = 0.016). The density curve determined that the optimal cutoff for breast volume was around 1300 cc. When accounting for potential confounding variables, multivariate regression analysis revealed that those whose breast volume > 1300 cc (vs. <1300 cc) were 2.5 times more likely to experience breast lymphedema after one year (OR = 2.53, p = 0.005). When volume was evaluated as a continuous variable, regression analysis revealed that for every 1cc increase in breast volume, the risk of breast lymphedema increases by 0.1% (OR = 1.001, P = 0.001). Conclusion: Chronic breast lymphedema presents a clinical concern for women undergoing lumpectomy with postoperative radiation, particularly women with larger breasts. Further studies should focus on preventative strategies, as well as the psychosocial and economic impact of this morbidity.

Radiation Oncology

Zhu S, **Ghanem AI**, **Morris ED**, and **Glide-Hurst C**. Inter-Fraction Cardiac Substructure Displacement Quantified by Magnetic Resonance (MR)-Guided Radiation Therapy. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):e324.

Purpose/Objective(s): Emerging evidence suggests that cardiac substructures are highly radiosensitive. However, the variability of substructure position after tumor localization has not been well characterized. This study quantifies the inter-fraction displacement of cardiac substructures by leveraging the excellent soft tissue contrast afforded by MR-guided radiation therapy. Materials/Methods: Sixteen patients who underwent radiotherapy for intrathoracic tumors with a 0.35 MR-guided Linac were retrospectively evaluated. Fourteen were treated at breath-hold (7 end-inhalation and 7 end-exhalation) using a 17-25 second TrueFISP scan (1.5 x 1.5 x 3 mm3) and 2 under free breathing condition (3-minute TrueFISP scan with 1.5 mm3 isotropic resolution). To mimic on-board IGRT, 3-4 daily MRIs (n = 63) were rigidly registered to the planning MR-simulation (MR-SIM) image based on tumor matching. Validated deep learning or atlas-based segmentation algorithms propagated 13 cardiac structures (e.g., whole heart, chambers, coronary arteries (CA), great vessels, etc.) to daily MRIs and contours were verified by 2 radiation oncologists. Daily centroid displacements from MR-SIM were quantified. Results: Across the heart and substructures, inter-fraction displacements for 17.2% (left-right (L-R)), 11.4% (anterior-posterior (A-P)), and 22.5% (superior-inferior (S-I)) fractions were > 5 mm. Fewer than 2.5% of all structures were displaced > 10 mm in any direction over the studied fractions, often due to lack of compliance with breath-hold conditions. Table 1 summarizes key results for the left/right ventricles (LV/RV), left anterior descending artery (LADA), and ascending aorta (AA), which are significant in the pathogenesis of

radiation-associated heart disease. For the chambers, the median absolute displacements were 2.4, 1.7, and 2.6 mm in the L-R, A-P, and S-I directions, respectively. Great vessels (superior vena cava, pulmonary artery, and AA) showed a tendency to have larger displacements in the S-I direction, with 46.6% of shifts > 3 mm whereas only 32.8 and 21.2% of displacements were observed in the L-R and A-P directions, respectively. Larger S-I displacements likely reflect the larger axial MRI slice thickness for most (14/16) patients. Conclusion: This exploratory work quantified the inter-fraction displacement of critical cardiac substructures and is a first step in deriving substructure-specific safety margins to ensure highly effective cardiac sparing. These findings require validation in a larger cohort for robust margin derivation and for applications in prospective clinical trials. [Formula presented]

Radiation Oncology

Zhu S, **Khalil R**, **Altairy O**, **Burmeister C**, **Dimitrova I**, and **Elshaikh MA**. The Prognostic Impact of Time Interval Between Hysterectomy and Initiation of Adjuvant Radiation Treatment in Women With Early-Stage Endometrial Carcinoma. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):e472.

Purpose/Objective(s): Adjuvant radiation therapy (ART) is indicated for women with endometrial carcinoma (EC) who are at high risk for recurrence. However, due to various reasons, some patients do not receive ART in a timely manner. In this study, we evaluated the prognostic impact of the time interval (TI) between hysterectomy and starting date of ART. Materials/Methods: After institutional review board approval, we queried our prospectively-maintained institutional database for women with uterine endometrioid EC of 2009 FIGO stages I-II who received ART without chemotherapy after surgical staging. The patients were classified into two groups, based on whether they received ART ≤8 weeks (group A) or >8 weeks (group B) after hysterectomy. We then compared the two groups with regards to the following survival endpoints: recurrence-free survival (RFS), disease-specific survival (DSS) and overall survival (OS). Univariate and multivariate analyses were also performed. Results: A total of 460 patients were identified. Median follow-up duration was 70.5 months. The median age for the entire cohort was 66.0 years. The cohort consisted of 176 patients with FIGO stage IA (38%), 207 (45%) with stage IB and 77 (17%) with stage II. Group A consisted of 354 (77%) patients, and group B had 106 (23%). The median TIs from hysterectomy to ART were 6 weeks and 10 weeks for groups A and B, respectively. There was no statistically significant difference between the groups in terms of baseline demographic and disease characteristics including age, race, grade, FIGO stage, extent of myometrial invasion, presence of lymphovascular space invasion and radiation treatment modality. A total of 52 patients experienced recurrences. Patients in group A (vs. group B) experienced significantly less recurrences overall (9% vs. 18%; p = 0.01). Rate of vaginal recurrence was significantly lower in group A (9% vs. 42%, p = 0.01). Univariate analysis showed that having RT ≤8 weeks was associated with significantly improved 5-year RFS rate, which was 89% and 80% for groups A and B (p = 0.04), respectively. The rates of 5-year OS (86% vs. 85% for groups A and B, respectively) and 5-year DSS (93% vs. 93% for groups A and B, respectively) were similar. In addition, multivariate analysis showed a statistical trend for improved 5-year RFS when receiving RT ≤8 weeks (p = 0.07). Conclusion: Our study suggests that delaying adjuvant radiation treatment beyond 8 weeks post-hysterectomy is associated with significantly more cancer recurrences for women with early-stage endometrial cancer.

Sleep Medicine

Liang E, **Morris ED**, **Vono J**, **Bazan L**, **Lu M**, Modh A, and **Glide-Hurst C**. Coupling Continuous Positive Airway Pressure (CPAP) and MR-guided Radiation Therapy. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):S169.

Purpose/Objective(s): Continuous positive airway pressure (CPAP) is a cost effective and readily available device that increases lung volumes and has shown promise in conventional x-ray-based radiation therapy (RT). However, limited data are available to quantify the impact of CPAP on lung reproducibility due to the use of ionizing radiation during imaging. We propose a novel pilot study combining CPAP with the powerful soft tissue capabilities of MR-guided RT to reduce the amount of radiation exposure to organs at risk, with the overarching goals of quantifying the impact of CPAP on lung stability under free-breathing (FB) and deep inspiration breath-hold (DIBH) conditions and assessing feasibility. Materials/Methods: An MR-safe configuration was devised by affixing several CPAP breathing circuits and verifying pressure maintenance using a manometer. Six healthy volunteers (median age 38,

range: 28-54) underwent MRIs of the thorax (25 second TrueFISP, 1.5×1.5×3 mm3 resolution) using a 0.35T MR-Linac. FB and 2 verbally coached DIBH acquisitions were performed at CPAP of 0, 6, 10, 12, and 15 cm H20. To define a mutual coordinate system between successive datasets, automated rigid registration was performed (translations only) based on bony anatomy to the reference condition (FB, CPAP 0 cm H20). To quantify the linear relationship between lung volume and pressure under FB conditions, R2 was estimated for each subject. To study positioning reproducibility that may depend on increased pressures in the setting of DIBH, a Spearman correlation coefficient was calculated based on the centroid differences in lung volume. A paired t-test was used to compare the difference between pressures of 0, 6, 10, 12, and 15 cm H20. Image quality with and without CPAP under FB conditions were assessed. Surveys about volunteer perceptions of CPAP were administered after initial CPAP tolerability screening and following the imaging session based on a ten-point scale (10 = least tolerable). Results: FB lung volumes increased as CPAP increased (R2 = 0.85 ± 0.13, range: 0.57 to 0.99) with visible reductions in motion artifacts. A significant negative correlation was observed between CPAP and the lung anterior/posterior centroid differences under DIBH, indicating a reduced difference on repeated measures (i.e., increased lung stability) as pressure increased. Paired t-tests showed significantly better reproducibility in lung volumes at pressures of 6, 10, 12, and 15 cm H20, as compared to 0 cm H20. Patient-reported difficulty tolerating CPAP was perceived to be lower after the study session (mean 2.0, range 1-4) than before (mean 2.83, range 1-5). Conclusion: This study confirms that integrating CPAP into MR-guided RT is feasible and well-tolerated. CPAP not only increases lung volumes under FB conditions, but also improves reproducibility of DIBH, offering potential for reducing treatment-related side effects regardless of treatment delivery platform.

Surgery

Gartrelle KJ, **Schaff EM**, **Kirsch C**, **Kwon D**, **Ajlouni M**, **Khan G**, **Shah R**, **Dobrosotskaya I**, **Parikh PJ**, and **Siddiqui F**. Racial Disparities Among Pancreatic Adenocarcinoma Patients: A Retrospective Survival Analysis of Non-Metastatic Pancreatic Cancer Patients. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):e431.

Purpose/Objective(s): It is predicted that in 2020, approximately 57,600 individuals will be diagnosed with pancreatic cancer (PaC). Based on SEER database analysis, there are conflicting opinions in literature about the overall treatment and outcomes in African-American patients with PaC. The purpose of this study was to determine if there was a racial disparity in overall survival rates between African Americans (AAs) and non-African Americans (non-AAs) diagnosed with PaC who received neoadjuvant radiation therapy (RT) in a tertiary-care cancer center with an established multi-disciplinary PaC tumor board and clinic. Materials/Methods: An IRB-approved retrospective chart analysis was completed on 100 patients who were diagnosed with pancreatic adenocarcinoma and treated with neoadjuvant RT between 2017-2019. Patients who were deemed resectable, borderline resectable (BR), or locally advanced/unresectable (LA) at initial diagnosis were included in the analysis. The following baseline characteristics were collected for each patient: staging, gender, age and ECOG score at initial diagnosis, tumor site and size, clinical T and N stage, CA19-9, and treatment variables (i.e., surgery, chemotherapy, and RT type). Overall survival was calculated from the RT start date. In order to identify any baseline differences among the AA group and the non-AA group, a two-sample t-test and Chi-square were employed. A log-rank test and Kaplan-Meier were used to determine any differences in overall survival among the two groups. Results: Of the 100 patients included in the analysis, 25 were AA and 58 were female. There were 17 (68%) BR and 8 (32%) LA patients in the AA group. In the non-AA group, there were 2 (3%) resectable, 47 (63%) BR, and 26 (35%) LA patients. There were no statistically significant differences detected in any of the baseline characteristics except a trend for increased CA19-9 values of 399.8 U/mL for AAs and 229 U/mL for non-AAs. There was no statistically significant difference in receipt of chemotherapy and RT between the two groups. The estimated median survival rates were 11.5 months for non-AAs and 8.4 months for AAs. One-year overall survival was 45% for AAs versus 48% for non-AAs ($p = 0.57$). Conclusion: There was no difference in overall survival among AAs and non-AAs who received neoadjuvant RT+/- chemotherapy for PaC at our institution between 2017-2019. Contrary to previous publications based on large SEER database analysis, there does not appear to be any difference in overall survival based on race if patients receive treatment in a comprehensive multi-disciplinary collaborative center.

Surgery

Kitajima T, **Kuno Y**, **Sukkarieh N**, **Suzuki Y**, **Shimada S**, **Flores A**, **Lisznyai E**, **Collins K**, **Yoshida A**, **Rizzari M**, **Moonka D**, **Abouljoud MS**, and **Nagai S**. EFFECTS OF AGING AND ACUTE-ON-CHRONIC LIVER FAILURE ON LIVER TRANSPLANT WAITLIST MORTALITY. *Hepatology* 2020; 72:800A-801A.

[Kitajima, Toshihiro; Kuno, Yasutaka; Sukkarieh, Nicole; Suzuki, Yukiko; Shimada, Shingo; Flores, Alexander; Lisznyai, Eric; Rizzari, Michael] Henry Ford Hosp, Div Transplant & Hepatobiliary Surg, Detroit, MI 48202 USA. [Collins, Kelly] Henry Ford Hlth Syst, Transplant & Hepatobiliary Surg, Detroit, MI USA. [Yoshida, Atsushi] Henry Ford Hosp, Transplant Inst, Detroit, MI 48202 USA. [Moonka, Dilip] Henry Ford Hosp, Gastroenterol, Detroit, MI 48202 USA. [Abouljoud, Marwan S.; Nagai, Shunji] Henry Ford Hosp, Transplant & Hepatobiliary Surg, Detroit, MI 48202 USA.

Background: Acute-on-chronic liver failure (ACLF) is characterized by multiple organ failure with high short-term mortality. However, the effect of the severity of ACLF on waitlist outcomes in age groups has not been well elucidated. We hypothesized that the negative effect of ACLF may be different between age groups and older patients may increase the risk of waitlist mortality compared to younger population. The aim of this study is to investigate the effects of ACLF on waitlist mortality according to recipient age. Methods: This study used data from the UNOS registry and evaluated adult patients listed for liver-only or liver-kidney transplant between 2014 and 2019. Patients listed as status 1A, multi- organ transplant, hepatocellular carcinoma, and re-transplant were excluded. We identified patients with ACLF using the European Association for the Study of the Liver-Chronic Liver Failure (EASL-CLIF) criteria. Ninety-day waitlist mortality was compared between ACLF grades 1, 2, and 3 in each age group at listing (age<50 [younger], 50-64 [mid], ≥65 [older]). The risks of 90-day waitlist mortality were analyzed in ACLF patients using Fine-Gray competing risk regression model. Risk was adjusted by recipient characteristics at listing. Results: Among the 30,486 patients eligible for the study, 6,316 (20.7%), 1,995 (6.5%) and 1,653 (5.4%) had ACLF 1,2 and 3, respectively. 7733 (25.3%) were in younger group, 17462 (57.3%) were in mid group, 5291 (17.4%) were in older group. In all age groups, ACLF 1, 2 and 3 groups showed significantly higher adjusted risk of 90-day waitlist mortality than those without ACLF (Figure). The adverse impact of ACLF on waitlist mortality was most significant in the older group. In patients with ACLF, higher grade of ACLF (ACLF- 2: adjusted hazard ratio [aHR] 1.33, P<0.001; ACLF-3: aHR 2.56, P<0.001; ref: ACLF-1) and older recipient age (mid: aHR 1.57, P<0.001: older: aHR 2.15, P<0.001; ref younger) independently increased the risk of 90-day waitlist mortality. Conclusion: While ACLF negatively affected 90-day mortality for patients of all age groups on waitlist, this effect was more prominent in the older populations. Given this fact and the higher risk of waitlist mortality for those with ACLF, increased priority in liver allocation to these patients should be considered.

Surgery

Kuno Y, **Kitajima T**, **Moonka D**, **Sukkarieh N**, **Flores A**, **Lisznyai E**, **Shimada S**, **Suzuki Y**, **Collins K**, **Rizzari M**, **Yoshida A**, **Abouljoud MS**, and **Nagai S**. LIVER TRANSPLANTATION IN OLDER PATIENTS WITH ACUTE-ON-CHRONIC LIVER FAILURE: AN ANALYSIS OF UNOS REGISTRY. *Hepatology* 2020; 72:819A-820A.

[Kuno, Yasutaka; Kitajima, Toshihiro; Sukkarieh, Nicole; Flores, Alexander; Lisznyai, Eric; Shimada, Shingo; Suzuki, Yukiko; Rizzari, Michael] Henry Ford Hosp, Detroit, MI 48202 USA. [Moonka, Dilip] Henry Ford Hosp, Gastroenterol, Detroit, MI 48202 USA. [Collins, Kelly] Henry Ford Hlth Syst, Transplant & Hepatobiliary Surg, Detroit, MI USA. [Yoshida, Atsushi] Henry Ford Hosp, Transplant Inst, Detroit, MI 48202 USA. [Abouljoud, Marwan S.; Nagai, Shunji] Henry Ford Hosp, Transplant & Hepatobiliary Surg, Detroit, MI 48202 USA.

Background: Acute on chronic liver failure (ACLF) patients undergoing liver transplantation (LT) may require additional consideration in selection and management due to their severity of illness. We hypothesized that older recipient age might increase the risk of graft loss in ACLF patients. We aimed to identify risk factors for post-transplant mortality in patients with ACLF, focusing on recipient age. Methods: Using data from the UNOS registry, this study evaluated adult liver or liver and kidney transplant recipients between 2014 and 2019. Patients with status 1A, multi-organ, hepatocellular carcinoma, and re-transplant were excluded. We identified patients with ACLF using European Association for the Study

of the Liver-Chronic Liver Failure (EASL-CLIF) criteria. One- year graft survival was compared between ACLF patients (ACLF grades 1, 2, 3) and those without ACLF for each age group (age<50 [younger], 50-64 [mid], ≥65 [older]). Risk factors for 1-year graft survival were analyzed in ACLF patients using Cox regression models. A subgroup analysis in older ACLF patients was performed based on identified risk factors. Risk was adjusted by donor and recipient characteristics at LT. Results: Among 17,148 patients eligible for the study, 3,836 (22.4%), 3,050 (17.8%) and 2,084 (12.2%) had ACLF 1,2 and 3. 2983 (17.4%) patients were in the older group. In all age groups, ACLF 1, 2 and 3 groups showed significantly higher risk of 1-year graft loss than those without ACLF (Figure). In patients with ACLF, older recipient (≥65 years, aHR 1.56, P<0.001, ref: <50 years) and ACLF-3 (aHR 1.57, P<0.001, ref: ACLF-1) were independent risk factors for one-year graft loss, along with black donor race (aHR 1.23, P=0.024, ref: white), DCD donor (aHR 2.00, P<0.001, ref: DBD), cold ischemia time (CIT)>8 hours (aHR 1.21, P=0.038), and older donor (>50 years: aHR 1.395, P<0.001, ref: ≤50 years). In older ACLF patients, risk of 1-year graft loss was decreased when graft was younger DBD donor with shorter CIT (<8hr) compared to those who did not meet all of these 3 [younger donor, DBD donor, and shorter CIT] factors (aHR 0.74, P=0.045). Conclusion: Liver transplant outcomes were significantly worse in patients with ACLF compared to those without ACLF regardless of recipient age. Donor selection and shortening cold ischemia time may mitigate risk of graft loss in older patients with ACLF.

Surgery

Nagai S, **Nallabasannagari AR**, **Moonka D**, **Reddiboina M**, **Nanna M**, **Chau LC**, **Yeddula S**, **Kitajima T**, **Bajjoka-Francis I**, and **Abouljoud MS**. USE OF NEURAL NETWORK MODELS TO PREDICT MORTALITY/ SURVIVAL AMONG PATIENTS ON THE LIVER TRANSPLANT WAITLIST. *Hepatology* 2020; 72:2A-3A.

[Nagai, Shunji; Chau, Lucy Ching; Yeddula, Sirisha; Kitajima, Toshihiro; Abouljoud, Marwan S.] Henry Ford Hosp, Transplant & Hepatobiliary Surg, Detroit, MI 48202 USA. [Nallabasannagari, Anubhav Reddy; Reddiboina, Madhu; Nanna, Michael] Henry Ford Hosp, Rediminds, Detroit, MI 48202 USA. [Moonka, Dilip] Henry Ford Hosp, Gastroenterol, Detroit, MI 48202 USA. [Bajjoka-Francis, Iman] Henry Ford Transplant Inst, Detroit, MI USA.

Background: While use of the MELD-Na scores have shown success in predicting waitlist mortality in liver transplant (LT), questions remain whether there are more efficacious models. The objective of this study is to develop Neural Network (NN) models that more accurately predict waitlist mortality. NNs are a type of Machine Learning algorithm. The fundamental building blocks of a NN are layers which are composed of units of calculation called neurons. NN performs calculations on input data and extracts meaningful patterns for the problem. Methods: This study used data from the OPTN/UNOS registry, which includes data for 194,299 patients listed for LT between Feb 27, 2002 and Dec 31, 2018. Subsets of the data were used for the creation of 4 separate NN models. These models were constructed to predict mortality at different timeframes at 30, 90, 180, and 365 days. We excluded patients who received LTs before the outcome timeline, patients with liver cancer, patients who received MELD exceptions, and patients who were listed for combined organ transplants other than kidney. The Liver Data and the Liver Wait List History files in the OPTN/UNOS registry were combined and a total of 44 variables were selected, including recipient characteristics, trend of liver and kidney function during waiting time, UNOS regions, and registration year. Age, ethnicity, and gender were not included in the NN model to avoid assigning waitlist priority based on these factors. For each model, the data were split using random sampling into training, validation, and test dataset in a 60:20:20 ratio. The performance of the models was assessed using Area Under Receiver Operating Curve (AUC-ROC) and Area Under Precision-Recall curve (PR-AUC). Results: According to NN prediction models, the AUC- ROC for 30-Day, 90-Day, 180-Day, and 365-Day Mortality was 0.949, 0.928, 0.915, and 0.899 and the PR-AUC was 0.689, 0.730, 0.769, and 0.823, respectively. The 90-Day Mortality NN model outperformed MELD score for both AUC-ROC and PR-AUC. It also outperformed MELD score for Recall (Sensitivity), Negative Predictive Value (NPV), and F-1 score. The 90-Day Mortality model specifically identified more waitlist deaths with a higher Recall (Sensitivity) of 0.833 vs 0.308 (P<0.001). MELD score performed better for Specificity and Precision. (Figure) The performance metrics were compared by breaking the test dataset into multiple subsets based on Ethnicity, Gender, Region, Age, Diagnosis Group, and Year of listing. The 90-Day Mortality NN model significantly outperformed MELD scores across all subsets of the data for predicting waitlist

mortality. Conclusion: Prediction models using NN more accurately identified waitlist mortality which outperformed MELD score. Using NN will improve predictive ability for waitlist mortality and lead to developing a more accurate and equitable allocation system with the ultimate goal of reducing LT waitlist mortality.

Surgery

Rama S, **Atisha D**, Evangelista M, **Cannella C**, **Barry R**, Ghosh S, **Luker J**, **Chen Y**, Zhu S, **Bensenhaver J**, **Levin KJ**, and **Walker EM**. The Effect of Oncoplastic Reduction on The Incidence of Post-Operative Lymphedema in Breast Cancer Patients Undergoing Lumpectomy. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):e45.

Purpose/Objective(s): In patients with macromastia, breast conservation surgery (BCS) followed by radiation therapy (RT) may be associated with increased radiation exposure and a different complication profile than those without macromastia. The oncoplastic reduction mammoplasty (ORM) procedure includes breast reduction at the time of BCS. The purpose of this study is to determine if women with macromastia who undergo ORM have a different complication profile compared to those who undergo BCS followed by RT. Materials/Methods: We performed a retrospective chart review on patients who underwent lumpectomy with RT from 2014 to 2017. Chronic breast lymphedema (CBL) was defined as swelling that persisted >1-year post-RT. Breast volumes (BV) were determined by contoured breast volumes or, if unavailable, estimated by the 95% isodose volumes from the RT treatment planning system. Univariate analysis was used to evaluate various patient factors and treatment outcomes in women with BV ≥1300 cc compared to <1300 cc. These same factors were compared in women who underwent ORM vs. BCS. Multivariate regression analysis was used to evaluate factors associated with ≥1 complication. Logistic regression was performed to identify factors associated with the development of CBL. Results: The total population included 785 patients, of which 28 (3.6%) underwent ORM and 757 (96.4%) underwent BCS. The total population was stratified into two groups, in which 289 (36.8%) patients had BV ≥1300 cc and 496 (63.2%) patients had a BV <1300 cc. Compared to patients with BV<1300 cc, those with BV ≥1300 cc had a higher percentage of African Americans (52.6% vs. 41.5%, P = 0.002), higher median BMI (34.96 vs. 27.87, P<0.001), higher incidence of diabetes (39.8% vs. 27.2%, P<0.001), higher incidence of hypertension (75.4% vs. 63.1%, P<0.001), and higher incidence of CBL (12.5% vs. 4.2%, P<0.001). Compared to BCS patients, ORM patients with BV ≥1300 cc had increased incidence of CBL (36.4% vs. 11.5%, P = 0.035). Logistic regression showed that the incidence of ≥1 complication was associated with BMI, presence of SLNB, and the number of lymph nodes removed in either SLNB or ALND. However, factors such as ORM and BV were not associated with an increased risk of ≥1 complication. Logistic regression demonstrated that having a BV ≥1300 cc was associated with 2.5 times increased odds of CBL compared to those with BV <1300 cc. Even though those who underwent ORM did not change the risk for CBL for the entire cohort, ORM patients with BV ≥1300 had a higher risk of CBL. Ultimately, logistic regression demonstrates that ORM does not increase the risk of CBL when adjusting for BV. Conclusion: In conclusion, axillary surgery contributed most significantly to the incidence of having ≥1 complication. However, BV was associated with an increased risk of CBL, regardless of the presence of ORM. Therefore, women with BV ≥1300 cc should be offered ORM at the time of lumpectomy in order to reduce their future risk of CBL.

Surgery

Schaff EM, **Gartrelle KJ**, **Kirsch C**, **Siddiqui F**, **Ajlouni M**, **Dragovic J**, **Aref I**, **Shah MM**, **Kwon D**, **Dobrosotskaya I**, **Shah R**, **Khan G**, and **Parikh PJ**. Magnetic Resonance Guided Stereotactic Ablative Radiation Therapy Versus External Beam RT with Chemotherapy For Pancreatic Cancer: Single Institution Toxicity Analysis Of Patients Treated In An Urban Academic Center. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):e582-e583.

Purpose/Objective(s): Several academic institutions have investigated stereotactic MR guided adaptive radiation therapy (SMART) to safely dose escalate for locally advanced and borderline resectable pancreatic cancer with initial favorable toxicity and survival outcomes. However, it is not clear that this treatment is safe or effective in more challenging populations, such as in an urban academic center. The purpose of this abstract was to review outcomes immediately before and after implementing dose escalated MR guided adaptive radiation therapy for pancreatic cancer. Materials/Methods: In this IRB

approved analysis, we retrospectively reviewed 57 consecutive patients from 2017-2019 with locally advanced or borderline resectable pancreatic cancer who were treated with neoadjuvant radiation therapy. Initially all patients received standard fractionated chemoradiation (chemoRT) to a dose of 50.4 Gy in 28 fractions. In September 2018 our institutional treatment guidelines were changed to recommend SMART (50Gy in 5 fractions) for these patients. Toxicity outcomes evaluated were grade 3+ GI toxicity based on CTCAE v5.0 as well as unplanned hospital admissions, both at 90 and 180 days. Treatment differences were analyzed using two sample t-test and chi-square test. Overall survival was evaluated at 180 days, and by Kaplan-Meier and log-rank test and was calculated from first day of radiation therapy. Results: 29 patients received chemoRT and 28 received SMART. Median follow up for the chemoRT group was 294 days and for SMART was 185 days. Groups did not have significant differences in age, performance status, stage, gender, CA 19-9, or neoadjuvant chemotherapy. Grade 3+ GI toxicity at 90 days was seen in 28% and 11% ($p = 0.11$) in the chemoRT and SMART groups, respectively. Types of toxicity were overall comparable with most being abdominal pain and duodenal bleeds. Hospital admissions at 90 days occurred in 38% and 21% of patients ($p = 0.17$) and at 180 days in 33% and 44% ($p = 0.48$). Surgical resection was achieved in 24% of chemoRT and 36% of SMART patients ($p = 0.34$). When evaluated using Kaplan-Meier and log-rank test there was a trend to overall survival benefit in the SMART group ($p = 0.07$). There was also a statistically significant 180-day survival improvement in SMART patients of 94% vs 70% in chemoRT patients ($p = 0.046$). Conclusion: Dose escalated SMART for locally advanced and borderline pancreatic cancer does not cause significant increase in GI grade 3+ GI toxicity at 90 days or hospitalization at 90 or 180 days as compared to chemoRT. Dose escalated SMART appears to be both safe and effective in our urban population. OS in the chemoRT group was comparable to previous trials such as LAP07. There is a trend to OS improvement on Kaplan-Meier analysis in the SBRT group ($p = 0.07$), as well as statistically significant improvement in 180-day survival; which supports the ongoing multi-institutional SMART study (NCT03621644). Updated results to be presented at the meeting.

Surgery

Shimada S, **Kitajima T**, **Lisznyai E**, **Suzuki Y**, **Kuno Y**, **Flores A**, **Sukkarieh N**, **Collins K**, **Rizzari M**, **Yoshida A**, **Abouljoud MS**, and **Nagai S**. FATE OF LIVER AND KIDNEY TRANSPLANT CANDIDATES BEFORE AND AFTER SIMULTANEOUS LIVER-KIDNEY TRANSPLANT ALLOCATION POLICY CHANGE. *Hepatology* 2020; 72:40A-40A.

[Shimada, Shingo; Kitajima, Toshihiro; Lisznyai, Eric; Suzuki, Yukiko; Kuno, Yasutaka; Flores, Alexander; Sukkarieh, Nicole; Rizzari, Michael] Henry Ford Hosp, Div Transplant & Hepatobiliary Surg, Detroit, MI 48202 USA. [Collins, Kelly] Henry Ford Hlth Syst, Transplant & Hepatobiliary Surg, Detroit, MI USA. [Yoshida, Atsushi] Henry Ford Hosp, Transplant Inst, Detroit, MI 48202 USA. [Abouljoud, Marwan S.; Nagai, Shunji] Henry Ford Hosp, Transplant & Hepatobiliary Surg, Detroit, MI 48202 USA.

Background: The OPTN/UNOS policy for kidney allocation to liver transplant (LT) recipients was implemented on August 10th, 2017. We investigated the impact of the policy change on outcomes on simultaneous liver-kidney transplantation (SLK) candidates. Methods: Using OPTN/UNOS data, we analyzed adult SLK candidates between January 2015 and March 2019. We excluded patients registered for retransplant. Patients were classified into two cohorts; cohort 1: from January 1st, 2015 to July 31st, 2017 (pre-policy group), cohort 2: from September 1st, 2017 to March 30th, 2019 (post-policy group). Waitlist outcomes, including 90-day mortality, transplant probability, and type of transplant (SLK vs. LT alone [LTA]) were compared between the two cohorts using a Fine-Gray competing risk regression model. Post-transplant outcomes were compared according to transplant type using a Cox regression model. Results: Of the 4641 patients eligible for this study, 2975 and 1666 were registered in cohorts 1 and 2, respectively. The average number of waitlisted patients (daily) was significantly lower in cohort 2 compared to cohort 1 (2.89/day vs. 3.25/day; p=0.013). In patients with MELD score >35, there was significantly higher 90-day transplant probability in cohort 2 (adjusted hazard ratio [aHR]:1.23, p=0.032); whereas no significant difference was observed in patients with MELD scores 30-34 or <29. The patients in cohort 2 with MELD scores ≥35 trended towards a lower 90- day waitlist mortality compared to patients in cohort 1 (aHR: 0.69, p=0.06). Regarding transplant type, the proportion of LTA in SLK candidates was significantly higher in cohort 2 compared to cohort 1; both overall (7.9% vs. 3.0%, P<0.001) and when stratified by MELD score (≤29, 30-34, ≥35; p=0.006, 0.008, 0.004, respectively) (Figure 1). Adjusted risk

of 1-year graft loss was significantly higher in LTA compared to SLK (aHR 2.01, p=0.012) (Figure 2). Conclusion: The new SLK policy significantly decreased the number of SLK transplants while significantly improving waitlist outcomes, especially in patients with higher MELD scores. After the policy change, patients who were initially registered for SLK more frequently received LTA, likely due to more stringent criteria. Because LTA outcomes were significantly worse than SLK in SLK candidates, the decision on transplant type for this patient population needs careful assessment.

Surgery

Suzuki Y, **Kitajima T**, **Flores A**, **Shimada S**, **Kuno Y**, **Lisznyai E**, **Sukkarieh N**, **Collins K**, **Rizzari M**, **Yoshida A**, **Abouljoud MS**, and **Nagai S**. PARADIGM CHANGE IN LIVER TRANSPLANT PRACTICE FOR PATIENTS WITH KIDNEY DYSFUNCTION AFTER THE IMPLEMENTATION OF THE NEW LIVER-KIDNEY ALLOCATION POLICY. *Hepatology* 2020; 72:1A-1A.

[Suzuki, Yukiko; Kitajima, Toshihiro; Flores, Alexander; Shimada, Shingo; Kuno, Yasutaka; Lisznyai, Eric; Sukkarieh, Nicole; Rizzari, Michael] Henry Ford Hosp, Div Transplant & Hepatobiliary Surg, Detroit, MI 48202 USA. [Collins, Kelly] Henry Ford Hlth Syst, Transplant & Hepatobiliary Surg, Detroit, MI USA. [Yoshida, Atsushi] Henry Ford Hosp Transplant Inst, Detroit, MI USA. [Abouljoud, Marwan S.; Nagai, Shunji] Henry Ford Hosp, Transplant & Hepatobiliary Surg, Detroit, MI 48202 USA.

Background: The new OPTN/UNOS policy regarding kidney allocation for liver transplant (LT) patients was implemented on Aug 10, 2017. Per the new policy, LT patients who developed kidney failure may be granted priority on the kidney transplant (KT) waitlist (Safety net). The aim of this study was to evaluate effects of the new policy on pre and post-transplant practice LT patients with kidney dysfunction. Methods: We analyzed adult primary LT alone (LTA) candidates who had kidney dysfunction at listing (Chronic kidney disease [CKD] stage 4 or higher) between January 2015 and March 2019 using data from the OPTN/UNOS. Impact of the new policy on the number of listings, waitlist outcomes, post-transplant outcomes, and KT listing after LTA were assessed. In post- LTA outcome analysis, patients were categorized according to kidney function at transplant (Group 1: CKD stage 4 without dialysis; Group 2: CKD stage 5 without dialysis; Group 3: dialysis requirement; Group 4: CKD stage 1-3 without dialysis). Results: A total of 3821 patients with CKD 4 or higher were registered for LTA. The daily number of patients on dialysis who were registered for LTA significantly increased in post- policy era compared with pre-policy era (1.21/day vs 0.95/ day, p <0.001). 90-day LT waitlist mortality (HR 0.99, p=0.94) or transplant probability (HR 1.07, p=0.25) was not changed in post-policy era, compared to pre-policy era. One-year liver graft survival in Groups 1, 2, 3, and 4 were comparable between before and after the policy implementation (Table 1). Of all LTA patients, the patients in post-policy era had a higher risk for KT listing after LTA than those in pre-policy era (6.2% vs 3.9%, odds ratio = 3.30, p <0.001), especially patients in Group 3, 8.4% vs 2.0% (odds ratio = 4.38, p <0.001) (Table 2). Among the 65 patients who were listed for KT in post- policy era, one-year KT probability, waitlist mortality rate, and removal rate due to clinical improvement rate were 61.1%, 1.5%, and 2.7%, respectively. Conclusion: The new policy significantly increased the number of LTA candidates with dialysis, did not affect their post-transplant survival, and increased KT listing after LTA. The safety-net rule led to high KT probability and low waitlist mortality rate in patients who were listed for KT after LTA. These results suggest that the new policy successfully stratified patients with kidney dysfunction for LTA and provided KT opportunities to patients post-LT kidney failure.

Surgery

Zhu S, **Atisha D**, **Evangelistia M**, **Barry R**, **Rama S**, Ghosh S, **Cannella C**, **Chen Y**, **Bensenhaver J**, **Levin KJ**, and **Walker EM**. Factors Associated with Chronic Breast Lymphedema After Adjuvant Radiation in Women Undergoing Breast Conservation Therapy. *International Journal of Radiation Oncology Biology Physics* 2020; 108(3):e32.

Purpose/Objective(s): Unlike temporary breast edema caused by post-lumpectomy radiation therapy (RT), the edema that persists beyond one year is not well defined and difficult to treat. The aim of this study is to define the incidence and risk factors for the development of chronic breast lymphedema in women undergoing lumpectomy with RT at a large metropolitan cancer center. Materials/Methods: A retrospective chart review was performed on all patients who underwent lumpectomy from 2014 to 2017.

Women who did not undergo RT at our institution and those with stage IV disease were excluded from the analysis. Patient demographics, comorbidities, operative data, RT data and postoperative complications were obtained. Chronic breast lymphedema (CBL) was defined as edema that persisted beyond one-year post completion of radiation therapy. Breast volumes were determined by contoured breast volumes or, if unavailable, estimated by the 95% isodose volumes from the RT treatment planning system. Using a density curve, the distribution of breast volumes was plotted for patients with and patients without CBL. Univariate analysis was used to evaluate factors associated with CBL. Multivariate regression analysis was used to evaluate factors associated with the risk of CBL while accounting for potential confounding variables as defined by the univariate analysis. Results: A total of 811 patients were included for analysis. Fifty-seven (7.0%) patients developed breast lymphedema beyond one year. For the entire cohort, mean age was 63.3 years old, mean BMI was 31.21 kg/m2, and mean breast volume was 1195 cc (SD = 643.25 cc). Compared to the cohort that did not develop CBL (n = 754), the CBL cohort (n = 57) had a higher BMI (33.10 kg/m2 vs. 29.84 kg/m2, p<0.001), higher percentage of black race (61.4% vs. 43.8%, P = 0.024), larger breast volume (1504 cc vs. 1081 cc, P<0.001), greater number of lymph nodes taken at time of surgery (3 vs. 1, P<0.001), higher percentage that had underwent ALND (12.3% vs. 5.2%, P = 0.036), and larger size of lumpectomy specimen (118.95 cm3 vs. 96.00 cm3, P = 0.016). The density curve determined that the optimal cutoff for breast volume was around 1300 cc. When accounting for potential confounding variables, multivariate regression analysis revealed that those whose breast volume > 1300 cc (vs. <1300 cc) were 2.5 times more likely to experience breast lymphedema after one year (OR = 2.53, p = 0.005). When volume was evaluated as a continuous variable, regression analysis revealed that for every 1cc increase in breast volume, the risk of breast lymphedema increases by 0.1% (OR = 1.001, P = 0.001). Conclusion: Chronic breast lymphedema presents a clinical concern for women undergoing lumpectomy with postoperative radiation, particularly women with larger breasts. Further studies should focus on preventative strategies, as well as the psychosocial and economic impact of this morbidity.

Books and Book Chapters

Pathology and Laboratory Medicine
Kostiuk M, and Burns B. "Trauma Assessment". StatPearls. Treasure Island (FL), StatPearls Publishing Copyright © 2020, StatPearls Publishing LLC.2020. PMID: 32310373. Full Text

Henry Ford Macomb Hospital
East Tennessee State University (ETSU)

Trauma is the leading cause of death worldwide. In the United States, trauma is the leading cause of death in young adults and accounts for ten percent of death in all men and women. In the U.S., there are approximately 50 million visits to the emergency department annually related to trauma. The most common causes of mortality in trauma victims include hemorrhage, cardiopulmonary arrest, and multiple organ dysfunction syndrome. The assessment of trauma victims requires an organized and systematic approach. When caring for a trauma victim, physicians, nurses, and support staff must work together and communicate effectively. The goal of assessing trauma victims is identifying immediate life threats and stabilizing the patient.

Surgery
Bennett B, and Rentea RM. "Thymectomy". StatPearls. Treasure Island (FL), StatPearls Publishing Copyright © 2020, StatPearls Publishing LLC. PMID: 33231972. Full Text

Henry Ford Allegiance Health
Children's Mercy

Thymectomy is the resection of the thymus gland. This anterior mediastinal organ can enlarge as in myasthenia gravis and thymoma and harbor malignant cells such as in thymic carcinoma or neuroendocrine tumors. The first thymectomies were performed incidentally in conjunction with thyroidectomies for Grave disease by Garre and Sauerbruch, but it was not until Blalock and colleagues that multiple series were performed with adequate results. This also included patients with myasthenia gravis but without thymomas. The gold standard approach for thymectomy is a median sternotomy or transsternal approach, but this has evolved to less invasive techniques such as upper partial sternotomy, transcervical, video-assisted thoracoscopic thymectomy, and robot-assisted approaches. Preoperative evaluation should include the functional status and pulmonary function tests, especially with single-lung ventilation in thoracoscopic approaches. Video-assisted and robot-assisted thoracoscopic thymectomies have shown to be superior to the traditional open approaches (transsternal or transcervical) in promoting shorter hospital length of stay and decreased morbidity and mortality.

HFHS Publications on COVID-19

Anesthesiology
Chhina AK, **Loyd GE**, **Szymanski TJ**, **Nowak KA**, **Peruzzi WT**, **Yeldo NS**, **Han X**, **Kerzabi LS**, **Galusca DM**, **Cazacu S**, **Brodie C**, and **Penning DH**. Frequency and Analysis of Unplanned Extubation in Coronavirus Disease 2019 Patients. *Crit Care Explor* 2020; 2(12):e0291. PMID: 33251520. Full Text

Center for Health Policy and Health Services Research
Gordon SC, **Rupp LB**, Boscarino JA, Daida Y, Schmidt MA, **Zhou YR**, **Trudeau S**, **Li J**, and **Lu M**. RISK FACTORS FOR SARS-COV-2 INFECTION AMONG PATIENTS WITH CHRONIC VIRAL HEPATITIS. *Hepatology* 2020; 72:299A-300A.

Center for Health Policy and Health Services Research
Lu M, **Rupp LB**, Boscarino JA, Schmidt MA, Daida Y, **Zhou YR**, **Trudeau S**, **Li J**, and **Gordon SC**. IMPACT OF HISTORY OF CHRONIC VIRAL HEPATITIS AND LIVER FIBROSIS ON RISK OF HOSPITALIZATION AND DEATH AMONG PATIENTS WITH SARS-COV-2 INFECTION. *Hepatology* 2020; 72:280A-281A.

Dermatology
Kashlan R, **Lyons AB**, Hivnor C, and **Ozog DM**. N95 Respirators for Dermatologic Surgery and Laser Procedures During COVID-19 and Beyond. *Dermatol Surg* 2020; 46(11):1441-1442. PMID: 33105244. Full Text

Gastroenterology
Gordon SC, **Rupp LB**, Boscarino JA, Daida Y, Schmidt MA, **Zhou YR**, **Trudeau S**, **Li J**, and **Lu M**. RISK FACTORS FOR SARS-COV-2 INFECTION AMONG PATIENTS WITH CHRONIC VIRAL HEPATITIS. *Hepatology* 2020; 72:299A-300A.

Gastroenterology
Lu M, **Rupp LB**, Boscarino JA, Schmidt MA, Daida Y, **Zhou YR**, **Trudeau S**, **Li J**, and **Gordon SC**. IMPACT OF HISTORY OF CHRONIC VIRAL HEPATITIS AND LIVER FIBROSIS ON RISK OF HOSPITALIZATION AND DEATH AMONG PATIENTS WITH SARS-COV-2 INFECTION. *Hepatology* 2020; 72:280A-281A.

Gastroenterology
Siddiqui MB, **Suresh S**, **Abu Ghanimeh M**, **Karrick M**, **Nimri F**, **Musleh M**, **Mendiratta V**, **Al-Shammari M**, **Simmer S**, **Jou J**, **Russell SM**, **Dang DY**, **Salgia RJ**, and **Zuchelli T**. LIVER INJURY IS ASSOCIATED WITH INCREASED MORBIDITY AND MORTALITY IN COVID-19 PATIENTS. *Hepatology* 2020; 72:287A-287A.

Gastroenterology
Suresh S, **Siddiqui MB**, **Abu Ghanimeh M**, **Nimri F**, **Karrick M**, **Musleh M**, **Mendiratta V**, **Russell SM**, **Jou J**, **Simmer S**, **Al-Shammari M**, **Dang D**, and **Zuchelli T**. CLINICAL OUTCOMES IN HOSPITALIZED COVID-19 PATIENTS WITH CHRONIC LIVER DISEASE AND CIRRHOSIS. *Hepatology* 2020; 72:263A-263A.

Hematology-Oncology
Tam S, **Wu VF**, **Williams AM**, **Girgis M**, **Sheqwara JZ**, **Siddiqui F**, and **Chang SS**. Disparities in the Uptake of Telemedicine During the COVID-19 Surge in a Multidisciplinary Head and Neck Cancer Population by Patient Demographic Characteristics and Socioeconomic Status. *JAMA Otolaryngol Head Neck Surg* 2020; Epub ahead of print. PMID: 33151289. Full Text

Infectious Diseases
Alangaden GJ, and **Mayur RS**. Response to "Is the outcome of SARS-CoV-2 infection in solid organ transplant recipients really similar to that of the general population?". *Am J Transplant* 2020; Epub ahead of print. PMID: 33249750. Full Text

Infectious Diseases
Tsang O, **Brar I**, Spinner C, Robinson P, Roestenberg M, Calmy A, Malvy D, Elboudwarej E, Tian Y, McDonald C, Tan S, Suri V, Hyland R, SenGupta D, Chokkalingam AP, Gaggar A, Osinusi AO, Brainard DM, Kim SW, Cooke G, Shan-Chwen SC, Nicastri E, Castano M, and Chai LYA. IMPACT OF BASELINE ALANINE AMINOTRANSFERASE LEVELS ON THE SAFETY AND EFFICACY OF REMDESIVIR IN MODERATE COVID-19 PATIENTS. *Hepatology* 2020; 72:88A-89A.

Internal Medicine
Siddiqui MB, **Suresh S**, **Abu Ghanimeh M**, **Karrick M**, **Nimri F**, **Musleh M**, **Mendiratta V**, **Al-Shammari M**, **Simmer S**, **Jou J**, **Russell SM**, **Dang DY**, **Salgia RJ**, and **Zuchelli T**. LIVER INJURY IS ASSOCIATED WITH INCREASED MORBIDITY AND MORTALITY IN COVID-19 PATIENTS. *Hepatology* 2020; 72:287A-287A.

Internal Medicine
Suresh S, **Siddiqui MB**, **Abu Ghanimeh M**, **Nimri F**, **Karrick M**, **Musleh M**, **Mendiratta V**, **Russell SM**, **Jou J**, **Simmer S**, **Al-Shammari M**, **Dang D**, and **Zuchelli T**. CLINICAL OUTCOMES IN HOSPITALIZED COVID-19 PATIENTS WITH CHRONIC LIVER DISEASE AND CIRRHOSIS. *Hepatology* 2020; 72:263A-263A.

Neurology
Anand SK, **Macki M**, Culver LG, **Wasade VS**, Hendren S, and **Schwalb JM**. Patient navigation in epilepsy care. *Epilepsy Behav* 2020; 113:107530. PMID: 33232897. Full Text

Neurology
Carneiro T, Dashkoff J, Leung LY, Nobleza COS, Marulanda-Londono E, Hathidara M, Koch S, Sur N, Boske A, Voetsch B, **Aboul Nour H**, **Miller DJ**, Daneshmand A, Shulman J, Curiale G, Greer DM, Romero JR, Anand P, and Cervantes-Arslanian AM. Intravenous tPA for Acute Ischemic Stroke in Patients with COVID-19. *J Stroke Cerebrovasc Dis* 2020; 29(11):105201. PMID: 33066885. Full Text

Neurology
Chaudhry F, **Bulka H**, **Rathnam AS**, Said OM, Lin J, **Lorigan H**, Bernitsas E, Rube J, Korzeniewski SJ, **Memon AB**, Levy PD, **Schultz L**, Javed A, Lisak R, and **Cerghet M**. COVID-19 in multiple sclerosis patients and risk factors for severe infection. *J Neurol Sci* 2020; 418:117147. PMID: 32980780. Full Text

Neurology
Lima M, Siokas V, Aloizou AM, Liampas I, Mentis AA, Tsouris Z, Papadimitriou A, **Mitsias PD**, Tsatsakis A, Bogdanos DP, Baloyannis SJ, and Dardiotis E. Unraveling the Possible Routes of SARS-COV-2 Invasion into the Central Nervous System. *Curr Treat Options Neurol* 2020; 22(11):37. PMID: 32994698. Full Text

Neurosurgery
Chhina AK, **Loyd GE**, **Szymanski TJ**, **Nowak KA**, **Peruzzi WT**, **Yeldo NS**, **Han X**, **Kerzabi LS**, **Galusca DM**, **Cazacu S**, **Brodie C**, and **Penning DH**. Frequency and Analysis of Unplanned Extubation in Coronavirus Disease 2019 Patients. *Crit Care Explor* 2020; 2(12):e0291. PMID: 33251520. Full Text

Otolaryngology
Tam S, **Wu VF**, **Williams AM**, **Girgis M**, **Sheqwara JZ**, **Siddiqui F**, and **Chang SS**. Disparities in the Uptake of Telemedicine During the COVID-19 Surge in a Multidisciplinary Head and Neck Cancer Population by Patient Demographic Characteristics and Socioeconomic Status. *JAMA Otolaryngol Head Neck Surg* 2020; Epub ahead of print. PMID: 33151289. Full Text

Public Health Sciences
Chhina AK, **Loyd GE**, **Szymanski TJ**, **Nowak KA**, **Peruzzi WT**, **Yeldo NS**, **Han X**, **Kerzabi LS**, **Galusca DM**, **Cazacu S**, **Brodie C**, and **Penning DH**. Frequency and Analysis of Unplanned Extubation in Coronavirus Disease 2019 Patients. *Crit Care Explor* 2020; 2(12):e0291. PMID: 33251520. Full Text

Public Health Sciences
Gordon SC, **Rupp LB**, Boscarino JA, Daida Y, Schmidt MA, **Zhou YR**, **Trudeau S**, **Li J**, and **Lu M**. RISK FACTORS FOR SARS-COV-2 INFECTION AMONG PATIENTS WITH CHRONIC VIRAL HEPATITIS. *Hepatology* 2020; 72:299A-300A.

Public Health Sciences
Lu M, **Rupp LB**, Boscarino JA, Schmidt MA, Daida Y, **Zhou YR**, **Trudeau S**, **Li J**, and **Gordon SC**. IMPACT OF HISTORY OF CHRONIC VIRAL HEPATITIS AND LIVER FIBROSIS ON RISK OF HOSPITALIZATION AND DEATH AMONG PATIENTS WITH SARS-COV-2 INFECTION. *Hepatology* 2020; 72:280A-281A.

Radiation Oncology
Tam S, **Wu VF**, **Williams AM**, **Girgis M**, **Sheqwara JZ**, **Siddiqui F**, and **Chang SS**. Disparities in the Uptake of Telemedicine During the COVID-19 Surge in a Multidisciplinary Head and Neck Cancer Population by Patient Demographic Characteristics and Socioeconomic Status. *JAMA Otolaryngol Head Neck Surg* 2020; Epub ahead of print. PMID: 33151289. Full Text

Sleep Medicine
Cheng P, Casement MD, **Kalmbach DA**, **Castelan AC**, and **Drake CL**. Digital Cognitive Behavioral Therapy for Insomnia Promotes Later Health Resilience During the Coronavirus Disease 19 (COVID-19) Pandemic. *Sleep* 2020; Epub ahead of print. PMID: 33249492. Full Text

Surgery
Brown CS, Albright J, Henke PK, Mansour MA, **Weaver M**, and Osborne NH. Modeling the Elective Vascular Surgery Recovery After COVID-19: Implications for Moving Forward. *J Vasc Surg* 2020; Epub ahead of print. PMID: 33248121. Full Text

Urology
Tandogdu Z, Collins J, Shaw G, Rohn J, Koves B, Sachdeva A, Ghazi A, Haese A, Mottrie A, Kumar A, Sivaraman A, Tewari A, Challacombe B, Rocco B, Giedelman C, Wagner C, **Rogers CG**, Murphy DG, Pushkar D, Ogaya-Pinies G, Porter J, Ramesh Seetharam K, Graefen M, Orvieto MA, Covas Moschovas M, Schatloff O, Wiklund P, Coelho R, Valero R, de Reijke TM, Ahlering T, Rogers T, van der Poel HG, Patel V, Artibani W, Wagenlehner F, Nathan S, Erik Bjerklund Johansens T, Hawkey P, and Kelly J. Management of patients who opt for radical prostatectomy during the COVID-19 pandemic: An International Accelerated Consensus Statement. *BJU Int* 2020; Epub ahead of print. PMID: 33185026. Full Text