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Henry Ford Health System

Henry Ford Health System Publication List – June 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 112 unique citations listed this month, 10 on COVID-19 from 12 departments. Articles are listed first, followed by conference abstracts, books and book chapters, and a bibliography of publications on COVID-19. Because of various limitations, this does not represent an exhaustive list of all published works by Henry Ford Health System authors.

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Articles

Administration

Kim DD, and **Sibai N**. The Current State of Opioid Prescribing and Drug Enforcement Agency (DEA) Action Against Physicians: An Analysis of DEA Database 2004-2017. *Pain Physician* 2020; 23(3):E297-e304. PMID: 32517406. Full Text

Pain Medicine Division, Department of Anesthesiology, Henry Ford Health System, Detroit MI.

BACKGROUND: Prescribing opioids has become a challenge. The US Drug Enforcement Agency (DEA) and Centers for Disease Control and Prevention (CDC) have become more involved, culminating in the March 2016 release of the CDC's "Guidelines for Prescribing Opioids for Chronic Pain." OBJECTIVES: Given the new guidelines, we wanted to see if there have been any changes in the numbers, demographics, physician risk factors, charges, and sanctions involving the DEA against physicians who prescribe opioids, when compared to a previous DEA database review from 1998 to 2006. STUDY DESIGN: This study involved an analysis of the DEA database from 2004 to 2017. SETTING: The review was conducted at the Henry Ford Health System Division of Pain Medicine. METHOD: After institutional review board approval at Henry Ford Health System, an analysis of the DEA database of criminal prosecutions of physician registrants from 2004-2017 was performed. The database was reviewed for demographic information such as age, gender, type of degree (doctor of medicine [MD] or doctor of osteopathic medicine [DO]), years of practice, state, charges, and outcome of prosecution (probation, sentencing, and length of sentencing). An internet-based search was performed on each registrant to obtain demographic data on specialty, years of practice, type of medical school (US vs foreign), board certification, and type of employment (private vs employed). RESULTS: Between 2004 and 2017, Pain Medicine (PM) had the highest percentage of in-specialty action at 0.11% (n = 5). There was an average of 18 prosecutions per year vs 14 in the previous review. Demographic risk factors for prosecution demonstrated the significance of the type of degree (MD vs. DO), gender, type of employment (private vs. employed), and board certification status for rates of prosecution. Having a DO degree and being male were associated with significantly higher risk as well as being in private practice and not having board certification (P < .001). In terms of type of criminal charges as a percent of cases, possession with intent to distribute (n = 90) was most prevalent, representing 52.3% of charges, with new charges being prescribing without medical purpose outside the usual course of practice (n = 71) representing 41.3% of charges. Comparison of US graduates (MD/DO) vs. foreign graduates showed higher rates of DEA action for foreign graduates but this was of borderline significance (P = .072). LIMITATIONS: State-by-state comparisons could not be made. Specialty type was sometimes self-reported, and information on all opioid prosecutions could not be obtained. The previous study by Goldenbaum et al included data beyond DEA prosecution, so direct comparisons may be limited. CONCLUSION: The overall risk of DEA action as a percentage of total physicians is small but not insignificant. The overall rates of DEA prosecution have increased. New risk factors include type of degree (DO vs. MD) and being in private practice with a subtle trend toward foreign graduates at higher risk. With the trend toward less prescribing by previously high-risk specialties such as Family Medicine, there has been an increase in the relative risk of DEA action for specialties treating patients with

pain such as PM, Physical Medicine and Rehabilitation, neurology, and neurosurgery bearing the brunt of prosecutions. New, more subtle charges have been added involving interpretation of the medical purpose of opioids and standard of care for their use. KEY WORDS: Certification, CDC, criminal, DEA, opioid, prescribing, prosecution, sanctions.

Behavioral Health Services/Psychiatry
Xiang X, **Ning Y**, and Kayser J. The Implications of COVID-19 for the Mental Health Care of Older Adults: Insights from Emergency Department Social Workers. *J Gerontol Soc Work* 2020; Epub ahead of print. PMID: 32543294. Request Article

University of Michigan School of Social Work , Ann Arbor, Michigan, USA, xiangxi@umich.edu.
Behavioral Health Social Worker, Henry Ford Allegiance Health , Jackson, Michigan, USA.
Clinical Social Worker, Departments of Social Work and Developmental Psychology, University of Michigan , Ann Arbor, Michigan, USA.

Cardiology/Cardiovascular Research
Ananthasubramaniam K, and **Karthikeyan V**. Lurking in the shadows: Asymptomatic bilateral lung involvement with novel corona virus 2019 identified on myocardial perfusion SPECT CT: Implications for interpreting physicians. *J Nucl Cardiol* 2020; Epub ahead of print. PMID: 32529532. Full Text

Heart and Vascular Institute, Henry Ford West Bloomfield Hospital, West Bloomfield, MI, USA. kananth1@hfhs.org.
Division of Nephrology, Henry Ford West Bloomfield Hospital, West Bloomfield, MI, USA.

Cardiology/Cardiovascular Research
Hernandez-Suarez DF, Ranka S, Kim Y, Latib A, Wiley J, Lopez-Candales A, Pinto DS, Gonzalez MC, Ramakrishna H, Sanina C, Nieves-Rodriguez BG, Rodriguez-Maldonado J, Feliu Maldonado R, Rodriguez-Ruiz IJ, da Luz Sant'Ana I, Wiley KA, Cox-Alomar P, **Villablanca PA**, and Roche-Lima A. Machine-learning-based in-hospital mortality prediction for transcatheter mitral valve repair in the United States. *Cardiovasc Revasc Med* 2020; Epub ahead of print. PMID: 32591310. Full Text

Division of Cardiovascular Medicine, Department of Medicine, University of Puerto Rico School of Medicine, San Juan, PR, USA. Electronic address: dagmar.hernandez@upr.edu.
Division of Cardiovascular Medicine, Department of Medicine, University of Kansas School of Medicine, Kansas City, KS, USA.
Division of Cardiovascular Medicine, Department of Medicine, Yale University School of Medicine, New Haven, CT, USA.
Division of Cardiology, Department of Medicine, Montefiore Medical Center/Albert Einstein College of Medicine, New York, NY, USA.
Division of Cardiology, Department of Medicine, University of Arkansas for Medical Sciences, Little Rock, AR, USA.
Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA.
Division of Cardiovascular and Thoracic Anesthesiology, Mayo Clinic, Rochester, MN, USA.
Center for Collaborative Research in Health Disparities, University of Puerto Rico School of Medicine, San Juan, PR, USA.
College of Agriculture and Life Sciences, Cornell University, Ithaca, NY, USA.
Division of Cardiology, Department of Medicine, Louisiana State University, New Orleans, LA, USA.
Division of Cardiovascular Medicine, Department of Medicine, Henry Ford Hospital, Detroit, MI, USA.

BACKGROUND: Transcatheter mitral valve repair(2) utilization has increased significantly in the United States over the last years. Yet, a risk-prediction tool for adverse events has not been developed. We aimed to generate a machine-learning-based algorithm to predict in-hospital mortality after TMVR. METHODS: Patients who underwent TMVR from 2012 through 2015 were identified using the National Inpatient Sample database. The study population was randomly divided into a training set (n = 636) and a testing set (n = 213). Prediction models for in-hospital mortality were obtained using five supervised machine-learning classifiers. RESULTS: A total of 849 TMVRs were analyzed in our study. The overall in-hospital mortality was 3.1%. A naïve Bayes (NB) model had the best discrimination for fifteen variables, with an area under the receiver-operating curve (AUC) of 0.83 (95% CI, 0.80-0.87), compared to 0.77 for logistic regression (95% CI, 0.58-0.95), 0.73 for an artificial neural network (95% CI, 0.55-0.91), and 0.67 for both a random forest and a support-vector machine (95% CI, 0.47-0.87). History of coronary artery disease, of chronic kidney disease, and smoking were the three most significant predictors of in-hospital mortality. CONCLUSIONS: We developed a robust machine-learning-derived model to predict in-hospital mortality in patients undergoing TMVR. This model is promising for decision-making and deserves further clinical validation.

Cardiology/Cardiovascular Research

Kang G, **Lee J**, **Song T**, **Pantelic M**, **Reeser N**, **Keimig T**, **Nadig J**, **Villablanca P**, **Frisoli T**, **Eng M**, **O'Neill W**, and **Wang DD**. Three-Dimensional CT Planning for Cerebral Embolic Protection in Structural Interventions. *JACC Cardiovasc Imaging* 2020; Epub ahead of print. PMID: 32563641. Full Text

Center for Structural Heart Disease, Henry Ford Health System, Detroit, Michigan.
Department of Radiology, Henry Ford Health System, Detroit, Michigan.
Center for Structural Heart Disease, Henry Ford Health System, Detroit, Michigan. Electronic address: dwang2@hfhs.org.

Cardiology/Cardiovascular Research

Lemor A, **Gorgis S**, **Villablanca PA**, **Basir MB**, **Voeltz M**, **Alaswad K**, and **O'Neill W**. Regional Variation in Procedural and Clinical Outcomes Among Patients With ST Elevation Myocardial Infarction With Cardiogenic Shock. *Am J Cardiol* 2020; 125(11):1612-1618. PMID: 32279842. Full Text

Division of Cardiology, Henry Ford Hospital, Detroit, Michigan; Centro de Investigación de Epidemiología Clínica y Medicina Basada en la Evidencia, Facultad de Medicina, Universidad de San Martín de Porres, Lima, Peru. Electronic address: alejandrolemor@outlook.com.
Division of Cardiology, Henry Ford Hospital, Detroit, Michigan.

There is limited data on regional differences in patient characteristics, practice patterns, and clinical outcomes in patients with ST elevation myocardial infarction (STEMI) with cardiogenic shock (CS) in the United States (US). We aimed to identify variations in treatment methods and clinical outcomes in patients with STEMI CS between the 4 US regions. Using the National Inpatient Sample database, we identified adult patients admitted with STEMI associated with CS between 2006 and 2015 using ICD-9-DM codes. Based on the US regions (Northeast, Midwest, South, and West), we divided patients in 4 cohorts and compared baseline patient characteristics, clinical outcomes and procedural outcomes. A total of 186,316 patients with STEMI CS were included; 32,303 (17.3%) were hospitalized in the Northeast, 43,634 (23.4%) in the Midwest, 70,036 (37.8%) in the South, and 40,043 (21.5%) in the West. Although nonstatistically significant, the in-hospital mortality was higher in Northeast region (37.7%), followed by the South (36.6%), West (35.7%), and Midwest (35.2%). Rates of percutaneous coronary intervention were higher in the Midwest (68.5%) and lower in the Northeast (56%). The use of percutaneous ventricular assist device and ECMO was higher in the Northeast (3.3% and 2.2%) and lower in the West (2.1% and 0.4%). The median length of stay was similar among all 4 cohorts (6 days) but median hospital costs were higher in the West ($36, 614) and lower in the South ($28,795). In conclusion, there are significant geographic variations in practice patterns, healthcare cost, and in-hospital outcomes in patients with STEMI complicated by CS between 4 US regions.

Cardiology/Cardiovascular Research

Lemor A, Patel N, **Jain T**, Baber U, Hernandez G, **Villablanca P**, **Basir MB**, **Alaswad K**, Mehran R, Dangas G, Sharma SK, and Kini A. Trends and Outcomes of Intravascular Imaging-guided Percutaneous Coronary Intervention in the United States. *Crit Pathw Cardiol* 2020; 19(2):69-74. PMID: 31895248. Full Text

From the Department of Cardiology, Henry Ford Hospital, Detroit, MI.
Universidad de San Martín de Porres, Facultad de Medicina, Centro de Investigación de Epidemiología Clínica y Medicina Basada en la Evidencia Lima, Peru.
Department of Cardiology, The Mount Sinai Hospital, New York, NY.
Department of Cardiology, University of Miami/Jackson Memorial Hospital, Miami, FL.

INTRODUCTION: Intravascular imaging-guided percutaneous coronary intervention (PCI) has shown to improve outcomes in randomized controlled trials. However, there are little real-world data about intravascular imaging utilization during PCI and its outcomes in the United States. METHODS: We conducted an observational analysis on the use of intravascular imaging (Intravascular Ultrasound or Optical Coherence Tomography)-guided PCI in 2,425,036 patients undergoing PCI between January 2010 and December 2014 from the Nationwide Inpatient Sample database. Utilizing propensity score matching, 83,988 matched pairs were identified. The primary outcome was in-hospital mortality. The secondary outcomes included cardiogenic shock and acute kidney injury. RESULTS: Among the 2,425,036 patients, 161,808 (6.7%) underwent imaging-guided PCI. Use of imaging-guidance increased from 6% in 2010 to 6.6% in 2014 (Ptrend < 0.001). The in-hospital mortality was significantly different between imaging-guided PCI and angiography-guided PCI [1.0% vs. 1.5%; adjusted OR: 0.67; 95% confidence interval (CI): 0.54-0.83, P < 0.001]. The rates of cardiogenic shock (2.5% vs. 3.1%; adjusted OR: 0.78; 95% CI: 0.66-0.93; P = 0.005) were significantly lower in imaging-guided PCI group and acute kidney injury rates (7.0% vs. 7.1%; adjusted OR: 0.99; 95% CI: 0.89-1.12; P = 0.919) were not significantly different. CONCLUSIONS: Imaging-guided PCI is associated with lower in-hospital mortality. Yet, a small proportion of patients undergoing PCI have imaging-guidance.

Cardiology/Cardiovascular Research
Nikolakopoulos I, Choi JW, **Alaswad K**, Khatri JJ, Krestyaninov O, Khelimskii D, Yeh RW, Jaffer FA, Toma C, Patel M, Mahmud E, Lembo NJ, Parikh M, Kirtane AJ, Ali ZA, Gkargkoulas F, Uretsky B, Sheikh AM, Vemmou E, Xenogiannis I, Rangan BV, Garcia S, Abdullah S, Banerjee S, Burke MN, Brilakis ES, and Karmpaliotis D. Equipment utilization in chronic total occlusion percutaneous coronary interventions: Insights from the PROGRESS-CTO registry. *Catheter Cardiovasc Interv* 2020; Epub ahead of print. PMID: 32597031. Full Text

Minneapolis Heart Institute and Minneapolis Heart Institute Foundation, Abbott Northwestern Hospital, Minneapolis, Minnesota, USA.
Baylor Heart and Vascular Hospital, Dallas, Texas, USA.
Henry Ford Hospital, Detroit, Michigan, USA.
Cleveland Clinic, Cleveland, Ohio, USA.
Meshalkin Novosibirsk Research Institute, Novosibirsk, Russia.
Beth Israel Deaconess Medical Center, Boston, Massachusetts, USA.
Massachusetts General Hospital, Boston, Massachusetts, USA.
University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania, USA.
VA San Diego Healthcare System and University of California San Diego, San Diego, California, USA.
Columbia University, New York, USA.
VA Central Arkansas Healthcare System, Little Rock, Arkansas, USA.
Wellstar Health System, Marietta, Georgia, USA.
VA North Texas Health Care System and University of Texas Southwestern Medical Center, Dallas, Texas, USA.

BACKGROUND: We examined guidewire and microcatheter utilization during chronic total occlusion (CTO) percutaneous coronary intervention (PCI). METHODS: We examined device utilization in 2,968 CTO PCIs performed in 2,936 patients at 19 US and two international center between January 2016 and January 2019. RESULTS: The median number of antegrade guidewires used per case declined (5 in 2016 vs 3 in 2019) and was higher in higher complexity lesions (2 in J-CTO 0 vs. 8 in J-CTO 4 or 5 score). In antegrade-only procedures, the most frequently used guidewires were the Pilot 200 (Abbott Vascular, 37%), Fielder XT (Asahi Intecc, 25%) and Gaia third (Asahi Intecc, 18%), while the most commonly used microcatheters were the Turnpike Spiral (Vascular Solutions, 18%) and Turnpike (Vascular Solutions, 16%). Compared with 2012-2015, during 2016-2019 use of novel equipment such as the Gaia guidewires and the Turnpike microcatheters led to decreased use of Confianza Pro 12 (Asahi Intecc) wire and Corsair (Asahi Intecc) family of microcatheters. In retrograde cases, the guidewires most commonly used were the Sion (44%), Pilot 200 (27%) and Fielder FC (26%), while the Corsair/Corsair Pro, Turnpike LP (Vascular Solutions) and Caravel (Asahi Intecc) were the most frequently used microcatheters for collateral crossing (29%, 26% and 22%, respectively). CONCLUSIONS: The most commonly used guidewires during CTO PCI are polymer-jacketed guidewires and the most commonly used microcatheters are torquable microcatheters.

Cardiology/Cardiovascular Research
Salih M, Ibrahim R, Tirunagiri D, Al-Ani H, and **Ananthasubramaniam K**. Loeffler's Endocarditis and Hypereosinophilic Syndrome. *Cardiol Rev* 2020; Epub ahead of print. PMID: 32520731. Full Text

Department of Internal Medicine and Cardiology, St Joseph Mercy Oakland Hospital, Pontiac MI.
The Heart and Vascular Institute, Henry Ford West Bloomfield Hospital, West Bloomfield MI.

Loeffler's endocarditis and hypereosinophilic syndromes are a unique group of infiltrative disorders characterized by hypereosinophilia and inflammatory thrombotic and ultimately fibrotic involvement of the heart, leading to multiple complications including valve involvement, thromboembolic phenomena and heart failure. Clinical recognition, comprehensive laboratory and multimodality imaging diagnostic workup, and early initiation of treatment have been shown to slow down the progression and promote remission. This review addresses a detailed analysis of Loeffler's endocarditis and hypereosinophilic syndromes.

Cardiology/Cardiovascular Research
Shah PB, Welt FGP, Mahmud E, Phillips A, Kleiman NS, Young MN, Sherwood M, Batchelor W, **Wang DD**, Davidson L, **Wyman J**, Kadavath S, Szerlip M, Hermiller J, Fullerton D, and Anwaruddin S. Triage Considerations for Patients Referred for Structural Heart Disease Intervention During the COVID-19 Pandemic: An ACC/SCAI Position Statement. *JACC Cardiovasc Interv* 2020; 13(12):1484-1488. PMID: 32250751. Full Text

American College of Cardiology Interventional Cardiology Section Leadership Council, Washington, DC; Division of Cardiovascular Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts. Electronic address: pbshah@partners.org.
American College of Cardiology Interventional Cardiology Section Leadership Council, Washington, DC; Cardiovascular Division, University of Utah Health, Salt Lake City, Utah.

Society for Cardiovascular Angiography and Interventions, Washington, DC; Division of Cardiovascular Medicine, University of California-San Diego, San Diego, California.
American College of Cardiology Cardiac Surgery Team and Leadership Council, Washington, DC; The Heart, Vascular, and Thoracic Institute, Cleveland Clinic, Cleveland, Ohio.
American College of Cardiology Interventional Cardiology Section Leadership Council, Washington, DC; Cardiovascular Division, Houston Methodist Hospital, Houston, Texas.
American College of Cardiology Interventional Cardiology Section Leadership Council, Washington, DC; Cardiovascular Division, Dartmouth-Hitchcock Medical Center, Geisel School of Medicine at Dartmouth, Lebanon, New Hampshire.
American College of Cardiology Interventional Cardiology Section Leadership Council, Washington, DC; Division of Cardiology, Inova Heart and Vascular Institute, Fairfax, Virginia.
Henry Ford Health System, Center for Structural Heart Disease, Wayne State University School of Medicine, Detroit, Michigan.
American College of Cardiology Interventional Cardiology Section Leadership Council, Washington, DC; Bluhm Cardiovascular Institute, Feinberg School of Medicine, Northwestern University, Chicago, Illinois.
American College of Cardiology Interventional Cardiology Section Leadership Council, Washington, DC; Henry Ford Health System, Center for Structural Heart Disease, Wayne State University School of Medicine, Detroit, Michigan.
American College of Cardiology Interventional Cardiology Section Leadership Council, Washington, DC; Department of Cardiovascular Medicine, University of Arkansas for Medical Sciences, Little Rock, Arkansas.
Society for Cardiovascular Angiography and Interventions, Washington, DC; Baylor Scott and White, The Heart Hospital Plano, Plano, Texas.
Society for Cardiovascular Angiography and Interventions, Washington, DC; Ascension Medical Group, Indianapolis, Indiana.
American College of Cardiology Cardiac Surgery Team and Leadership Council, Washington, DC; Division of Cardiothoracic Surgery, University of Colorado School of Medicine, Denver, Colorado.
American College of Cardiology Interventional Cardiology Section Leadership Council, Washington, DC; Cardiovascular Division, The Hospital of the University of Pennsylvania, Perelman School of Medicine, Philadelphia, Pennsylvania.

The coronavirus disease-2019 (COVID-19) pandemic has strained health care resources around the world, causing many institutions to curtail or stop elective procedures. This has resulted in an inability to care for patients with valvular and structural heart disease in a timely fashion, potentially placing these patients at increased risk for adverse cardiovascular complications, including CHF and death. The effective triage of these patients has become challenging in the current environment as clinicians have had to weigh the risk of bringing susceptible patients into the hospital environment during the COVID-19 pandemic against the risk of delaying a needed procedure. In this document, the authors suggest guidelines for how to triage patients in need of structural heart disease interventions and provide a framework for how to decide when it may be appropriate to proceed with intervention despite the ongoing pandemic. In particular, the authors address the triage of patients in need of transcatheter aortic valve replacement and percutaneous mitral valve repair. The authors also address procedural issues and considerations for the function of structural heart disease teams during the COVID-19 pandemic.

Cardiology/Cardiovascular Research
Ya'qoub L, and **Eng MH**. Bioprosthetic valve infective endocarditis: why is it important? *Heart* 2020; Epub ahead of print. PMID: 32546509. Full Text

Department of Cardiology, Louisiana State University Health Sciences Center Shreveport, Shreveport, Louisiana, USA yaqoublina1989@gmail.com.
Division of structural heart disease, Henry Ford Health System, Detroit, Michigan, USA.

Center for Health Policy and Health Services Research
Hu J, and **Nerenz DR**. Performance of Multihospital Health Systems' Flagship Hospitals in the CMS Star Rating Program. *J Hosp Med* 2020; Epub ahead of print. PMID: 32584246. Full Text

Center for Health Policy & Health Services Research, Henry Ford Health System, Detroit, Michigan.

Using the Hospital Compare overall hospital quality star ratings and other publicly available data on acute care hospitals, we examined star ratings for the flagship hospitals of a set of multihospital health systems in the United States. We compared star ratings and hospital characteristics of flagship and nonflagship hospitals across and within 113 health systems. The system flagship hospitals had significantly lower star ratings than did nonflagship hospitals, and they did not generally have the highest star ratings in their own systems. Higher teaching intensity, larger bed size, higher uncompensated care, and higher disproportionate share hospital (DSH) patient percentage were all significantly associated with lower star ratings of flagship hospitals when compared with nonflagship hospitals across

all health systems; the flagship hospital of a system was more likely to have the lowest star rating in its system if the difference in DSH percentage was relatively large between the flagship and nonflagship hospitals in that system.

Dermatology
Fransen F, Spuls P, Alam M, Badawi A, Boixeda P, Haedersdal M, **Hamzavi I**, Hedelund L, Kelly KM, Kono T, Laubach HJ, Manuskiatti W, Marini L, Nouri K, Paasch U, Passeron T, Prinsen C, Verner I, and Wolkerstorfer A. Generic outcome set for the international registry on Laser trEAtments in Dermatology (LEAD): a protocol for a Delphi study to achieve consensus on what to measure. *BMJ Open* 2020; 10(6). PMID: 32595165. Full Text

Dermatology, Amsterdam UMC, Amsterdam, Noord-Holland, The Netherlands frederikefransen@gmail.com m-alam@northwestern.edu.
Dermatology, Amsterdam UMC, Amsterdam, Noord-Holland, The Netherlands.
Department of Dermatology, Amsterdam Public Health, Infection and Immunity, Amsterdam University Medical Center, Amsterdam, The Netherlands.
Department of Dermatology, Feinberg School of Medicine, Northwestern University, Chicago, Illinois (IL), United States frederikefransen@gmail.com m-alam@northwestern.edu.
Department of Dermatology, Northwestern Memorial Hospital, Arkes Family Pavilion, Chicago, Illinois (IL), United States.
Dermatology Unit, Department of Medical Applications of Lasers, National Institute of Laser Enhanced Sciences, Cairo University, Giza, Egypt.
Dermatology Department, Ramón y Cajal Hospital, Madrid, Spain.
Dermatology, Copenhagen University Hospital Bispebjerg, Copenhagen, Denmark.
Massachusetts General Hospital, Harvard Medical School Boston, Boston, United States.
Department of Dermatology, Henry Ford Hospital, Detroit, Michigan, USA.
Dermatology, Aarhus Universitetshospital, Aarhus, Denmark.
Beckman Laser Institute, University of California, Irvine, California, USA.
Department of Plastic and Reconstructive Surgery, Tokai University School of Medicine, Isehera, Japan.
Dermatology and Venereology, Hopitaux Universitaires de Geneve, Geneva, Switzerland.
Faculty of Medicine Siriraj Hospital, Department of Dermatology, Mahidol University, Bangkok, Thailand.
Dermatology, SDC-The Skin Doctors' Center, Trieste, Italy.
Dermatology and Cutaneous Surgery, University of Miami School of Medicine, Miami, Florida, USA.
University of Leipzig, Leipzig, UK.
Dermatology, Centre Hospitalier Universitaire de Nice, Nice, Provence-Alpes-Côte d'Azu, France.
Department of Epidemiology and Biostatistics, Amsterdam Public Health research institute, Amsterdam UMC, VU University Medical Center, Amsterdam, The Netherlands.
Dermatology, Verner clinic, Tel Aviv, Israel.

INTRODUCTION: While laser technology has expanded the armamentarium of treatment for various skin diseases during the past years, heterogeneity in study outcomes hampers comparability and appropriate evidence synthesis. Part of these issues can be addressed by developing a generic outcome set. Using the Delphi method, this study aims to seek consensus between key stakeholders on relevant generic outcomes (what to measure) for implementation in the international registry on Laser trEAtments in Dermatology (LEAD). The registry is focused on collecting research data on various laser treatments for skin disorders. METHODS AND ANALYSIS: By reviewing the literature and involvement of key stakeholder groups and adult patients in need or after laser surgery and health professionals, a preliminary list of outcomes will be generated and categorised into domains. Using these outcomes, an international three-round Delphi study will be performed to rate the importance of outcomes in the selection of a generic outcome set. Participants are allowed to provide new outcomes to the preliminary list for revisions during the first Delphi round. Finally, results will be discussed during a consensus meeting to agree on generic outcomes to be used in the LEAD registry. ETHICS AND DISSEMINATION: An ethics approval was not applicable (W19_290 # 18.336). The study is registered with the Cochrane Skin Core OUtcome Set INitiative) and the Core Outcome Measures in Effectiveness Trials initiative. Procedures will be conducted according to the Declaration of Helsinki. The findings will be disseminated through peer-reviewed publications and conference presentations.

Dermatology
Freeman EE, McMahon DE, Hruza GJ, Irvine AD, Spuls PI, Smith CH, Mahil SK, Castelo-Soccio L, Cordoro KM, Lara-Corrales I, Naik HB, Alhusayen R, Ingram JR, Feldman SR, Balogh EA, Kappelman MD, Wall D, Meah N, Sinclair R, Beylot-Barry M, Fitzgerald M, French LE, **Lim HW**, Griffiths CEM, and Flohr C. International Collaboration and Rapid Harmonization across Dermatologic COVID-19 Registries. *J Am Acad Dermatol* 2020; Epub ahead of print. PMID: 32562840. Full Text

Department of Dermatology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA; Medical Practice Evaluation Center, Mongan Institute, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA. Electronic address: efreeman@mgh.harvard.edu.
Department of Dermatology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA.
Department of Dermatology, Saint Louis University School of Medicine, Saint Louis, MO.
Clinical Medicine, Trinity College Dublin, Dublin, Ireland.
Department of Dermatology, Public Health and Epidemiology; Immunity and Infections, Amsterdam University Medical Centers, location Academic Medical Center, Amsterdam, the Netherlands.
St John's Institute of Dermatology, King's College London and Guy's & St Thomas' NHS Foundation Trust, London, UK.
Section of Pediatric Dermatology, Children's Hospital of Philadelphia, Philadelphia, PA, USA.
Department of Dermatology, University of California, San Francisco, CA, USA.
Section of Pediatric Dermatology, Hospital for Sick Children, Toronto, Canada.
Sunnybrook Research Institute, Dermatology Division, Department of Medicine, University of Toronto, Toronto, ON, Canada.
Department of Dermatology & Academic Wound Healing, Division of Infection and Immunity, Cardiff University, Cardiff CF14 4XN, UK.
Center for Dermatology Research, Department of Dermatology, Wake Forest School of Medicine, Winston Salem, NC, USA.
Department of Pediatrics, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA.
Hair Restoration Blackrock, Dublin, Ireland; National and International Skin Registry Solutions (NISR), Charles Institute of Dermatology, Dublin, Ireland.
Sinclair Dermatology, East Melbourne, Victoria 3002, Australia.
French Society of Dermatology and Department of Dermatology, University Hospital of Bordeaux, France.
American Academy of Dermatology, Rosemont, IL, USA.
Department of Dermatology, University Hospital, Munich University of Ludwig Maximilian, Munich, Germany.
Department of Dermatology, Henry Ford Health System, Detroit, MI, USA.
Dermatology Centre, Salford Royal Hospital, NIHR Manchester Biomedical Research Centre, University of Manchester, Manchester UK.
Unit for Population-Based Dermatology Research, St John's Institute of Dermatology, King's College London and Guy's & St Thomas' NHS Foundation Trust, London, UK.

Dermatology
Narla S, Price KN, Sachdeva M, Shah M, Shi V, **Hamzavi I**, Alavi A, and Lowe MA. Proceeding report of the fourth Symposium on Hidradenitis Suppurativa Advances (SHSA) 2019. *J Am Acad Dermatol* 2020; Epub ahead of print. PMID: 32497690. Full Text

Department of Dermatology, Henry Ford Health System, Detroit, MI. Electronic address: shanthi.narla1@gmail.com.
University of Illinois College of Medicine, Chicago, IL.
Faculty of Medicine, University of Toronto, Toronto, ON, Canada.
Division of Dermatology, Department of Medicine, University of Arizona, Tucson, AZ.
Department of Dermatology, Henry Ford Health System, Detroit, MI.
Division of Dermatology, University of Toronto, Women's College Hospital, Toronto, ON, Canada.
The Rockefeller University, New York, NY.

The 4(th) Annual Symposium on Hidradenitis Suppurativa (SHSA) took place on 1-3 November 2019 at the Westin Book Cadillac Hotel in Detroit, Michigan, U.S.A. This symposium was a joint meeting of the United States Hidradenitis Suppurativa Foundation (HSF) and the Canadian Hidradenitis Suppurativa Foundation (CHSF). This cross-disciplinary meeting with experts from around the world was an opportunity to discuss the most recent advances in the study of hidradenitis suppurativa (HS) pathogenesis, clinical trials, classification, scoring systems, complementary/ alternative medical treatments (CAM), diet, pain management, surgical and laser treatment, and ultrasound assessment. A special pre-conference workshop was held on the use of neodymium-doped yttrium aluminum garnet (Nd:YAG) laser hair reduction, sinus tract deroofing, carbon dioxide (CO(2)) laser excision with ultrasound mapping and tumescent anesthesia for the treatment of HS. The focused workshops on establishing an HS clinic, setting up an HS support group, Hidradenitis Suppurativa PRospective Observational REgistry and bioSpecimen RepoSitory (HS PROGRESS), and wound care were held during the meeting. A special program called HS Ambassadors was established for patients who may have questions about the conference presentations and in addition, a meet and greet for patients and HS Ambassadors was arranged. To facilitate networking between those early in their career and clinical and research experts, a mentoring reception was held.

Dermatology
Ozog DM. Commentary on Treatment of Hypertrophic Burn and Traumatic Scars With 2940 mm Fractional Ablative Er: YAG. *Dermatol Surg* 2020; 46(6):794-795. PMID: 32452977. Full Text

Division of Mohs and Dermatological Surgery, Henry Ford Hospital, Detroit, Michigan.

Dermatology
Paller AS, **Gold LS**, Soung J, Tallman AM, Rubenstein DS, and Gooderham M. Efficacy and Patient-Reported Outcomes from a Phase IIb, Randomized Clinical Trial of Tapinarof Cream for the Treatment of Adolescents and Adults with Atopic Dermatitis. *J Am Acad Dermatol* 2020; Epub ahead of print. PMID: 32502588. Full Text

Northwestern University Feinberg School of Medicine, Chicago, IL, USA. Electronic address: apaller@northwestern.edu.
Henry Ford Health System, Detroit, MI, USA.
Southern California Dermatology, Santa Ana, CA, USA.
Dermavant Sciences, Inc., Long Beach, CA, USA.
Dermavant Sciences, Inc., Durham, NC, USA.
SKiN Centre for Dermatology, Probity Medical Research and Queen's University, Peterborough, ON, Canada.

BACKGROUND: Tapinarof is a topical therapeutic aryl hydrocarbon receptor modulating agent (TAMA) under investigation for atopic dermatitis (AD) and psoriasis treatment. METHODS: Phase IIb, double-blind, vehicle-controlled study randomized adolescents and adults with AD to receive tapinarof cream 0.5%, 1%, or vehicle, once (QD) or twice daily (BID) for 12 weeks with 4-week follow-up. Outcomes included Investigator Global Assessment (IGA), Eczema Area and Severity Index (EASI), body-surface area (BSA) affected, pruritus numeric rating scale scores, subject impressions of AD and pruritus symptom severity, and Patient-Oriented Eczema Measure (POEM) scores. RESULTS: 191/247 randomized subjects completed the study. Week-12 IGA responses were higher in tapinarof groups vs vehicle, reaching statistical significance with tapinarof 1%BID; ≥75/90% improvement in EASI from baseline were significantly higher in tapinarof groups (except 0.5%QD and 0.5%BID, respectively); EASI scores were significantly improved in all tapinarof groups; BSA affected was significantly reduced in tapinarof groups (except 0.5%BID). More subjects reported AD and pruritus symptom severity as very/moderately improved in tapinarof groups and POEM improvements were observed in all groups. Most adverse events were mild or moderate. LIMITATIONS: Larger prospective studies are required to confirm reported analyses. CONCLUSIONS: Tapinarof is a potential important advance in topical medicine development for AD.

Dermatology
Teran VA, **McHargue CA**, and Gru AA. Photodistributed Rash Progressing to Erythroderma: Answer. *Am J Dermatopathol* 2020; 42(6):463-465. PMID: 32433320. Full Text

Department of Dermatology, University of Virginia Health System, Charlottesville, VA.
Department of Dermatology, Henry Ford Hospital, Detroit, MI.
Section of Dermatopathology, Department of Pathology, University of Virginia Health System, Charlottesville, VA.

Dermatology
Zhou L, **Adrianto I**, **Wang J**, **Wu X**, **Datta I**, and **Mi QS**. Single-Cell RNA-Seq Analysis Uncovers Distinct Functional Human NKT Cell Sub-Populations in Peripheral Blood. *Frontiers in Cell and Developmental Biology* 2020; 8. PMID: Not assigned. Full Text

L. Zhou, Center for Cutaneous Biology and Immunology Research, Department of Dermatology, Henry Ford Health System, Detroit, MI, United States
Q.-S. Mi, Center for Cutaneous Biology and Immunology Research, Department of Dermatology, Henry Ford Health System, Detroit, MI, United States
L. Zhou, Immunology Research Program, Henry Ford Cancer Institute, Henry Ford Health System, Detroit, MI, United States
Q.-S. Mi, Immunology Research Program, Henry Ford Cancer Institute, Henry Ford Health System, Detroit, MI, United States

Vα24-invariant human natural killer T (NKT) cells comprise a unique subset of CD1d-restricted T cells with potent immune regulatory function and are involved in the development of a variety of human diseases. However, the lack of comprehensive molecular subset identities limits their objective classification and clinical application. Using unbiased single-cell RNA sequencing (scRNA-seq) of over 4000 unstimulated and 7000 stimulated human peripheral blood NKT cells, we identified four and five clusters of NKT cells from each NKT group, respectively. Our study uncovers multiple previously unrecognized NKT subsets with potential functional specificities, including a cluster of NKT cells

with regulatory T cell property. Flow cytometry and Ingenuity Pathway Analysis confirmed the existence of these NKT populations and indicated the related functional capacities. Our study provides the unbiased and more comprehensive molecular identities of human NKT subsets, which will eventually lead the way to tailored therapies targeting selected NKT subsets.

Diagnostic Radiology

Gadde R, **Arora K**, Felicella MM, Arora S, Cheng L, **Park H**, **Gupta NS**, Salamat MS, and **Williamson SR**. Cystic Trophoblastic Tumor in a Primary Central Nervous System Post-Chemotherapy Germ Cell Tumor: The First Case Report. *Int J Surg Pathol* 2020; Epub ahead of print. PMID: 32498578. Full Text

Henry Ford Health System, Henry Ford Hospital, Detroit, MI, USA.
These authors contributed equally to the study.
Barrow Neurological Institute, Phoenix, AZ, USA.
Indiana University, Indianapolis, IN, USA.
University of Wisconsin, Madison, WI, USA.
Wayne State University, Detroit, MI, USA.

Cystic trophoblastic tumor (CTT) is an uncommon trophoblastic proliferation of germ cell tumor origin, mostly reported in post-chemotherapy metastases of testicular germ cell tumors and rarely primary untreated testicular tumors. To date, we are not aware of occurrence in a non-testicular tumor. A 12-year-old boy presented with limb swelling, increased appetite, weight gain, and precocious puberty. Evaluation revealed right frontal lobe mass and elevated α-fetoprotein and β-human chorionic gonadotrophin. After response to neoadjuvant chemotherapy, the tumor was resected. Microscopically, the resection contained predominantly smooth muscle tissue with scattered small foci of glandular teratoma and CTT. Immunohistochemistry (SALL4, glypican 3) revealed no residual yolk sac tumor. Fluorescence in situ hybridization revealed gain of chromosome 12p. The patient has been disease-free for 13 years. This report expands the spectrum of primary central nervous system germ cell tumors with the occurrence of CTT in this site.

Diagnostic Radiology

Kang G, **Lee J**, **Song T**, **Pantelic M**, **Reeser N**, **Keimig T**, **Nadig J**, **Villablanca P**, **Frisoli T**, **Eng M**, **O'Neill W**, and **Wang DD**. Three-Dimensional CT Planning for Cerebral Embolic Protection in Structural Interventions. *JACC Cardiovasc Imaging* 2020; Epub ahead of print. PMID: 32563641. Full Text

Center for Structural Heart Disease, Henry Ford Health System, Detroit, Michigan.
Department of Radiology, Henry Ford Health System, Detroit, Michigan.
Center for Structural Heart Disease, Henry Ford Health System, Detroit, Michigan. Electronic address: dwang2@hfhs.org.

Diagnostic Radiology

Pandey AS, Daou BJ, Tsai JP, Zaidi SF, Salahuddin H, Gemmete JJ, Oliver MJ, Singer J, Elder TA, Mbabuike N, Adel JG, Gujrati Y, Saleemi MA, Siddiqui FM, Elias AE, **Rehman MF**, **Marin H**, **Chebl AB**, **Kole M**, Wilseck JM, Kazmierczak CD, Mick JM, Majjhoo AQ, Naravetla BR, Rayes M, Luqman AW, Richards BF, Kelkar P, Burgess R, Thompson BG, Chaudhary N, Mazaris PA, Qahwash O, Razak MA, and Jumaa MA. Letter: COVID-19 Pandemic-The Bystander Effect on Stroke Care in Michigan. *Neurosurgery* 2020; Epub ahead of print. PMID: 32496518. Full Text

Department of Neurosurgery University of Michigan Ann Arbor, Michigan.
Spectrum Health West Michigan Grand Rapids, Michigan.
ProMedica Neurosciences Institute Toledo, Ohio.
Department of Neurology University of Toledo Toledo, Ohio.
Department of Radiology University of Michigan Ann Arbor, Michigan.
Field Neuroscience Institute Saginaw, Michigan.
Ascension St. Mary's Hospital Saginaw, Michigan.
Michigan State University East Lansing, Michigan.
Sparrow Health System East Lansing, Michigan.
Metro Health-University of Michigan Wyoming, Michigan.
Henry Ford Health System Detroit, Michigan.
Oakland University William Beaumont School of Medicine Auburn Hills, Michigan.
McLaren Health System Grand Blanc, Michigan.
Detroit Medical Center Wayne State University Detroit, Michigan.
Ascension Providence Hospitals Livonia, Michigan.
Lansing Neurosurgery East Lansing, Michigan.

Emergency Medicine

Dean DJ, **Sabagha N**, **Rose K**, **Weiss A**, France J, **Asmar T**, **Rammal JA**, **Beyer M**, **Bussa R**, **Ross J**, **Chaudhry K**, Smoot T, **Wilson K**, and **Miller J**. A Pilot Trial of Topical Capsaicin Cream for Treatment of Cannabinoid Hyperemesis Syndrome. *Acad Emerg Med* 2020; Epub ahead of print. PMID: 32569429. Full Text

Department of Emergency Medicine, Henry Ford Hospital, Detroit, MI, USA.
Michigan Poison Center, Detroit, MI, USA.
Central Michigan University College of Medicine, Mount Pleasant, MI, USA.
Wayne State University, Detroit, MI, USA.
Frederick Memorial Hospital, Frederick, MD, USA.

BACKGROUND: Patients with cannabinoid hyperemesis syndrome (CHS) present frequently to the emergency department. Previous case studies suggest dramatic symptomatic improvement with topical capsaicin treatment. This exploratory study examined the potential effectiveness of topical capsaicin in patients with nausea and vomiting due to a suspected CHS exacerbation. METHODS: This was a double-blind, randomized placebo-controlled pilot trial. Adults who presented with vomiting suspected to be from CHS were eligible for enrollment. We excluded pregnant women and those with resolution of symptoms. Following randomization, topical 0.1% capsaicin or placebo cream was applied to the anterior abdomen in a uniform manner. The primary outcome was the severity of nausea on a visual analog scale (VAS) of 0-10 cm assessed at 30 minutes. Secondary outcomes were adverse events, occurrence of post-treatment vomiting, nausea by VAS at 60 minutes, and hospital admission. RESULTS: This pilot trial enrolled 30 patients; 17 in the capsaicin arm and 13 in the placebo arm. One patient in the capsaicin arm did not tolerate treatment due to skin irritation. Mean nausea severity at 30 minutes was 4.1 ±2.3 cm in the capsaicin arm and 6.1 ±3.3 cm in the placebo arm (difference -2.0 cm, 95% CI, 0.2 to -4.2 cm). At 60 minutes, mean nausea severity was 3.2 ±3.2 cm versus 6.4 ±2.8 cm (difference -3.2 cm, 95% CI, -0.9 to -5.4 cm). The percent reduction in nausea at 60 minutes from baseline was 46.0% in the capsaicin arm and 24.9% in the placebo arm (difference 21.1%, 95% CI, -5.6% to 47.9%). A higher proportion of capsaicin group patients (29.4% vs. 0%) had complete resolution of nausea (RR 3.4, 95% CI, 1.6 to 7.1). CONCLUSION: In this pilot trial, the application of topical capsaicin cream was associated with a significant reduction in nausea at 60 minutes but not at 30 minutes and provided more complete relief of nausea.

Emergency Medicine

Suleyman G, **Fadel RA**, **Malette KM**, **Hammond C**, **Abdulla H**, **Entz A**, **Demertzis Z**, **Hanna Z**, **Failla A**, **Dagher C**, **Chaudhry Z**, **Vahia A**, **Abreu Lanfranco O**, **Ramesh M**, **Zervos MJ**, **Alangaden G**, **Miller J**, and **Brar I**. Clinical Characteristics and Morbidity Associated With Coronavirus Disease 2019 in a Series of Patients in Metropolitan Detroit. *JAMA Netw Open* 2020; 3(6). PMID: 32543702. Full Text

Department of Infectious Diseases, Henry Ford Hospital, Detroit, Michigan.
Department of Internal Medicine, Henry Ford Hospital, Detroit, Michigan.
School of Medicine, Wayne State University, Detroit, Michigan.
Department of Emergency Medicine, Henry Ford Hospital, Detroit, Michigan.

IMPORTANCE: In late December 2019, an outbreak caused by a novel severe acute respiratory syndrome coronavirus 2 emerged in Wuhan, China. Data on the clinical characteristics and outcomes of infected patients in urban communities in the US are limited. OBJECTIVES: To describe the clinical characteristics and outcomes of patients with coronavirus disease 2019 (COVID-19) and to perform a comparative analysis of hospitalized and ambulatory patient populations. DESIGN, SETTING, AND PARTICIPANTS: This study is a case series of 463 consecutive patients with COVID-19 evaluated at Henry Ford Health System in metropolitan Detroit, Michigan, from March 9 to March 27, 2020. Data analysis was performed from March to April 2020. EXPOSURE: Laboratory-confirmed severe acute respiratory syndrome coronavirus 2 infection. MAIN OUTCOMES AND MEASURES: Demographic data, underlying comorbidities, clinical presentation, complications, treatment, and outcomes were collected. RESULTS: Of 463 patients with COVID-19 (mean [SD] age, 57.5 [16.8] years), 259 (55.9%) were female, and 334 (72.1%) were African American. Most patients (435 [94.0%]) had at least 1 comorbidity, including hypertension (295 patients [63.7%]), chronic kidney disease (182 patients [39.3%]), and diabetes (178 patients [38.4%]). Common symptoms at presentation were cough (347 patients [74.9%]), fever (315 patients [68.0%]), and dyspnea (282 patients [60.9%]). Three hundred fifty-five patients (76.7%) were hospitalized; 141 (39.7%) required intensive care unit management and 114 (80.8%) of those patients required invasive mechanical ventilation. Male sex (odds ratio [OR], 2.0; 95% CI, 1.3-3.2; P = .001), severe obesity (OR, 2.0; 95% CI, 1.4-3.6; P = .02), and chronic kidney disease (OR, 2.0; 95% CI, 1.3-3.3; P = .006) were independently associated with intensive care unit admission. Patients admitted to the intensive care unit had longer length of stay and higher incidence of respiratory failure and acute respiratory distress syndrome requiring invasive mechanical ventilation, acute kidney injury requiring dialysis, shock, and mortality (57 patients [40.4%] vs 15 patients [7.0%]) compared with patients in the general practice unit. Twenty-nine (11.2%) of those discharged from the hospital were readmitted and, overall, 20.0% died

within 30 days. Male sex (OR, 1.8; 95% CI, 1.1-3.1; P = .03) and age older than 60 years (OR, 5.3; 95% CI, 2.9-9.7; P < .001) were significantly associated with mortality, whereas African American race was not (OR, 0.98; 95% CI, 0.54-1.8; P = .86). CONCLUSIONS AND RELEVANCE: In this review of urban metropolitan patients with COVID-19, most were African American with a high prevalence of comorbid conditions and high rates of hospitalization, intensive care unit admission, complications, and mortality due to COVID-19.

Endocrinology and Metabolism

Kruger D, and Valentine V. Canagliflozin for the Treatment of Diabetic Kidney Disease and Implications for Clinical Practice: A Narrative Review. *Diabetes Ther* 2020; 11(6):1237-1250. PMID: 32405876. Full Text

Henry Ford Health System, Detroit, MI, USA. dkruger1@hfhs.org.
Clinica La Esperanza, Albuquerque, NM, USA.

Type 2 diabetes mellitus (T2DM) affects millions of people worldwide, elevating their risk of developing a range of complications, including chronic kidney disease (CKD). People with T2DM and CKD (i.e., diabetic kidney disease, DKD) have an increased risk of progressing to end-stage kidney disease (ESKD), experiencing cardiovascular complications, and premature death. Despite this, DKD is primarily addressed through management of risk factors, and there are few pharmaceutical treatments capable of reversing or delaying disease progression. Canagliflozin is a sodium glucose co-transporter 2 inhibitor that was initially developed as a blood glucose-lowering agent for people with T2DM. Evidence from clinical trials of canagliflozin in people with T2DM, as well as evidence from cardiovascular outcomes trials in people with T2DM and high cardiovascular risk, provided preliminary evidence suggesting that it may also have beneficial renal effects. The Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation (CREDENCE) trial was a dedicated renal outcomes trial of canagliflozin that assessed its renal effects in people with DKD. Overall, the CREDENCE trial demonstrated that canagliflozin improves renal outcomes and slows early disease progression in people with DKD. These data supported the approval of canagliflozin for the treatment DKD, the first new treatment in almost 20 years; therefore, it is important for clinicians to understand how to implement this treatment in their clinical practice.

Endocrinology and Metabolism

Pratley RE, Kanapka LG, Rickels MR, Ahmann A, Aleppo G, Beck R, Bhargava A, Bode BW, Carlson A, Chaytor NS, Fox DS, Goland R, Hirsch IB, **Kruger D**, Kudva YC, Levy C, McGill JB, Peters A, Philipson L, Philis-Tsimikas A, Pop-Busui R, Shah VN, Thompson M, Vendrame F, Verdejo A, Weinstock RS, Young L, and Miller KM. Effect of Continuous Glucose Monitoring on Hypoglycemia in Older Adults With Type 1 Diabetes: A Randomized Clinical Trial. *Jama* 2020; 323(23):2397-2406. PMID: 32543682. Full Text

AdventHealth Translational Research Institute, Orlando, Florida.
Jaeb Center for Health Research, Tampa, Florida.
Rodebaugh Diabetes Center, University of Pennsylvania Perelman School of Medicine, Philadelphia.
Oregon Health and Science University, Portland.
Feinberg School of Medicine, Northwestern University, Chicago, Illinois.
Iowa Diabetes and Endocrinology Research Center, Des Moines.
Atlanta Diabetes Associates, Atlanta, Georgia.
Park Nicollet International Diabetes Center, Minneapolis, Minnesota.
Elson S. Floyd College of Medicine, Washington State University, Spokane.
University of South California, School of Pharmacy, Los Angeles.
Naomi Berri Diabetes Center, Columbia University, New York, New York.
University of Washington, Seattle.
Henry Ford Health System, Detroit, Michigan.
Mayo Clinic, Rochester, Minnesota.
Icahn School of Medicine at Mount Sinai, New York, New York.
Washington University School of Medicine in St Louis, St Louis, Missouri.
Keck School of Medicine, University of Southern California, Los Angeles.
University of Chicago, Chicago, Illinois.
Scripps Whittier Diabetes Institute, La Jolla, California.
University of Michigan, Ann Arbor.
Barbara Davis Center for Diabetes, University of Colorado Anschutz Medical Campus, Aurora.
University of Massachusetts Medical School, Worcester.
University of Miami, Miami, Florida.
SUNY Upstate Medical University, Syracuse, New York.
University of North Carolina at Chapel Hill, Chapel Hill.

IMPORTANCE: Continuous glucose monitoring (CGM) provides real-time assessment of glucose levels and may be beneficial in reducing hypoglycemia in older adults with type 1 diabetes. OBJECTIVE: To determine whether CGM is effective in reducing hypoglycemia compared with standard blood glucose monitoring (BGM) in older adults with type 1 diabetes. DESIGN, SETTING, AND PARTICIPANTS: Randomized clinical trial conducted at 22 endocrinology practices in the United States among 203 adults at least 60 years of age with type 1 diabetes. INTERVENTIONS: Participants were randomly assigned in a 1:1 ratio to use CGM (n = 103) or standard BGM (n = 100). MAIN OUTCOMES AND MEASURES: The primary outcome was CGM-measured percentage of time that sensor glucose values were less than 70 mg/dL during 6 months of follow-up. There were 31 prespecified secondary outcomes, including additional CGM metrics for hypoglycemia, hyperglycemia, and glucose control; hemoglobin A1c (HbA1c); and cognition and patient-reported outcomes, with adjustment for multiple comparisons to control for false-discovery rate. RESULTS: Of the 203 participants (median age, 68 [interquartile range {IQR}, 65-71] years; median type 1 diabetes duration, 36 [IQR, 25-48] years; 52% female; 53% insulin pump use; mean HbA1c, 7.5% [SD, 0.9%]), 83% used CGM at least 6 days per week during month 6. Median time with glucose levels less than 70 mg/dL was 5.1% (73 minutes per day) at baseline and 2.7% (39 minutes per day) during follow-up in the CGM group vs 4.7% (68 minutes per day) and 4.9% (70 minutes per day), respectively, in the standard BGM group (adjusted treatment difference, -1.9% (-27 minutes per day); 95% CI, -2.8% to -1.1% [-40 to -16 minutes per day]; P <.001). Of the 31 prespecified secondary end points, there were statistically significant differences for all 9 CGM metrics, 6 of 7 HbA1c outcomes, and none of the 15 cognitive and patient-reported outcomes. Mean HbA1c decreased in the CGM group compared with the standard BGM group (adjusted group difference, -0.3%; 95% CI, -0.4% to -0.1%; P <.001). The most commonly reported adverse events using CGM and standard BGM, respectively, were severe hypoglycemia (1 and 10), fractures (5 and 1), falls (4 and 3), and emergency department visits (6 and 8). CONCLUSIONS AND RELEVANCE: Among adults aged 60 years or older with type 1 diabetes, continuous glucose monitoring compared with standard blood glucose monitoring resulted in a small but statistically significant improvement in hypoglycemia over 6 months. Further research is needed to understand the long-term clinical benefit. TRIAL REGISTRATION: ClinicalTrials.gov Identifier: NCT03240432.

Gastroenterology
Gordon SC, Kachru N, Parker E, Korrer S, Ozbay AB, and Wong RJ. Health Care Use and Costs Among Patients With Nonalcoholic Steatohepatitis With Advanced Fibrosis Using the Fibrosis-4 Score. *Hepatology Communications* 2020; Epub ahead of print. PMID: Not assigned. Full Text

S.C. Gordon, Department of Gastroenterology and Hepatology, Henry Ford Hospital, Wayne State University School of Medicine, Detroit, MI, United States

Limited evidence exists on the clinical and economic burden of advanced fibrosis in patients with nonalcoholic fatty liver disease/nonalcoholic steatohepatitis (NAFLD/NASH) due to the invasiveness of liver biopsies for accurately staging liver disease. The fibrosis-4 (FIB-4) score allows for noninvasive assessment of liver fibrosis by using clinical and laboratory data alone. This study aimed to characterize the comorbidity burden, health care resource use (HCRU), and costs among patients with NAFLD/NASH with FIB-4-defined F3 (bridging fibrosis) and F4 (compensated cirrhosis) fibrosis. Using the Optum Research Database, a retrospective cohort study was conducted among 251,725 commercially insured adult patients with ≥1 NAFLD/NASH diagnosis from January 1, 2008, to August 31, 2016, and laboratory data required to calculate FIB-4 scores. Five criteria using varying FIB-4 score cutoffs were identified based on expert clinical opinion and published literature. Date of the first valid FIB-4 score marked the index date. Mean annual HCRU and costs were calculated during the pre-index and post-index periods. The prevalence of FIB-4-based F3 and F4 fibrosis was 0.40%-2.72% and 1.03%-1.61%, respectively. Almost 50% of patients identified with FIB-4-based F3 or F4 had type 2 diabetes, cardiovascular disease, or renal impairment. Total all-cause health care costs increased significantly from pre-index to post-index for patients with FIB-4-based F3 fibrosis across most criteria (17%-29% increase) and patients with FIB-4-based F4 fibrosis across all criteria (47%-48% increase). Inpatient costs were the primary drivers of this increment. Conclusion: Significant increases in HCRU and costs were observed following FIB-4-based identification of F3 and F4 fibrosis among U.S. adults with NAFLD/NASH. These data suggest the importance of early identification and management of NAFLD/NASH that may halt or reduce the risk of disease progression and limit the underlying burden.

Gastroenterology
Kitajima T, Hibi T, **Moonka D**, Sapisochin G, **Abouljoud MS**, and **Nagai S**. Center Experience Affects Liver Transplant Outcomes in Patients with Hilar Cholangiocarcinoma. *Ann Surg Oncol* 2020; Epub ahead of print. PMID: 32495286. Full Text

Division of Transplant and Hepatobiliary Surgery, Henry Ford Hospital, Detroit, MI, USA.
Department of Pediatric Surgery and Transplantation, Kumamoto University Hospital, Kumamoto, Japan.
Gastroenterology and Hepatology, Henry Ford Hospital, Detroit, MI, USA.

Multi-Organ Transplant and Hepato-Pancreato-Biliary Surgical Oncology, University Health Network, University of Toronto, Toronto, ON, Canada.
Division of Transplant and Hepatobiliary Surgery, Henry Ford Hospital, Detroit, MI, USA. snagai1@hfhs.org.

BACKGROUND: Based on favorable outcomes reported by experienced centers, perihilar cholangiocarcinoma (Ph-CCA) has become an accepted indication for liver transplantation (LT). What is less clear is if the reported outcomes have been reproduced nationwide in the US. OBJECTIVE: The aim of this study was to evaluate post-transplant outcomes in patients with Ph-CCA and to determine prognostic factors. METHODS: Patients who underwent LT with Model for End-stage Liver Disease exception scores for Ph-CCA between 2010 and 2017 were evaluated. Transplant centers were classified into well- and less-experienced groups: Group 1 [well-experienced (≥ 6 LTs), 7 centers]; Group 2 [less-experienced (< 6 LTs), 23 centers]. Post-transplant mortality due to all-cause and recurrence of Ph-CCA were set as endpoints. RESULTS: Post-transplant outcomes were significantly better in Group 1 than in Group 2, with 1-, 3-, and 5-year patient survival rates of 91.8%, 56.9%, and 45.8%, versus 65.6%, 48.8%, and 26.0%, respectively. Group 2 showed a significantly higher risk of 1-, 3-, and 5-year all-cause mortality and 1-year mortality associated with Ph-CCA recurrence. Center experience was an independent risk factor for post-transplant mortality. In intention-to-treat analysis, a positive prognostic effect of LT was significant and LT decreased the mortality risk by 86% in the well-experienced group [hazard ratio (HR) 0.14, $p < 0.001$], whereas this effect was not observed in the less-experienced group (HR 1.35, $p = 0.47$). CONCLUSIONS: Risk of recurrence of malignancy and mortality was significantly higher in the less-experienced center group. Center effects on post-transplant outcomes in patients with Ph-CCA should be recognized, and the introduction of center approval for LT for Ph-CCA may be justified to achieve comparable outcomes between centers.

Gastroenterology
Lawitz E, Landis CS, Flamm SL, Bonacini M, Ortiz-Lasanta G, Huang J, Zhang J, Kirby BJ, De-Oertel S, Hyland RH, Osinusi AO, Brainard DM, Robson R, Maliakkal BJ, **Gordon SC**, and Gane EJ. Sofosbuvir plus ribavirin and sofosbuvir plus ledipasvir in patients with genotype 1 or 3 hepatitis C virus and severe renal impairment: a multicentre, phase 2b, non-randomised, open-label study. *Lancet Gastroenterol Hepatol* 2020; Epub ahead of print. PMID: 32531259. Request Article

Texas Liver Institute, University of Texas Health San Antonio, San Antonio, TX, USA.
Department of Medicine, University of Washington, Seattle, WA, USA.
Northwestern University, Chicago, IL, USA.
Mission Gastroenterology and Hepatology, University of California, San Francisco, CA, USA.
Fundación de Investigación, San Juan, Puerto Rico.
University of Rochester, Rochester, NY, USA.
Gilead Sciences, Foster City, CA, USA.
Christchurch Clinical Studies Trust, Christchurch, New Zealand.
Henry Ford Health System, Detroit, MI, USA.
Auckland Clinical Studies, Auckland, New Zealand. Electronic address: EdGane@adhb.govt.nz.

BACKGROUND: There is a medical need for highly effective, safe, and well tolerated treatments for patients infected with hepatitis C virus (HCV) with severe renal impairment. We investigated the safety and efficacy of sofosbuvir with ribavirin or ledipasvir combined with sofosbuvir in a prospective study of patients with genotype 1 or 3 HCV infection and stage 4-5 chronic kidney disease (creatinine clearance by Cockcroft-Gault ≤30 mL/min) who were not on dialysis. METHODS: This phase 2b, open-label, non-randomised, multicentre study in the USA and New Zealand investigated three sequentially enrolled cohorts of patients. Patients were recruited from ten hospitals and clinical research centres and were included if they had genotype 1 or 3 HCV infection, a creatinine clearance less than or equal to 30 mL/min, and were not on dialysis. In cohorts 1 and 2, patients received sofosbuvir (200 mg in cohort 1 and 400 mg in cohort 2) plus ribavirin 200 mg once per day for 24 weeks. In cohort 3, 18 patients received ledipasvir combined with sofosbuvir (90 mg ledipasvir and 400 mg sofosbuvir) once per day for 12 weeks. The primary efficacy endpoint was the proportion of patients achieving sustained virological response 12 weeks after the end of treatment (SVR12). Safety and pharmacokinetic data were also collected. The trial is registered with ClinicalTrials.gov, number NCT01958281, and is completed. FINDINGS: This study was done between Oct 7, 2013, and Oct 29, 2017. In the sofosbuvir plus ribavirin cohorts, 32 patients were screened, of whom 20 were enrolled and assessed for efficacy and safety (ten patients in each cohort). In the ledipasvir plus sofosbuvir cohort, 33 patients were screened, of whom 18 were enrolled and assessed for treatment efficacy and safety. Four (40%, 95% CI 12-74) of ten patients in cohort 1 and six (60%, 26-88) of ten patients in cohort 2 achieved SVR12. All 18 (100%, 82-100) patients in cohort 3 achieved SVR12. Adverse events were mostly mild or moderate in severity. The most commonly reported adverse events overall were headache (eight [21%] of 38 patients), anaemia (seven [18%] of 38 patients), and fatigue (six [16%] of 38 patients). Eight patients had serious adverse events, none of which were treatment related. There were no treatment-related cardiac events or clinically significant changes in echocardiographic parameters or creatinine clearance by Cockcroft-Gault. INTERPRETATION: In this phase 2b study, ledipasvir combined with sofosbuvir for 12

weeks was safe and effective in patients with genotype 1 HCV infection and stage 4-5 chronic kidney disease who were not on dialysis. FUNDING: Gilead Sciences.

Gastroenterology
Loomba R, Wong R, Fraysse J, Shreay S, Li S, Harrison S, and **Gordon SC**. Editorial: how widespread and serious is non-alcoholic fatty liver disease in the real world? Authors' reply. *Aliment Pharmacol Ther* 2020; 51(11):1200-1201. PMID: 32424927. Full Text

Department of Medicine, NAFLD Research Center, La Jolla, CA, USA.
Division of Gastroenterology, Department of Medicine, University of California, San Diego, La Jolla, CA, USA.
Division of Gastroenterology and Hepatology, Alameda Health System, Highland Hospital, Oakland, CA, USA.
Health Economics Outcomes Research, Gilead Sciences, Foster City, CA, USA.
Chronic Disease Research Group, Minneapolis, MN, USA.
Pinnacle Clinical Research, San Antonio, TX, USA.
Department of Gastroenterology and Hepatology, Henry Ford Hospital, Wayne State University School of Medicine, Detroit, MI, USA.

Gastroenterology
Mittal C, **Dang D**, Stoffel E, Menees S, Scott FI, Ahnen D, and Patel SG. Underutilization of Lynch Syndrome Screening at Two Large Veterans Affairs Medical Centers. *Dig Dis Sci* 2020; Epub ahead of print. PMID: 32500284. Full Text

University of Colorado Anschutz Medical Center, 12631 E 17th Avenue, Room 7614, Campus Box 158, 80045, Aurora, CO, USA.
Parkview Cancer Institute, Fort Wayne, IN, USA.
Veterans Affairs Hospital, Ann Arbor, MI, USA.
Henry Ford Medical Center, Detroit, MI, USA.
University of Michigan, Ann Arbor, MI, USA.
University of Colorado Anschutz Medical Center, 12631 E 17th Avenue, Room 7614, Campus Box 158, 80045, Aurora, CO, USA. Swati.Patel@cuanschutz.edu.
Veterans Affairs Hospital, Aurora, CO, USA. Swati.Patel@cuanschutz.edu.

BACKGROUND: Lynch syndrome (LS) is the most common hereditary colorectal cancer (CRC) syndrome, yet is grossly under-recognized. Multiple professional societies recommend screening all CRCs for LS by performing tumor testing. The veterans affairs system has not adopted universal tumor testing as a national performance metric and leaves screening for LS to clinical care at individual sites. AIMS: Describe adherence to LS screening in the VA system. METHODS: Dual-center, retrospective review of all CRCs diagnosed between 2010 and 2016. Rates of tumor testing, personal and family history of cancer were extracted from the medical record. Univariate and multivariate regression analysis was performed to determine predictors of tumor-based screening for LS. RESULTS: A total of 421 cancers were reviewed. 15.1% of all cancers underwent either MSI and/or IHC for LS screening over the study period. There was improvement in LS screening from 3% of all CRCs in 2010 to 45% of all CRCs in 2016. 34% and 70% of patients did not have documentation of CRC in first- and second-degree relatives, respectively. Of the 73 patients who met one of the Revised Bethesda Criteria or had a PREMM1,2,6 score of ≥ 5, 34% and 56% underwent tumor testing, respectively. Younger age, non-Caucasian race, meeting Bethesda or PREMM1,2,6 criteria and right-sided tumor location were predictors of undergoing tumor testing. CONCLUSIONS: CRC tumor screening for LS is grossly inadequate when left to routine clinical care. Our results lend support to implementation of reflexive universal tumor testing within the VA system.

Gastroenterology
Reddy CA, Tavakkoli A, Chen VL, Korsnes S, Bedi AO, Carrott PW, Chang AC, Lagisetty KH, Kwon RS, Elmunzer BJ, Orringer MB, **Piraka C**, Prabhu A, Reddy RM, Wamsteker E, and Rubenstein JH. Long-Term Quality of Life Following Endoscopic Therapy Compared to Esophagectomy for Neoplastic Barrett's Esophagus. *Dig Dis Sci* 2020; Epub ahead of print. PMID: 32519141. Full Text

Barrett's Esophagus Program, Division of Gastroenterology, University of Michigan, 1500 E Medical Center Dr., Ann Arbor, MI, 48109, USA. shanreddy13@gmail.com.
Division of Gastroenterology, UT Southwestern, Dallas, TX, USA.
Barrett's Esophagus Program, Division of Gastroenterology, University of Michigan, 1500 E Medical Center Dr., Ann Arbor, MI, 48109, USA.
Division of Thoracic Surgery, Baylor College of Medicine, Houston, TX, USA.
Section of Thoracic Surgery, University of Michigan, Ann Arbor, MI, USA.
Division of Gastroenterology, Medical University of South Carolina, Charleston, SC, USA.

Division of Gastroenterology, Henry Ford Health System, Detroit, MI, USA.

INTRODUCTION: Endoscopic therapy (ET) and esophagectomy result in similar survival for Barrett's esophagus (BE) with high-grade dysplasia (HGD) or T1a esophageal adenocarcinoma (EAC), but the long-term quality of life (QOL) has not been compared. AIMS: We aimed to compare long-term QOL between patients who had undergone ET versus esophagectomy. METHODS: Patients were included if they underwent ET or esophagectomy at the University of Michigan since 2000 for the treatment of HGD or T1a EAC. Two validated survey QOL questionnaires were mailed to the patients. We compared QOL between and within groups (ET = 91, esophagectomy = 62), adjusting for covariates. RESULTS: The median time since initial intervention was 6.8 years. Compared to esophagectomy, ET patients tended to be older, had a lower prevalence of EAC, and had a shorter duration since therapy. ET patients had worse adjusted physical and role functioning than esophagectomy patients. However, the adjusted odds ratio (OR) of having symptoms was significantly less with ET for diarrhea (0.287; 95% confidence interval [CI] = 0.114, 0.724), trouble eating (0.207; 0.0766, 0.562), choking (0.325; 0.119, 0.888), coughing (0.291; 0.114, 0.746), and speech difficulty (0.306; 0.0959, 0.978). Amongst the ET patients, we found that the number of therapy sessions and need for dilation were associated with worse outcomes. DISCUSSION: Multiple measures of symptom status were better with ET compared to esophagectomy following treatment of BE with HGD or T1a EAC. We observed worse long-term physical and role functioning in ET patients which could reflect unmeasured baseline functional status rather than a causal effect of ET.

Global Health Initiative

Selitsky L, **Markowitz N**, **Baxa DM**, **Kaljee L**, **Miree CA**, **Islam N**, **Burse C**, **Newaz R**, **Dankerlui D**, **Jacobsen G**, and **Joseph C**. Self-report of domestic violence and forced sex are related to sexual risk behaviors in a sample of juvenile detainees. *Health Justice* 2020; 8(1):15. PMID: 32577955. Full Text

Internal Medicine, Johns Hopkins Hospital, Baltimore, USA.
Division of Infectious Diseases, Henry Ford Health System and School of Medicine, Wayne State University, Detroit, USA.
William Beaumont School of Medicine, Oakland University, Rochester, USA.
Division of Infectious Diseases, Henry Ford Health System, Detroit, USA.
Global Health Initiative, Henry Ford Health System, Detroit, USA.
Department of Public Health Sciences, Henry Ford Health System, 1 Ford Place, Detroit, Michigan, USA.
Department of Public Health Sciences, Henry Ford Health System, 1 Ford Place, Detroit, Michigan, USA.
cjoseph1@hfhs.org.

BACKGROUND: Justice-involved youth have higher rates of sexually transmitted infections (STIs), and a higher prevalence of the associated sexual risk behaviors. Sexual risk behaviors are also associated with alcohol and drug use. Research suggests that a history of trauma is an important predictor of alcohol and drug use in youth offenders, and therefore is a likely contributor to sexual risk behavior in this population. The objective of this analysis is to determine the association of trauma, specifically, domestic violence and forced sex, to six sexual risk behaviors and a history of chlamydia among detained youth. METHODS: The analysis uses data from a convenience sample of detainees assenting to HIV testing conducted December 2016 - August 2017 using the state-certified Voluntary Counseling Testing and Referral (VCTR) process. RESULTS: Of the 379 youth that received VCTR at the facility, 308 (81.3%) were used in this analysis. Report of domestic violence was significantly associated with sex under the influence of alcohol and was also significantly associated with sex under the influence of marijuana. Forced sex was associated with a sexual partner of unknown HIV status. CONCLUSIONS: Traumatic experiences were related to sexual risk behaviors in this analysis, and substance use was strongly implicated in the association. Trauma is known to be a catalyst to sexual risk behaviors, substance use, and delinquency in adolescence. Results support the findings of other investigators and re-iterate the need for trauma-informed interventions that can improve the life trajectories of detained youth.

Hematology/Oncology

Sankar K, **Gadgeel SM**, and Qin A. Molecular therapeutic targets in non-small cell lung cancer. *Expert Rev Anticancer Ther* 2020; Epub ahead of print. PMID: 32580596. Request Article

University of Michigan , C300 Med Inn, SPC 5848, 1500 E. Medical Center Dr, Ann Arbor, MI 48109-5848.
Henry Ford Cancer Institute , Hematology/Oncology-CFP-5, 2799 West Grand Boulevard, Detroit, MI 48202.

INTRODUCTION: Several targetable genetic alterations have been identified in non-small cell lung cancers (NSCLC) and drugs targeting these alterations have been approved for the management of advanced NSCLC patients. Driver mutations with emerging clinical trial data include EGFR exon 20 insertion mutations, MET amplification, KRAS G12C point mutations, RET rearrangements, HER2 amplification and mutations, and FGFR amplification and translocations. AREAS COVERED: We reviewed English-language articles indexed in Medline and PubMed up to the

1(st) of June 2020. In addition, the proceedings of major conferences were reviewed for relevant abstracts. We report data published regarding targeted therapies which are currently approved and for those which are emerging in advanced or metastatic NSCLC. EXPERT REVIEW: While these drugs have been shown to be efficacious and tolerable, resistance almost always develops. Though next-generation tyrosine kinase inhibitors (TKIs) have been developed, the appropriate sequencing of these drugs is not clear. Evaluating combination therapies to prevent or delay the onset of resistance and understanding mechanisms of resistance are critical areas of emerging research.

Hospital Medicine
Segon YS, **Summey RD**, Slawski B, and **Kaatz S**. Surgical Venous Thromboembolism Prophylaxis: Clinical Practice Update. *Hosp Pract (1995)* 2020; Epub ahead of print. PMID: 32589468. Request Article

Division of General Internal Medicine, Medical College of Wisconsin , Milwaukee, Wisconsin.
Division of Hospital Medicine, Henry Ford Hospital , Detroit, Michigan.

Background: Perioperative medicine continues to evolve as new literature emerges. This article provides an update on prevention of venous thromboembolism (VTE) in surgical patients. METHODS: We reviewed articles on VTE prevention in surgical patients published in peer reviewed journals since the publication of 2012 ACCP guidelines on VTE prevention in surgical patients. RESULTS: Methods of VTE prophylaxis include aggressive ambulation, mechanical prophylaxis and pharmacological prophylaxis. In non-orthopedic surgery, the overall approach remains assessment of thrombosis risk with the recommendation to use a risk assessment tool such as the modified Caprini score. Low molecular weight heparin (LMWH) appears to be more effective than unfractionated heparin (UFH) for VTE prophylaxis in non-orthopedic surgery. For orthopedic surgery, recent studies now recognize aspirin as an option for VTE prophylaxis after total hip arthroplasty, total knee arthroplasty and hip fracture surgery. Extended prophylaxis with LMWH reduces the risk of symptomatic VTE in high risk abdominal and pelvic cancer surgery without an appreciable increase in risk of bleeding and decreased symptomatic VTE in major orthopedic surgery but with more minor but not major bleeding. Prophylactic Inferior vena cava (IVC) filter placement or surveillance compression ultrasonography is not recommended in management or detection of VTE in surgical patients. CONCLUSIONS: This article aims to provide insight into data from last several years which has potential to change clinical practices in perioperative setting.

Hypertension and Vascular Research
Roy B, **Sundar K**, and **Palaniyandi SS**. 4-hydroxy-2-nonenal decreases coronary endothelial cell migration: Potentiation by aldehyde dehydrogenase 2 inhibition. *Vascul Pharmacol* 2020; Epub ahead of print. PMID: 32585188. Full Text

Division of Hypertension and Vascular Research, Department of Internal Medicine, Henry Ford Health System, Detroit, MI 48202, United States of America; Department of Physiology, Wayne State University, Detroit, MI 48202, United States of America.
Division of Hypertension and Vascular Research, Department of Internal Medicine, Henry Ford Health System, Detroit, MI 48202, United States of America.
Division of Hypertension and Vascular Research, Department of Internal Medicine, Henry Ford Health System, Detroit, MI 48202, United States of America; Department of Physiology, Wayne State University, Detroit, MI 48202, United States of America. Electronic address: spalani2@hfhs.org.

4-hydroxynonenal (4HNE) is a reactive aldehyde, which is involved in oxidative stress associated pathogenesis. The cellular toxicity of 4HNE is mitigated by aldehyde dehydrogenase (ALDH) 2. Thus, we hypothesize that ALDH2 inhibition exacerbates 4HNE-induced decrease in coronary endothelial cell (EC) migration in vitro. To test our hypothesis, we pharmacologically inhibited ALDH2 in cultured mouse coronary ECs (MCECs) by disulfiram (DSF) (2.5 μM) before challenging the cells with different doses of 4HNE (25, 50 and 75 μM) for 4, 12, 16 and 24 h. We evaluated MCEC migration by scratch wound migration assay. 4HNE attenuated MCEC migration significantly relative to control ($P < .05$), which was exacerbated with DSF pretreatment ($P < .05$). DSF pretreatment exacerbated 4HNE-induced decrease in ALDH2 activity in MCECs. Next, we showed that 75 μM 4HNE significantly decreased the intracellular mRNA levels of vascular endothelial growth factor (VEGF), VEGF receptor 2 (VEGFR2), focal adhesion kinase (FAK) and other promigratory genes compared to control, which were further decreased by DSF pretreatment. 75 μM 4HNE also decreased the protein levels of VEGFR2, FAK, phospho-FAK, Src and paxillin in MCECs. Thus, we conclude that ALDH2 inhibition potentiates 4HNE-induced decrease in MCECs migration in vitro.

Infectious Diseases
Alangaden G, and **Ramesh MS**. Reply to Fernandez Cruz. *Clin Infect Dis* 2020; Epub ahead of print. PMID: 32589700. Full Text

Infectious Diseases, Henry Ford Hospital, West Grand Blvd, Detroit, MI, USA.

Infectious Diseases

Selitsky L, **Markowitz N**, **Baxa DM**, **Kaljee L**, **Miree CA**, **Islam N**, **Burse C**, **Newaz R**, **Dankerlui D**, **Jacobsen G**, and **Joseph C**. Self-report of domestic violence and forced sex are related to sexual risk behaviors in a sample of juvenile detainees. *Health Justice* 2020; 8(1):15. PMID: 32577955. Full Text

Internal Medicine, Johns Hopkins Hospital, Baltimore, USA.
Division of Infectious Diseases, Henry Ford Health System and School of Medicine, Wayne State University, Detroit, USA.
William Beaumont School of Medicine, Oakland University, Rochester, USA.
Division of Infectious Diseases, Henry Ford Health System, Detroit, USA.
Global Health Initiative, Henry Ford Health System, Detroit, USA.
Department of Public Health Sciences, Henry Ford Health System, 1 Ford Place, Detroit, Michigan, USA.
Department of Public Health Sciences, Henry Ford Health System, 1 Ford Place, Detroit, Michigan, USA.
cjoseph1@hfhs.org.

BACKGROUND: Justice-involved youth have higher rates of sexually transmitted infections (STIs), and a higher prevalence of the associated sexual risk behaviors. Sexual risk behaviors are also associated with alcohol and drug use. Research suggests that a history of trauma is an important predictor of alcohol and drug use in youth offenders, and therefore is a likely contributor to sexual risk behavior in this population. The objective of this analysis is to determine the association of trauma, specifically, domestic violence and forced sex, to six sexual risk behaviors and a history of chlamydia among detained youth. METHODS: The analysis uses data from a convenience sample of detainees assenting to HIV testing conducted December 2016 - August 2017 using the state-certified Voluntary Counseling Testing and Referral (VCTR) process. RESULTS: Of the 379 youth that received VCTR at the facility, 308 (81.3%) were used in this analysis. Report of domestic violence was significantly associated with sex under the influence of alcohol and was also significantly associated with sex under the influence of marijuana. Forced sex was associated with a sexual partner of unknown HIV status. CONCLUSIONS: Traumatic experiences were related to sexual risk behaviors in this analysis, and substance use was strongly implicated in the association. Trauma is known to be a catalyst to sexual risk behaviors, substance use, and delinquency in adolescence. Results support the findings of other investigators and re-iterate the need for trauma-informed interventions that can improve the life trajectories of detained youth.

Infectious Diseases

Suleyman G, **Fadel RA**, **Malette KM**, **Hammond C**, **Abdulla H**, **Entz A**, **Demertzis Z**, **Hanna Z**, **Failla A**, **Dagher C**, **Chaudhry Z**, **Vahia A**, **Abreu Lanfranco O**, **Ramesh M**, **Zervos MJ**, **Alangaden G**, **Miller J**, and **Brar I**. Clinical Characteristics and Morbidity Associated With Coronavirus Disease 2019 in a Series of Patients in Metropolitan Detroit. *JAMA Netw Open* 2020; 3(6). PMID: 32543702. Full Text

Department of Infectious Diseases, Henry Ford Hospital, Detroit, Michigan.
Department of Internal Medicine, Henry Ford Hospital, Detroit, Michigan.
School of Medicine, Wayne State University, Detroit, Michigan.
Department of Emergency Medicine, Henry Ford Hospital, Detroit, Michigan.

IMPORTANCE: In late December 2019, an outbreak caused by a novel severe acute respiratory syndrome coronavirus 2 emerged in Wuhan, China. Data on the clinical characteristics and outcomes of infected patients in urban communities in the US are limited. OBJECTIVES: To describe the clinical characteristics and outcomes of patients with coronavirus disease 2019 (COVID-19) and to perform a comparative analysis of hospitalized and ambulatory patient populations. DESIGN, SETTING, AND PARTICIPANTS: This study is a case series of 463 consecutive patients with COVID-19 evaluated at Henry Ford Health System in metropolitan Detroit, Michigan, from March 9 to March 27, 2020. Data analysis was performed from March to April 2020. EXPOSURE: Laboratory-confirmed severe acute respiratory syndrome coronavirus 2 infection. MAIN OUTCOMES AND MEASURES: Demographic data, underlying comorbidities, clinical presentation, complications, treatment, and outcomes were collected. RESULTS: Of 463 patients with COVID-19 (mean [SD] age, 57.5 [16.8] years), 259 (55.9%) were female, and 334 (72.1%) were African American. Most patients (435 [94.0%]) had at least 1 comorbidity, including hypertension (295 patients [63.7%]), chronic kidney disease (182 patients [39.3%]), and diabetes (178 patients [38.4%]). Common symptoms at presentation were cough (347 patients [74.9%]), fever (315 patients [68.0%]), and dyspnea (282 patients [60.9%]). Three hundred fifty-five patients (76.7%) were hospitalized; 141 (39.7%) required intensive care unit management and 114 (80.8%) of those patients required invasive mechanical ventilation. Male sex (odds ratio [OR], 2.0; 95% CI, 1.3-3.2; P = .001), severe obesity (OR, 2.0; 95% CI, 1.4-3.6; P = .02), and chronic kidney disease (OR, 2.0; 95% CI, 1.3-3.3; P = .006) were independently associated with intensive care unit admission. Patients admitted to the intensive care unit had longer length of stay and higher incidence of respiratory failure and acute respiratory distress syndrome requiring invasive mechanical ventilation, acute kidney injury requiring

dialysis, shock, and mortality (57 patients [40.4%] vs 15 patients [7.0%]) compared with patients in the general practice unit. Twenty-nine (11.2%) of those discharged from the hospital were readmitted and, overall, 20.0% died within 30 days. Male sex (OR, 1.8; 95% CI, 1.1-3.1; P = .03) and age older than 60 years (OR, 5.3; 95% CI, 2.9-9.7; P < .001) were significantly associated with mortality, whereas African American race was not (OR, 0.98; 95% CI, 0.54-1.8; P = .86). CONCLUSIONS AND RELEVANCE: In this review of urban metropolitan patients with COVID-19, most were African American with a high prevalence of comorbid conditions and high rates of hospitalization, intensive care unit admission, complications, and mortality due to COVID-19.

Internal Medicine
Battisha A, **Altibi AM**, Madoukh B, Sheikh O, Sawalha K, Shaikh S, and Al-Sadawi M. Spontaneous Biliary Pericardial Tamponade: A Case Report and Literature Review. *Curr Cardiol Rev* 2020; Epub ahead of print. PMID: 32525780. Request Article

University Of Massachusetts Medical School - Baystate, Springfield, MA. United States.
Henry Ford Allegiance Health Hospital, Jackson, Michigan. United States.
Overland Park Regional Medical Center, Overland Park, KS. United States.
University of Texas Health Science Center at San Antonio, San Antonio, TX. United States.
State University of New York: Downstate Medical Center, Brooklyn, NY. United States.

BACKGROUND: Biliary pericardial tamponade (BPT) is a rare form of pericardial tamponade, characterized by yellowish-greenish pericardial fluid upon pericardiocentesis. Historically, BPT reported to occur in the setting of an associated pericardio-biliary fistula. However, BPT in the absence of a detectable fistula is extremely rare. CASE PRESENTATION: A 75-year-old Hispanic male presenting with dyspnea and diagnosed with cardiac tamponade. Subsequent pericardiocentesis revealed biliary pericardial fluid (bilirubin of 7.6 mg/dl). Patient underwent extensive workup to identify a potential fistula between hepatobiliary system and the pericardial space, which was non-revealing. The mechanism of bile entry into the pericardial space remains to be unidentified. LITERATURE REVIEW: A total of six previously published BPT were identified: all were males, mean age of 53.3 years (range: 31-73). Mortality was reported in two out of the six cases. The underlying etiology for pericardial tamponade varied across the cases: incidental pericardio-biliary fistula, traumatic pericardial injury, and presence of associated malignancy. - Conclusion: Biliary pericardial tamponade is a rare form of tamponade that warrants a prompt workup (e.g., Hepatobiliary Iminodiacetic Acid - HIDA scan) for an iatrogenic vs. traumatic pericardio-biliary fistula. As a first case in the literature, our case exhibits a biliary tamponade in the absence of an identifiable fistula.

Internal Medicine
Battisha A, Sawalha K, **Altibi AM**, Madoukh B, Al-Akchar M, and Patel B. Cardiogenic shock in autoimmune rheumatologic diseases: an insight on etiologies, management, and treatment outcomes. *Heart Fail Rev* 2020; Epub ahead of print. PMID: 32562022. Full Text

University of Massachusetts Medical School - Baystate, Springfield, MA, USA.
Harvard T.H. Chan School of Public Health, Harvard University, Boston, MA, USA.
Henry Ford Health System (HFHS), Jackson, MI, USA.
Overland Park Regional Medical Center - HCA Midwest Health, Kansas City, MO, USA.
Southern Illinois University School of Medicine, Springfield, IL, USA.
Heart and Vascular Institute, West Virginian University, 1 Medical Center Dr., Morgantown, WV, 26505, USA.
Brijesh.patel@wvumedicine.org.

Autoimmune rheumatological disorders are known to have an increased risk for cardiovascular diseases including coronary artery disease (CAD), myocarditis, pericarditis, valvulopathy, and in consequence cardiogenic shock. Data on cardiogenic shock in rheumatological diseases are scarce; however, several reports have highlighted this specific entity. We sought to review the available literature and highlight major outcomes and the management approaches in each disease. Systematic literature search, including PubMed, Ovid/Medline, Cochrane Library, and Web of Science, was conducted between January 2000 and December 2009. We reviewed all cases reporting cardiogenic shock with rheumatologic conditions, including systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), Takayasu's arteritis (TA), granulomatosis with polyangiitis (GPA), giant cell arteritis (GCA), and antiphospholipid syndrome (APS). We selected 45 papers reporting a total of 48 cases. Mean age was 39 ± 7.3 years and 68.8% were females. Most common rheumatologic conditions associated with cardiogenic shock were SLE (31%), GPA (23%), TA (14.6%), APA (10.4%), and RA (8.3%). Cardiogenic shock was found to be caused by eosinophilic myocarditis in 58% of cases, CAD in 19% of cases, and valvulopathy in 6% of cases. Most patient required high-dose steroids and second immunosuppressant therapy. Mechanical circulatory supported was required in 23 cases, IABP in 16 cases, and ECMO in 12 cases. Complete recovery occurred in 37 patients while 9 patients died and 2 required heart transplant. Responsible for two-thirds of cases, eosinophilic myocarditis should be suspected in young cardiogenic shock patients with underlying rheumatologic conditions. Lupus and GPA are the two most common conditions.

Internal Medicine

Suleyman G, **Fadel RA**, **Malette KM**, **Hammond C**, **Abdulla H**, **Entz A**, **Demertzis Z**, **Hanna Z**, **Failla A**, **Dagher C**, **Chaudhry Z**, **Vahia A**, **Abreu Lanfranco O**, **Ramesh M**, **Zervos MJ**, **Alangaden G**, **Miller J**, and **Brar I**. Clinical Characteristics and Morbidity Associated With Coronavirus Disease 2019 in a Series of Patients in Metropolitan Detroit. *JAMA Netw Open* 2020; 3(6). PMID: 32543702. Full Text

Department of Infectious Diseases, Henry Ford Hospital, Detroit, Michigan.
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School of Medicine, Wayne State University, Detroit, Michigan.
Department of Emergency Medicine, Henry Ford Hospital, Detroit, Michigan.

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Internal Medicine

Venkatesulu BP, Giridhar P, Malouf TD, Trifletti DM, and Krishnan S. A systematic review of the role of carbon ion radiation therapy in recurrent rectal cancer. *Acta Oncol* 2020; Epub ahead of print. PMID: 32476538. Request Article

Department of Internal medicine, Henry Ford Hospital, Detroit, MI, USA.
Department of Radiation Oncology, All India Institute of medical sciences, New Delhi, India.
Department of Radiation Oncology, Mayo Clinic Florida, Jacksonville, FL, USA.

Background: Colorectal cancer is the fourth leading cause of cancer-associated death in the world. The 5-year local recurrence rates in patients undergoing multimodality therapy are approximately 5-10%. The standard approach to treat locally recurrent rectal is re-irradiation followed by surgical resection. Recent reports have suggested that the treatment outcomes with carbon ion radiation therapy (CIRT) in recurrent rectal cancer are promising and have superior results compared to photon therapy. Hence, we performed a systematic review to evaluate the patterns of care and treatment outcomes of recurrent rectal cancer patients treated with CIRT.Methodology: We performed a systematic search to identify the articles that reported on CIRT use in recurrent rectal cancer.Results: Systematic search of PubMed and Cochrane Central resulted in 98 abstracts. Eight studies fulfilled the predefined inclusion criteria. Among eight studies, one study is a prospective phase I/II study done in Japan; three prospective studies are ongoing (PANDORA-01 trial, HIMAT1351trial, and a phase II study of reirradiation for prior CIRT), and five studies are institutional reports on role of CIRT. These studies were predominantly reported from Japan and Germany. All reports except one were performed in patients who have not received prior radiation. The most commonly utilized treatment prescription was 73.4 Gy (RBE) in 16 fractions over 4 weeks in patients without any prior history of radiation and 36 Gy in 12 fractions over 3 weeks at 3 Gy per fraction in patients with prior photon radiation to the pelvis. There is one ongoing trial assessing the role of carbon ion re-irradiation in patients who had prior CIRT for rectal

cancer.Conclusion: CIRT holds immense promise in improving outcomes in locally recurrent rectal cancer. There is a need for more multi-institutional prospective clinical trials to assess the role of CIRT.

Nephrology
Ananthasubramaniam K, and **Karthikeyan V**. Lurking in the shadows: Asymptomatic bilateral lung involvement with novel corona virus 2019 identified on myocardial perfusion SPECT CT: Implications for interpreting physicians. *J Nucl Cardiol* 2020; Epub ahead of print. PMID: 32529532. Full Text

Heart and Vascular Institute, Henry Ford West Bloomfield Hospital, West Bloomfield, MI, USA. kananth1@hfhs.org.
Division of Nephrology, Henry Ford West Bloomfield Hospital, West Bloomfield, MI, USA.

Nephrology
Andrews AM, Zhang N, Smith AH, Loughery C, Resnicow K, Chapman R, Jenkins Riley H, Stav S, and **Yee J**. A Clustered Randomized Trial Informing Patients on Dialysis About Their Ability to Donate Organs and Tissues. *Prog Transplant* 2020; Epub ahead of print. PMID: 32567518. Full Text

National Kidney Foundation of Michigan, Ann Arbor, MI, USA.
Division of Biostatistics and Epidemiology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA.
Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, OH, USA.
Greenfield Health Systems, Bingham Farms, MI, USA.
Department of Health Behavior & Health Education, University of Michigan School of Public Health, Ann Arbor, MI, USA.
Gift of Life Michigan, Minority Organ and Tissue Transplant Education Program, Ann Arbor, MI, USA.
Henry Ford Health System, Detroit, MI, USA.

INTRODUCTION: The transplant waiting list exceeds the number of organs available. One means of increasing the organ pool is to broaden potential donors to include those with chronic diseases. RESEARCH QUESTIONS: The study tested the effectiveness of using peer mentors to encourage individuals on dialysis to enroll on an organ donor registry. DESIGN: Dialysis units were pair-matched by size and racial composition and then randomized to one of 2 interventions: meetings with a peer mentor (experimental intervention) or organ donation mailings (control). Peer mentors were trained to discuss organ donation with individuals on dialysis during in-person meetings at dialysis units. The primary outcome was verified registration in the state's donor registry. RESULTS: After adjusting for age, gender, race, income, and education and accounting for correlation within the dialysis center, there was a significant intervention effect. Among individuals in the intervention group, the odds of enrolling (verified) on the donor registry were 2.52 times higher than those in the control group. DISCUSSION: The use of peer mentors to discuss donating organs after death with individuals on dialysis can increase enrollment on a donor registry. Dispelling myths about chronic illness and donation can counter widely held misconceptions and help persons make an informed choice about end-of-life decisions and present an opportunity to increase the number of organs and tissues available for transplant.

Neurology
LeWitt PA. Dopamine Metabolite Biomarkers and Testing for Disease Modification in Parkinson Disease. *JAMA Neurol* 2020; Epub ahead of print. PMID: 32597929. Full Text

Department of Neurology, Wayne State University School of Medicine, Detroit, Michigan.
Henry Ford Hospital, Detroit, Michigan.

Neurology
Li L, **Li R**, **Zacharek A**, **Wang F**, **Landschoot-Ward J**, **Chopp M**, **Chen J**, and **Cui X**. ABCA1/ApoE/HDL Signaling Pathway Facilitates Myelination and Oligodendrogenesis after Stroke. *Int J Mol Sci* 2020; 21(12). PMID: 32575457. Full Text

Department of Neurology, Henry Ford Hospital, Detroit, MI 48202, USA.
Department of Physics, Oakland University, Rochester, MI 48309, USA.

ATP-binding cassette transporter A1 (ABCA1) plays an important role in the regulation of apolipoprotein E (ApoE) and the biogenesis of high-density lipoprotein (HDL) cholesterol in the mammalian brain. Cholesterol is a major source for myelination. Here, we investigate whether ABCA1/ApoE/HDL contribute to myelin repair and oligodendrogenesis in the ischemic brain after stroke. Specific brain ABCA1-deficient (ABCA1(-B/-B)) and ABCA1-floxed (ABCA1(fl/fl)) control mice were subjected to permanent distal middle-cerebral-artery occlusion (dMCAo) and were intracerebrally administered (1) artificial mouse cerebrospinal fluid (CSF) as vehicle control, (2) human plasma HDL3, and (3) recombined human ApoE2 starting 24 h after dMCAo for 14 days. All stroke mice were sacrificed 21

days after dMCAo. The ABCA1(-B/-B)-dMCAo mice exhibit significantly reduced myelination and oligodendrogenesis in the ischemic brain as well as decreased functional outcome 21 days after stroke compared with ABCA1(fl/fl) mice; administration of human ApoE2 or HDL3 in the ischemic brain significantly attenuates the deficits in myelination and oligodendrogenesis in ABCA1(-B/-B)-dMCAo mice ($p < 0.05$, $n = 9$/group). In vitro, ABCA1(-B/-B) reduces ApoE expression and decreases primary oligodendrocyte progenitor cell (OPC) migration and oligodendrocyte maturation; HDL3 and ApoE2 treatment significantly reverses ABCA1(-B/-B)-induced reduction in OPC migration and oligodendrocyte maturation. Our data indicate that the ABCA1/ApoE/HDL signaling pathway contributes to myelination and oligodendrogenesis in the ischemic brain after stroke.

Neurology

LoCastro E, Paudyal R, Mazaheri Y, Hatzoglou V, Oh JH, Lu Y, Konar AS, Vom Eigen K, Ho A, **Ewing JR**, Lee N, Deasy JO, and Shukla-Dave A. Computational Modeling of Interstitial Fluid Pressure and Velocity in Head and Neck Cancer Based on Dynamic Contrast-Enhanced Magnetic Resonance Imaging: Feasibility Analysis. *Tomography* 2020; 6(2):129-138. PMID: 32548289. Full Text

Departments of Medical Physics and.
Radiology, Memorial Sloan Kettering Cancer Center, New York, NY.
Department of Radiology, Medical College of Wisconsin, Milwaukee, WI.
Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY.
Departments of Neurology and.
Neurosurgery, Henry Ford Hospital, Detroit, MI; and.
Department of Radiation Oncology, Memorial Sloan Kettering Cancer Center, New York, NY.

We developed and tested the feasibility of computational fluid modeling (CFM) based on dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) for quantitative estimation of interstitial fluid pressure (IFP) and velocity (IFV) in patients with head and neck (HN) cancer with locoregional lymph node metastases. Twenty-two patients with HN cancer, with 38 lymph nodes, underwent pretreatment standard MRI, including DCE-MRI, on a 3-Tesla scanner. CFM simulation was performed with the finite element method in COMSOL Multiphysics software. The model consisted of a partial differential equation (PDE) module to generate 3D parametric IFP and IFV maps, using the Darcy equation and Ktrans values (min(-1), estimated from the extended Tofts model) to reflect fluid influx into tissue from the capillary microvasculature. The Spearman correlation (ρ) was calculated between total tumor volumes and CFM estimates of mean tumor IFP and IFV. CFM-estimated tumor IFP and IFV mean ± standard deviation for the neck nodal metastases were 1.73 ± 0.39 (kPa) and 1.82 ± 0.9 × (10(-7) m/s), respectively. High IFP estimates corresponds to very low IFV throughout the tumor core, but IFV rises rapidly near the tumor boundary where the drop in IFP is precipitous. A significant correlation was found between pretreatment total tumor volume and CFM estimates of mean tumor IFP ($\rho = 0.50$, $P = 0.004$). Future studies can validate these initial findings in larger patients with HN cancer cohorts using CFM of the tumor in concert with DCE characterization, which holds promise in radiation oncology and drug-therapy clinical trials.

Neurology

Mac Grory B, Nackenoff A, Poli S, Spitzer MS, Nedelmann M, Guillon B, Preterre C, Chen CS, Lee AW, Yaghi S, Stretz C, Azher I, Paddock J, Bakaeva T, Greer DM, Shulman JG, **Kowalski RG**, Lavin P, Mistry E, Espaillat K, Furie K, Kirshner H, and Schrag M. Intravenous Fibrinolysis for Central Retinal Artery Occlusion: A Cohort Study and Updated Patient-Level Meta-Analysis. *Stroke* 2020; 51(7):2018-2025. PMID: 32568646. Full Text

Department of Neurology (B.M.G., C.S., I.A., J.P., T.B., K.F.), Warren Alpert Medical School of Brown University, Providence, RI.
Department of Neurology (A.N., P.L., E.M., K.E., H.K., M.S.), Vanderbilt University School of Medicine, Nashville, TN.
Department of Neurology with Focus on Neurovascular Diseases, and Hertie Institute for Clinical Brain Research, University Hospital Tübingen, Germany (S.P.).
Eye Clinic, University Hospital Hamburg-Eppendorf, Germany (M.S.S.).
Department of Neurology, Sana Regio Klinikum, Pinneberg, Germany (M.N.).
Department of Neurology, CHU de Nantes - Laennec Nantes, France (B.G., C.P.).
Department of Ophthalmology, Flinders Medical Center and Flinders University, Adelaide, Australia (C.S.C.).
Department of Neurology, Flinders University and the Calvary Wakefield Hospital, Adelaide, Australia (A.W.L.).
Department of Neurology, New York University School of Medicine (S.Y.).
Division of Ophthalmology, Department of Surgery (T.B.), Warren Alpert Medical School of Brown University, Providence, RI.
Massachusetts Eye and Ear Infirmary, Harvard Medical School, Boston (T.B.).
Department of Neurology, Boston University School of Medicine, MA (D.M.G., J.G.S.).
Department of Neurology, Henry Ford Hospital, Detroit, MI (R.G.K.).
Department of Ophthalmology and Visual Sciences (P.L.), Vanderbilt University School of Medicine, Nashville, TN.

BACKGROUND AND PURPOSE: Central retinal artery occlusion results in sudden, painless, usually permanent loss of vision in the affected eye. There is no proven, effective treatment to salvage visual acuity and a clear, unmet need for an effective therapy. In this work, we evaluated the efficacy of intravenous tissue-type plasminogen activator (IV alteplase) in a prospective cohort study and an updated systematic review and meta-analysis. METHODS: We enrolled consecutive patients with acute central retinal artery occlusion within 48 hours of symptoms onset and with a visual acuity of <20/200 from January 2009 until May 2019. The primary outcomes were safety and functional visual acuity recovery. We compared rates of visual recovery between those treated with alteplase within 4.5 hours of symptom onset to those who did not receive alteplase (including an analysis restricted to untreated patients presenting within the window for treatment). We incorporated these results into an updated systematic review and patient-level meta-analysis. RESULTS: We enrolled 112 patients, of whom 25 (22.3% of the cohort) were treated with IV alteplase. One patient had an asymptomatic intracerebral hemorrhage after IV alteplase treatment. Forty-four percent of alteplase-treated patients had recovery of visual acuity when treated within 4.5 hours versus 13.1% of those not treated with alteplase (P=0.003) and 11.6% of those presenting within 4 hours who did not receive alteplase (P=0.03). Our updated patient-level meta-analysis of 238 patients included 67 patients treated with alteplase within 4.5 hours since time last known well with a recovery rate of 37.3%. This favorably compares with a 17.7% recovery rate in those without treatment. In linear regression, earlier treatment correlated with a higher rate of visual recovery (P=0.01). CONCLUSIONS: This study showed that the administration of intravenous alteplase within 4.5 hours of symptom onset is associated with a higher likelihood of a favorable visual outcome for acute central retinal artery occlusion. Our results strongly support proceeding to a randomized, placebo-controlled clinical trial.

Neurology
Pandey AS, Daou BJ, Tsai JP, Zaidi SF, Salahuddin H, Gemmete JJ, Oliver MJ, Singer J, Elder TA, Mbabuike N, Adel JG, Gujrati Y, Saleemi MA, Siddiqui FM, Elias AE, **Rehman MF**, **Marin H**, **Chebl AB**, **Kole M**, Wilseck JM, Kazmierczak CD, Mick JM, Majjhoo AQ, Naravetla BR, Rayes M, Luqman AW, Richards BF, Kelkar P, Burgess R, Thompson BG, Chaudhary N, Mazaris PA, Qahwash O, Razak MA, and Jumaa MA. Letter: COVID-19 Pandemic-The Bystander Effect on Stroke Care in Michigan. *Neurosurgery* 2020; Epub ahead of print. PMID: 32496518. Full Text

Department of Neurosurgery University of Michigan Ann Arbor, Michigan.
Spectrum Health West Michigan Grand Rapids, Michigan.
ProMedica Neurosciences Institute Toledo, Ohio.
Department of Neurology University of Toledo Toledo, Ohio.
Department of Radiology University of Michigan Ann Arbor, Michigan.
Field Neuroscience Institute Saginaw, Michigan.
Ascension St. Mary's Hospital Saginaw, Michigan.
Michigan State University East Lansing, Michigan.
Sparrow Health System East Lansing, Michigan.
Metro Health-University of Michigan Wyoming, Michigan.
Henry Ford Health System Detroit, Michigan.
Oakland University William Beaumont School of Medicine Auburn Hills, Michigan.
McLaren Health System Grand Blanc, Michigan.
Detroit Medical Center Wayne State University Detroit, Michigan.
Ascension Providence Hospitals Livonia, Michigan.
Lansing Neurosurgery East Lansing, Michigan.

Neurology
Qian Y, **Chopp M**, and **Chen J**. Emerging role of microRNAs in ischemic stroke with comorbidities. *Exp Neurol* 2020; 331. PMID: 32561412. Full Text

Department of Neurology, Henry Ford Hospital, Detroit, MI, United States of America.
Department of Neurology, Henry Ford Hospital, Detroit, MI, United States of America; Department of Physics, Oakland University, Rochester, MI, United States of America. Electronic address: mchopp1@hfhs.org.
Department of Neurology, Henry Ford Hospital, Detroit, MI, United States of America. Electronic address: jchen4@hfhs.org.

Ischemic stroke is one of the major causes of global disability and death. Comorbidities in stroke are not only risk factors for an increased incidence of stroke, but also adversely impact stroke outcome. Stroke patients with co-morbidities have worse deficit, long term disability and high mortality rate and extended hospitalization stay. MicroRNAs (miRNAs) are noncoding RNA molecules, and are emerging as key molecular mediators of ischemic stroke and other diseases. Thus, focusing on the treatment of stroke and its comorbidities with miRNAs appears to be particularly important. In this review article, we provide an overview of the common comorbidities of hypertension, diabetes mellitus (DM) and hyperlipidemia in ischemic stroke. We also discuss specific miRNAs, including miR-126,

miR-223, and miR-124 which are important in regulating ischemic stroke and describetheir effects as related to stroke and comorbidities. In addition, we provide an overview of roles of long non-coding RNAs (lncRNAs) and circular RNAs (circRNAs) in stroke with comorbidities.

Neurology
Sico JJ, Sarwal A, Benish SM, Busis NA, Cohen BH, Das RR, Finsilver S, **Halperin JJ**, Kelly AG, Meunier L, Phipps MS, Thirumala PD, Villanueva R, von Gaudecker J, Bennett A, and Shenoy AM. Quality improvement in neurology: Neurology Outcomes Quality Measurement Set. *Neurology* 2020; 94(22):982-990. PMID: 32398356. Full Text

From the Departments of Neurology (J.J.S.), Internal Medicine, and the Center for NeuroEpidemiological and Clinical Neurological Research, Yale School of Medicine, New Haven, CT; and Neurology Service and Pain Research, Informatics, Multi-morbidities, and Education (PRIME) Health Services Research Center (J.J.S.), VA Connecticut Healthcare System, West Haven, CT; Department of Neurology (A.S.), Wake Forest School of Medicine, Winston Salem, NC; Department of Neurology (S.M.B.), University of Minnesota School of Medicine and Physicians Minneapolis, MN; Department of Neurology (N.A.B.), University of Pittsburgh School of Medicine, PA; Department of Pediatrics (B.H.C.), The Rebecca D. Considine Research Institute, Akron Children's Hospital, Akron, OH and The Northeast Ohio Medical University (B.H.C.), Rootstown, OH; Department of Neurology (R.R.D), University of Texas Southwestern Medical Center, Dallas, TX; International Essential Tremor Foundation (S.F.), Member of Henry Ford Health System Foundation Board, Member of Henry Ford Health System Neuroscience Institute Council of Advisors; Department of Neurosciences (J.J.H.), Atlantic Health, Summit, NJ; Department of Neurology (A.G.K.), University of Rochester, NY; Epilepsy Foundation of Minnesota (L.M.), Minneapolis, MN; Departments of Neurology and Epidemiology and Public Health (M.S.P.), University of Maryland School of Medicine, Baltimore, MD; Department of Neurology (P.D.T.), University of Pittsburgh Medical Center, PA; Neurology (R.V.), University of Rochester Medical Center, Rochester, NY; Indiana University School of Nursing (J.v.G.), Indianapolis, IN; American Academy of Neurology (A.B.), Minneapolis, MN; and Division of Neurology (A.M.S.), Mount Auburn Hospital, Cambridge, MA.

Neurology
Singh J, and **Ali A**. Headache as the Presenting Symptom in 2 Patients with COVID-19 and a History of Migraine: 2 Case Reports. *Headache* 2020; Epub ahead of print. PMID: 32521062. Full Text

Henry Ford Health System, Department of Neurology, Detroit, MI, United States.

The Coronavirus disease 2019 (COVID-19) pandemic has now affected more than five million people globally. Typical symptoms include fever, cough, and shortness of breath. Patients with underlying medical comorbidities such as cardiovascular disease and diabetes are more likely to become severely ill. To date there is limited information on how COVID-19 affects patients with a history migraine. Here, we present the cases of 2 women with a history of migraine whose first symptom of COVID-19 was a severe persistent headache.

Neurology
Zahoor I, and **Giri S**. Specialized Pro-Resolving Lipid Mediators: Emerging Therapeutic Candidates for Multiple Sclerosis. *Clin Rev Allergy Immunol* 2020; Epub ahead of print. PMID: 32495237. Full Text

Department of Neurology, Research Division, Education & Research Building, Henry Ford Hospital, Room 4023, 2799 W Grand Blvd, Detroit, MI, 48202, USA. izahoor1@hfhs.org.
Department of Neurology, Research Division, Education & Research Building, Henry Ford Hospital, Room 4051, 2799 W Grand Blvd, Detroit, MI, 48202, USA. SGiri1@hfhs.org.

Multiple sclerosis (MS) is a neuroinflammatory disease in which unresolved and uncontrolled inflammation disrupts normal cellular homeostasis and leads to a pathological disease state. It has long been recognized that endogenously derived metabolic by-products of omega fatty acids, known as specialized pro-resolving lipid mediators (SPMs), are instrumental in resolving the pathologic inflammation. However, there is minimal data available on the functional status of SPMs in MS, despite the fact that MS presents a classical model of chronic inflammation. Studies to date indicate that dysfunction of the SPM biosynthetic pathway is responsible for their altered levels in patient-derived biofluids, which contributes to heightened inflammation and disease severity. Collectively, current findings suggest the contentious role of SPMs in MS due to variable outcomes in biological matrices across studies conducted so far, which could, in part, also be attributed to differences in population characteristics. It seems that SPMs have neuroprotective action on MS by exerting proresolving effects on brain microglia in its preclinical model; however, there are no reports demonstrating the direct effect of SPMs on oligodendrocytes or neurons. This reveals that "one size does not fit all" notion holds significance for MS in terms of the status of SPMs in other inflammatory conditions. The lack of clarity served as the impetus for this review, which is the first of its kind to summarize the relevant data regarding the role of SPMs in MS and the potential to target them for biomarker development and future alternative

therapies for this disease. Understanding the mechanisms behind biological actions of SPMs as resolution mediators may prevent or even cure MS and other neurodegenerative pathologies.

Neurosurgery
Hatcher SE, and **Air EL**. Catastrophic failure of spinal cord stimulator paddle electrodes in the cervical spine. *Clin Neurol Neurosurg* 2020; 196. PMID: 32563977. Full Text

Henry Ford Health System, 2799 W. Grand Blvd, Detroit, MI, 48202, USA.
Henry Ford Health System, 2799 W. Grand Blvd, Detroit, MI, 48202, USA. Electronic address: eair1@hfhs.org.

Neurosurgery
Pandey AS, Daou BJ, Tsai JP, Zaidi SF, Salahuddin H, Gemmete JJ, Oliver MJ, Singer J, Elder TA, Mbabuike N, Adel JG, Gujrati Y, Saleemi MA, Siddiqui FM, Elias AE, **Rehman MF**, **Marin H**, **Chebl AB**, **Kole M**, Wilseck JM, Kazmierczak CD, Mick JM, Majjhoo AQ, Naravetla BR, Rayes M, Luqman AW, Richards BF, Kelkar P, Burgess R, Thompson BG, Chaudhary N, Mazaris PA, Qahwash O, Razak MA, and Jumaa MA. Letter: COVID-19 Pandemic-The Bystander Effect on Stroke Care in Michigan. *Neurosurgery* 2020; Epub ahead of print. PMID: 32496518. Full Text

Department of Neurosurgery University of Michigan Ann Arbor, Michigan.
Spectrum Health West Michigan Grand Rapids, Michigan.
ProMedica Neurosciences Institute Toledo, Ohio.
Department of Neurology University of Toledo Toledo, Ohio.
Department of Radiology University of Michigan Ann Arbor, Michigan.
Field Neuroscience Institute Saginaw, Michigan.
Ascension St. Mary's Hospital Saginaw, Michigan.
Michigan State University East Lansing, Michigan.
Sparrow Health System East Lansing, Michigan.
Metro Health-University of Michigan Wyoming, Michigan.
Henry Ford Health System Detroit, Michigan.
Oakland University William Beaumont School of Medicine Auburn Hills, Michigan.
McLaren Health System Grand Blanc, Michigan.
Detroit Medical Center Wayne State University Detroit, Michigan.
Ascension Providence Hospitals Livonia, Michigan.
Lansing Neurosurgery East Lansing, Michigan.

Neurosurgery
Zakaria HM, **Wilkinson BM**, Pennington Z, Saadeh YS, Lau D, **Chandra A**, Ahmed AK, **Macki M**, **Anand SK**, **Abouelleil MA**, Fateh JA, Rick JW, Morshed RA, Deng H, Chen KY, **Robin A**, **Lee IY**, **Kalkanis S**, Chou D, Park P, Sciubba DM, and **Chang V**. Sarcopenia as a Prognostic Factor for 90-Day and Overall Mortality in Patients Undergoing Spine Surgery for Metastatic Tumors: A Multicenter Retrospective Cohort Study. *Neurosurgery* 2020; Epub ahead of print. PMID: 32592483. Full Text

Department of Neurosurgery, Henry Ford Hospital, Detroit, Michigan.
Johns Hopkins University, Baltimore, Maryland.
University of Michigan, Ann Arbor, Michigan.
University of California, San Francisco, San Francisco, California.
Department of Neurosurgery, Neurological Institute, Taichung Veterans General Hospital, Taichung, Taiwan.

BACKGROUND: Novel methods in predicting survival in patients with spinal metastases may help guide clinical decision-making and stratify treatments regarding surgery vs palliative care. OBJECTIVE: To evaluate whether the frailty/sarcopenia paradigm is predictive of survival and morbidity in patients undergoing surgery for spinal metastasis. METHODS: A total of 271 patients from 4 tertiary care centers who had undergone surgery for spinal metastasis were identified. Frailty/sarcopenia was defined by psoas muscle size. Survival hazard ratios were calculated using multivariate analysis, with variables from demographic, functional, oncological, and surgical factors. Secondary outcomes included improvement of neurological function and postoperative morbidity. RESULTS: Patients in the smallest psoas tertile had shorter overall survival compared to the middle and largest tertile. Psoas size (PS) predicted overall mortality more strongly than Tokuhashi score, Tomita score, and Karnofsky Performance Status (KPS). PS predicted 90-d mortality more strongly than Tokuhashi score, Tomita score, and KPS. Patients with a larger PS were more likely to have an improvement in deficit compared to the middle tertile. PS was not predictive of 30-d morbidity. CONCLUSION: In patients undergoing surgery for spine metastases, PS as a surrogate for frailty/sarcopenia predicts 90-d and overall mortality, independent of demographic, functional, oncological, and surgical characteristics. The frailty/sarcopenia paradigm is a stronger predictor of survival at these time points than

other standards. PS can be used in clinical decision-making to select which patients with metastatic spine tumors are appropriate surgical candidates.

Obstetrics, Gynecology, and Women's Health

Saeed H, **Hong L**, **Smith N**, and **Shaman M**. Ovarian torsion in utero diagnosed at 37 weeks of pregnancy: A case report. *Case Rep Womens Health* 2020; 27. PMID: 32577405. Full Text

Department of Obstetrics and Gynecology, Henry Ford Hospital, Detroit, MI, United States of America.

BACKGROUND: Fetal ovarian masses are common abdominal anomalies in female fetuses, often diagnosed in the third trimester. Most masses are benign and tend to resolve spontaneously within a few months after birth, but larger masses may present complications such as torsion. CASE: A 21-year-old primagravid woman was noted to have a complex avascular solid mass in the fetal left pelvis, which was consistent with complex fetal left ovarian torsion. The patient underwent induction of labor at 39 weeks for possible intervention. The infant underwent surgery at 5 weeks of age and a torsed, necrotic ovary was discovered. CONCLUSION: The diagnosis of ovarian torsion in utero is rare, and prenatal and postnatal guidelines are needed on frequency of monitoring, timing of delivery, and postnatal follow-up.

Ophthalmology and Eye Care Services

Hamad AE, Moinuddin O, Blair MP, Schechet SA, Shapiro MJ, Quiram PA, Mammo DA, Berrocal AM, Prakhunhungsit S, Cernichiaro-Espinosa LA, Mukai S, Yonekawa Y, Ung C, Holz ER, Harper CA, 3rd, Young RC, Besirli CG, Nagiel A, Lee TC, Gupta MP, Walsh MK, Khawly JA, Campbell JP, Kychenthal A, Nudleman ED, Robinson JE, Hartnett ME, Calvo CM, and Chang EY. Late-Onset Retinal Findings and Complications in Untreated Retinopathy of Prematurity. *Ophthalmol Retina* 2020; 4(6):602-612. PMID: 32059986. Full Text

Retina and Vitreous of Texas, Houston, Texas; Henry Ford Health System, Detroit, Michigan.
Kellogg Eye Center, University of Michigan School of Medicine, Ann Arbor, Michigan.
Department of Ophthalmology and Visual Science, University of Chicago, Chicago, Illinois; Retina Consultants, Ltd, Chicago, Illinois.
Department of Ophthalmology and Visual Science, University of Chicago, Chicago, Illinois.
VitreoRetinal Surgery, PA, Minneapolis, Minnesota; Department of Ophthalmology and Visual Neurosciences, University of Minnesota, Minneapolis, Minnesota.
Department of Ophthalmology and Visual Neurosciences, University of Minnesota, Minneapolis, Minnesota.
Bascom Palmer Eye Institute, University of Miami, Miami, Florida.
Department of Ophthalmology, Massachusetts Eye and Ear Infirmary, Harvard Medical School, Boston, Massachusetts; Pediatric Retina Surgery Service, Boston Children's Hospital, Harvard Medical School, Boston, Massachusetts.
Department of Ophthalmology, Massachusetts Eye and Ear Infirmary, Harvard Medical School, Boston, Massachusetts.
Retina and Vitreous of Texas, Houston, Texas.
Austin Retina Associates, Austin, Texas.
USC Roski Eye Institute, Department of Ophthalmology, Keck School of Medicine, University of Southern California, Los Angeles, California; The Vision Center, Department of Surgery, Children's Hospital Los Angeles, Los Angeles, California.
Department of Ophthalmology, Weill Cornell Medical College, New York, New York.
Retina Associates, Tucson, Arizona.
Casey Eye Institute, Oregon Health and Science University, Portland, Oregon.
KYDOFT Foundation, Santiago, Chile.
Shiley Eye Institute, University of California San Diego School of Medicine, San Diego, California.
Palmetto Retina Center, West Columbia, South Carolina.
John A. Moran Eye Center, University of Utah School of Medicine, Salt Lake City, Utah.
Retina and Vitreous of Texas, Houston, Texas. Electronic address: emanmdphd@gmail.com.

PURPOSE: To investigate late retinal findings and complications of eyes with a history of retinopathy of prematurity (ROP) that did not meet treatment criteria and did not receive treatment during infancy. DESIGN: Retrospective, nonconsecutive, noncomparative, multicenter case series. PARTICIPANTS: Three hundred sixty-three eyes of 186 patients. METHODS: Data were requested from multiple providers on premature patients with a history of ROP and no treatment during infancy who demonstrated late retinal findings or complications and included age, gender, gestational age and weight, zone and stage at infancy, visual acuity, current retina vascularization status, vitreous character, presence of peripheral retinal findings such as lattice retinal tears and detachments (RDs), retinoschisis, and fluorescein findings. MAIN OUTCOME MEASURES: Rate of RDs and factors conferring a higher risk of RDs. RESULTS: The average age was 34.5 years (range, 7-76 years), average gestational age was 26.6 weeks (range,

23-34 weeks), and average birth weight was 875 g (range, 425-1590 g). Findings included lattice in 196 eyes (54.0%), atrophic holes in 126 eyes (34.7%), retinal tears in 111 eyes (30.6%), RDs in 140 eyes (38.6 %), tractional retinoschisis in 44 eyes (11.9%), and visible vitreous condensation ridge-like interface in 112 eyes (30.5%). Fluorescein angiography (FA) was performed in 113 eyes, of which 59 eyes (52.2%) showed leakage and 16 eyes (14.2%) showed neovascularization. Incomplete vascularization posterior to zone 3 was common (71.6% of eyes). Retinal detachments were more likely in patients with a gestational age of 29 weeks or less ($P < 0.05$) and in eyes with furthest vascularization to posterior zone 2 eyes compared with zone 3 eyes ($P = 0.009$). CONCLUSIONS: Eyes with ROP not meeting the treatment threshold during infancy showed various late retinal findings and complications, of which RDs were the most concerning. Complications were seen in all age groups, including patients born after the Early Treatment for Retinopathy of Prematurity Study. Contributing factors to RDs included atrophic holes within peripheral avascular retina, visible vitreous condensation ridge-like interface with residual traction, and premature vitreous syneresis. We recommend regular examinations and consideration of ultra-widefield FA examinations. Prospective studies are needed to explore the frequency of complications and benefit of prophylactic treatment and if eyes treated with anti-vascular endothelial growth factor therapy are at risk of similar findings and complications.

Orthopedics/Bone and Joint

Lee ECS, Roach NT, Clouthier AL, Bicknell RT, **Bey MJ**, Young NM, and Rainbow MJ. Three-dimensional scapular morphology is associated with rotator cuff tears and alters the abduction moment arm of the supraspinatus. *Clin Biomech (Bristol, Avon)* 2020; 78. PMID: 32580097. Full Text

Department of Mechanical and Materials Engineering, Queen's University, Kingston, ON, Canada. Electronic address: erin.lee@queensu.ca.
Department of Human Evolutionary Biology, Harvard University, Cambridge, MA, USA.
School of Human Kinetics, University of Ottawa, Ottawa, ON, Canada.
Department of Surgery, Kingston Health Sciences Centre, Kingston, Canada.
Department of Orthopaedic Surgery, Henry Ford Hospital, Detroit, MI, USA.
Department of Orthopaedic Surgery, University of California San Francisco, CA, USA.
Department of Mechanical and Materials Engineering, Queen's University, Kingston, ON, Canada.

BACKGROUND: Numerous studies have reported an association between rotator cuff injury and two-dimensional measures of scapular morphology. However, the mechanical underpinnings explaining how these shape features affect glenohumeral joint function and lead to injury are poorly understood. We hypothesized that three-dimensional features of scapular morphology differentiate asymptomatic shoulders from those with rotator cuff tears, and that these features would alter the mechanical advantage of the supraspinatus. METHODS: Twenty-four individuals with supraspinatus tears and twenty-seven age-matched controls were recruited. A statistical shape analysis identified scapular features distinguishing symptomatic patients from asymptomatic controls. We examined the effect of injury-associated morphology on mechanics by developing a morphable model driven by six degree-of-freedom biplanar videoradiography data. We used the model to simulate abduction for a range of shapes and computed the supraspinatus moment arm. FINDINGS: Rotator cuff injury was associated with a cranial orientation of the glenoid and scapular spine ($P = .011$, $d = 0.75$) and/or decreased subacromial space ($P = .001$, $d = 0.94$). The shape analysis also identified previously undocumented features associated with superior inclination and subacromial narrowing. In our computational model, warping the scapula from a cranial to a lateral orientation increased the supraspinatus moment arm at 20° of abduction and decreased the moment arm at 160° of abduction. INTERPRETATIONS: Three-dimensional analysis of scapular morphology indicates a stronger relationship between morphology and cuff tears than two-dimensional measures. Insight into how morphological features affect rotator cuff mechanics may improve patient-specific strategies for prevention and treatment of cuff tears.

Orthopedics/Bone and Joint

Okoroha KR, **Ussef N**, **Jildeh TR**, **Khalil LS**, Hasan L, Bench C, **Zeni F**, **Eller E**, and **Moutzouros V**. Comparison of Tendon Lengthening With Traditional Versus Accelerated Rehabilitation After Achilles Tendon Repair: A Prospective Randomized Controlled Trial. *Am J Sports Med* 2020; 48(7):1720-1726. PMID: 32203675. Full Text

Department of Orthopaedic Surgery, Henry Ford Hospital, Detroit, Michigan, USA.
Tulane University Medical School, New Orleans, Louisiana, USA.
Wayne State University School of Medicine, Detroit, Michigan, USA.

BACKGROUND: Early weightbearing protocols after Achilles tendon repair promote mobilization, yet little is known about their effect on tendon lengthening. PURPOSE: To evaluate tendon lengthening after Achilles tendon repair with accelerated rehabilitation. STUDY DESIGN: Randomized controlled trial; Level of evidence, 1. METHODS: Patients undergoing primary repair for acute Achilles tendon ruptures consented to have tantalum beads placed within the tendon. Patients were randomized into either a traditional (weightbearing at 6 weeks) or accelerated (graduated weightbearing at 2 weeks) rehabilitation group. The primary outcome of the study was postoperative tendon

elongation as measured by radiostereometric beads. Secondary outcomes included Achilles Tendon Total Rupture Score (ATRS) and Patient-Reported Outcomes Measurement Information System Pain Interference Short Form (PROMIS PI-SF) score. RESULTS: All 18 patients included in the final analysis were found to have significant tendon lengthening after surgery, with a mean lengthening of 15.9 mm. No significant differences were found in overall lengthening between the traditional and accelerated rehabilitation groups (15.3 ± 4.5 vs 16.4 ± 4.7 mm, respectively; P = .33) at final follow-up. The repair site in each group was found to lengthen more than the intratendinous site (traditional group, 13.2 vs 2.1 mm; accelerated group, 16.8 vs -0.4 mm); however, no difference in lengthening was seen between groups (P = .82 and P = .31, respectively). The greatest amount of lengthening occurred between 2 and 6 weeks, and the least amount of lengthening occurred between 6 and 12 weeks, with no difference between the traditional and accelerated groups at these time points (P = .84 and P = .38, respectively). No differences were noted in ankle range of motion (dorsiflexion, P = .16; plantarflexion, P = .08) or outcome scores (ATRS, P = .56; PROMIS PI-SF, P = .54). CONCLUSION: This study's findings demonstrate that all patients undergoing operative repair of Achilles tendon ruptures had lengthening after surgery. No difference was found in tendon lengthening (repair site or intratendinous) at any time point between patients undergoing traditional versus accelerated rehabilitation postoperatively. The greatest amount of lengthening was found to occur between 2 and 6 weeks postoperatively, and tendon lengthening decreased significantly after 6 weeks. REGISTRATION: NCT04050748 (ClinicalTrials.gov identifier).

Orthopedics/Bone and Joint

Rahman TM, Frisch NB, **Darrith B**, Patel I, and **Silverton CD**. Incidence of Pseudotumors in a Dual Modular Stem Construct With and Without Metal-on-Metal Bearing Surface. *J Am Acad Orthop Surg* 2020; Epub ahead of print. PMID: 32568995. Full Text

From the Wayne State University School of Medicine, Detroit, MI (Dr. Rahman and Dr. Patel), the Ascension Providence Rochester Hospital, Rochester, MI (Dr. Frisch), and the Department of Orthopaedic Surgery, Henry Ford Health System, Detroit, MI (Dr. Darrith and Dr. Silverton).

BACKGROUND: The purpose of this study was to compare the incidence of pseudotumors in metal-on-metal (MoM) titanium modular neck hip arthroplasties to non-MoM modular neck hip arthroplasties. A secondary goal was to determine whether a correlation exists between elevated metal concentrations and pseudotumor incidence. METHODS: The data were collected and evaluated from 49 MoM joints and 26 non-MoM joints between the years 2012 and 2017. Hip ultrasonography was done after a minimum of 5 years postimplantation. Whole serum metal (titanium, cobalt, and chromium) concentrations were measured at the hip ultrasonography study. RESULTS: The average time elapsed between surgery and ultrasonography visit was 7.6 years. In the 49 patients with MoM joints, 22.4% (n = 11) had a pseudotumor. In the 26 patients with non-MoM joints, 9.1% of metal-on-polyethylene hips (n = 1) and 0% of ceramic-on-ceramic/polyethylene hips developed a pseudotumor. No significant statistical correlation was observed between serum metal concentrations and pseudotumor formation (P > 0.05). A significant correlation was observed of serum titanium concentration to pseudotumor size (P = 0.024). CONCLUSION: The incidence of pseudotumor formation in MoM total hip arthroplasties was more than five times the incidence associated with non-MoM bearings. The correlation between serum titanium concentration and pseudotumor size suggests that titanium levels may be a useful indicator for pseudotumor formation in patients with this particular titanium modular neck femoral implant. No notable correlation was observed between serum cobalt and chromium concentration and pseudotumor formation or size.

Otolaryngology

Craig JR, Tataryn RW, Aghaloo TL, Pokorny AT, Gray ST, Mattos JL, and Poetker DM. Management of odontogenic sinusitis: multidisciplinary consensus statement. *Int Forum Allergy Rhinol* 2020; Epub ahead of print. PMID: 32506807. Full Text

Department of Otolaryngology, Henry Ford Health System, Detroit, MI.
Tataryn Endodontics, Spokane, WA.
Department of Endodontics, School of Dentistry, Loma Linda University, Loma Linda, CA.
University of California, Los Angeles (UCLA) School of Dentistry, UCLA, Los Angeles, CA.
Spokane ENT Clinic, Spokane, WA.
Department of Otolaryngology, University of Washington, Seattle, WA.
Department of Otolaryngology-Head and Neck Surgery, Harvard Medical School, Boston, MA.
Department of Otolaryngology, University of Virginia, Charlottesville, VA.
Department of Otolaryngology, Medical College of Wisconsin, Milwaukee, WI.

BACKGROUND: Odontogenic sinusitis (ODS) can present a therapeutic dilemma because multiple treatment strategies have been reported. ODS review articles have been published, but they have lacked multidisciplinary collaboration and an evidence-based methodology. The purpose of this article was to perform an evidence-based

review of ODS management options, and develop a multidisciplinary consensus statement on ODS management options. METHODS: An evidence-based review of dental and medical literature on ODS management was performed using PubMed, EMBASE, and Cochrane Review Databases up to December 2019. Exclusion criteria included non-English-language articles, case series with fewer than 10 patients, fungal sinusitis, and studies that did not report treatment success rates. Because aggregate levels of evidence for recommendations were no higher than level C, a clinical consensus statement was conducted using a modified Delphi method. RESULTS: Sixteen articles met inclusion criteria for the evidence-based review on the following ODS management options: dental treatment alone or combined with ESS for various dental pathologies, and endoscopic sinus surgery (ESS) alone for dental implant-related ODS. Strong consensus was achieved for 9 of the 10 clinical statements, the strongest being the use of shared decision-making for selecting management strategies. No consensus was reached for determining the extent of ESS necessary for uncomplicated ODS. CONCLUSION: Strong consensus was reached that ODS management should involve shared decision-making between the otolaryngologist, dental provider, and patient, where the benefits and risks of dental treatment and ESS are discussed. Higher-quality studies are necessary to develop evidence-based treatment recommendations for ODS.

Pathology
Gadde R, **Arora K**, Felicella MM, Arora S, Cheng L, **Park H**, **Gupta NS**, Salamat MS, and **Williamson SR**. Cystic Trophoblastic Tumor in a Primary Central Nervous System Post-Chemotherapy Germ Cell Tumor: The First Case Report. *Int J Surg Pathol* 2020; Epub ahead of print. PMID: 32498578. Full Text

Henry Ford Health System, Henry Ford Hospital, Detroit, MI, USA.
These authors contributed equally to the study.
Barrow Neurological Institute, Phoenix, AZ, USA.
Indiana University, Indianapolis, IN, USA.
University of Wisconsin, Madison, WI, USA.
Wayne State University, Detroit, MI, USA.

Cystic trophoblastic tumor (CTT) is an uncommon trophoblastic proliferation of germ cell tumor origin, mostly reported in post-chemotherapy metastases of testicular germ cell tumors and rarely primary untreated testicular tumors. To date, we are not aware of occurrence in a non-testicular tumor. A 12-year-old boy presented with limb swelling, increased appetite, weight gain, and precocious puberty. Evaluation revealed right frontal lobe mass and elevated α-fetoprotein and β-human chorionic gonadotrophin. After response to neoadjuvant chemotherapy, the tumor was resected. Microscopically, the resection contained predominantly smooth muscle tissue with scattered small foci of glandular teratoma and CTT. Immunohistochemistry (SALL4, glypican 3) revealed no residual yolk sac tumor. Fluorescence in situ hybridization revealed gain of chromosome 12p. The patient has been disease-free for 13 years. This report expands the spectrum of primary central nervous system germ cell tumors with the occurrence of CTT in this site.

Pathology
Rodgers SA, and **Williamson SR**. Xanthogranulomatous Ureteritis Mimicking Ureteral Involvement by Cancer in a Radical Cystectomy Specimen. *Int J Surg Pathol* 2020; Epub ahead of print. PMID: 32493143. Full Text

Henry Ford Health System, Detroit, MI, USA.
Wayne State University, Detroit, MI, USA.

Xanthogranulomatous pyelonephritis is well established as a renal mass-forming inflammatory process. However, a ureteral counterpart is minimally recognized. In this article, we present a case of xanthogranulomatous ureteritis in an 81-year-old woman, mimicking ureteral involvement by cancer in a radical cystectomy specimen for invasive urothelial carcinoma. Similar to the pathogenesis of xanthogranulomatous pyelonephritis, the patient was noted to have ureteral obstruction by calculus and had urine culture positive for Klebsiella pneumoniae. To our knowledge, this is the first report of xanthogranulomatous ureteritis associated with this pathogen and the only report associated with concurrent bladder cancer. Increased pathologist and urologist awareness of xanthogranulomatous ureteritis expands the spectrum of pseudotumoral processes of the ureter.

Pathology
Williamson SR, and **Rodgers SA**. Xanthogranulomatous Ureteritis Mimicking Ureteral Involvement by Cancer in a Radical Cystectomy Specimen. *International Journal of Surgical Pathology* 2020; Epub ahead of print. PMID: Not assigned. Full Text

S.R. Williamson, Henry Ford Health System, Detroit, MI, United States

Xanthogranulomatous pyelonephritis is well established as a renal mass-forming inflammatory process. However, a ureteral counterpart is minimally recognized. In this article, we present a case of xanthogranulomatous ureteritis in an 81-year-old woman, mimicking ureteral involvement by cancer in a radical cystectomy specimen for invasive urothelial carcinoma. Similar to the pathogenesis of xanthogranulomatous pyelonephritis, the patient was noted to have ureteral obstruction by calculus and had urine culture positive for Klebsiella pneumoniae. To our knowledge, this is the first report of xanthogranulomatous ureteritis associated with this pathogen and the only report associated with concurrent bladder cancer. Increased pathologist and urologist awareness of xanthogranulomatous ureteritis expands the spectrum of pseudotumoral processes of the ureter.

Pharmacy
Cheng JWM, Colucci V, **Kalus JS**, and Spinler SA. Focused Updates: SGLT2 Inhibitors in Patients With Heart Failure and/or Chronic Kidney Disease. *Ann Pharmacother* 2020; Epub ahead of print. PMID: 32536199. Full Text

MCPHS University, Boston, MA, USA.
Brigham and Women's Hospital, Boston, MA, USA.
University of Montana, Missoula, MT, USA.
Henry Ford Hospital, Detroit, MI, USA.
Binghamton University, Binghamton, NY, USA.

Sodium-glucose cotransporter (SGLT2) inhibitors have demonstrated cardiovascular (CV) benefits in large-scale clinical trials of people who have type 2 diabetes and either established CV disease or multiple CV risk factors. These studies also indicated early signals in benefiting heart failure (HF) patients and those with chronic kidney diseases. This article reviews recent and future clinical studies that focus on evaluation of the use of SGLT2 inhibitors in HF management and renal protection.

Pharmacy
Hanni C, Petrovitch E, Ali M, Gibson W, Giuliano C, Holzhausen J, **Makowski C**, Pallisco A, **Patel N**, Sutter D, **To L**, and Yost R. Outcomes associated with apixaban vs warfarin in patients with renal dysfunction. *Blood Adv* 2020; 4(11):2366-2371. PMID: 32463871. Full Text

Pharmacy Department, Beaumont Health, Royal Oak, MI.
Pharmacy Department, Detroit Medical Center, Detroit, MI.
Pharmacy Department, Baycare Health Systems, St. Petersburg, FL.
Wayne State University Eugene Applebaum College of Pharmacy, Detroit, MI.
Pharmacy Department, Ascension St. John Hospital, Detroit, MI; and.
Pharmacy Department, Henry Ford Hospital, Detroit, MI.

Apixaban in patients with impaired renal function is supported by limited data. Landmark clinical trials evaluating apixaban in patients with atrial fibrillation and/or acute venous thromboembolism excluded patients with creatinine clearance (CrCl) <25 mL/min. This multicenter, retrospective chart review was conducted to evaluate the safety and effectiveness of apixaban compared with warfarin in patients with CrCl <25 mL/min. Included patients were newly initiated on apixaban or warfarin for at least 45 days with a CrCl <25 mL/min. Patients were evaluated for thrombosis and bleeding outcomes 6 months following initiation of anticoagulation. The primary outcome was the time to first bleeding or thrombosis event. A total of 128 patients met inclusion criteria in the apixaban group and 733 patients in the warfarin group. Time to first bleeding or thrombosis event was significantly different between the apixaban and warfarin groups. Cox proportional hazards model was conducted to control for potential confounding factors for the primary outcome. After controlling for atrial fibrillation and coronary artery bypass grafting, risk of thrombotic and bleeding events was lower in the apixaban group (hazard ratio, 0.47; 95% confidence interval, 0.25-0.92). There was not a statistical difference between time to thrombosis (83 days vs 54 days, P = .648), rate of thrombosis (5.5% vs 10.3%, P = .08), time to bleeding (46 days vs 54 days, P = .886), or rate of bleeding (5.5% vs 10.9%, P = .06). The severity of bleeding and thrombotic events was not different between groups. Apixaban may serve as a reasonable alternative compared with warfarin in patients with severe renal dysfunction.

Pharmacy
Martirosov AL, **Smith ZR**, **Hencken L**, **MacDonald NC**, **Griebe K**, **Fantuz P**, **Grafton G**, **Hegab S**, **Ismail R**, **Jackson B**, **Kelly B**, **Miller M**, and **Awdish R**. Improving transitions of care for critically ill adult patients on pulmonary arterial hypertension medications. *Am J Health Syst Pharm* 2020; 77(12):958-965. PMID: 32495842. Full Text

Wayne State University, Detroit, MI, and Henry Ford Hospital, Detroit, MI.
Henry Ford Hospital, Detroit, MI.
Henry Ford Hospital, Detroit, MI, and Wayne State University School of Medicine, Detroit, MI.

PURPOSE: The purpose of this report is to describe the activities of critical care and ambulatory care pharmacists in a multidisciplinary transitions-of-care (TOC) service for critically ill patients with pulmonary arterial hypertension (PAH) receiving PAH medications. SUMMARY: Initiation of medications for treatment of PAH involves complex medication access steps. In the ambulatory care setting, multidisciplinary teams often have a process for completing these steps to ensure access to PAH medications. Patients with PAH are frequently admitted to an intensive care unit (ICU), and their home PAH medications are continued and/or new medications are initiated in the ICU setting. Inpatient multidisciplinary teams are often unfamiliar with the medication access steps unique to PAH medications. The coordination and completion of medication access steps in the inpatient setting is critical to ensure access to medications at discharge and prevent delays in care. A PAH-specific TOC bundle for patients prescribed a PAH medication who are admitted to the ICU was developed by a multidisciplinary team at an academic teaching hospital. The service involves a critical care pharmacist completing a PAH medication history, assessing for PAH medication access barriers, and referring patients to an ambulatory care pharmacist for postdischarge telephone follow-up. In collaboration with the PAH multidisciplinary team, a standardized workflow to be initiated by the critical care pharmacist was developed to streamline completion of PAH medication access steps. Within 3 days of hospital discharge, the ambulatory care pharmacist calls referred patients to ensure access to PAH medications, provide disease state and medication education, and request that the patient schedule a follow-up office visit to take place within 14 days of discharge. CONCLUSION: Collaboration by a PAH multidisciplinary team, critical care pharmacist, and ambulatory care pharmacist can improve TOC related to PAH medication access for patients with PAH. The PAH TOC bundle serves as a model that may be transferable to other health centers.

Pharmacy

Mohammad I, Berlie HD, Lipari M, **Martirosov AL**, Duong AA, Faraj M, **Bacon O**, and Garwood CL. Ambulatory Care Practice in the COVID-19 Era: Redesigning Clinical Services and Experiential Learning. *JACCP Journal of the American College of Clinical Pharmacy* 2020; Epub ahead of print. PMID: Not assigned. Full Text

C.L. Garwood, Department of Pharmacy Practice, Eugene Applebaum College of Pharmacy and Health Sciences Wayne State University, Detroit, MI, United States
C.L. Garwood, Ambulatory Care Clinical Pharmacy Specialist, Department of Pharmacy, Harper University Hospital, Detroit Medical Center, Detroit, MI, United States

The Coronavirus Disease (COVID -19) has created a variety of challenges for healthcare professionals, including ambulatory care clinical pharmacists. High-quality remote and minimal-contact care has become a necessity. Ambulatory care clinical pharmacists around the nation have adjusted their practice. In many cases, this included implementation of telehealth programs for comprehensive medication management. The redesign of ambulatory care Advanced Pharmacy Practice Experiences (APPE) also required quick adaptation. In this paper, we describe the clinical practice and experiential education challenges encountered by an ambulatory care clinical pharmacist workgroup in a COVID -19 “hotspot,” with an emphasis on solutions and guidance. We discuss how to adapt ambulatory care clinical pharmacy practices including methods of minimal-contact care, reimbursement opportunities, tracking outcomes, and restructuring ambulatory care APPE. As ambulatory care clinical pharmacists continue to expand the services they provide in response to COVID -19, we also describe opportunities to promote pharmacists as providers during times of pandemic and into the future.

Pharmacy

Morrison AR, **Kenney RM**, and **Davis SL**. Outpatient Clostridioides difficile infections: An opportunity for antimicrobial stewardship programs. *Infect Control Hosp Epidemiol* 2020; Epub ahead of print. PMID: 32484121. Full Text

Department of Pharmacy, Henry Ford Hospital, Detroit, Michigan.
Eugene Applebaum College of Pharmacy and Health Sciences, Detroit, Michigan.

Public Health Sciences

Belsky JB, Filbin MR, **Rivers EP**, **Bobbitt KR**, **Jaehne AK**, Wisnik CA, Maciejewski KR, Li F, and **Morris DC**. F-Actin is associated with a worsening qSOFA score and intensive care unit admission in emergency department patients at risk for sepsis. *Biomarkers* 2020; 25(5):391-396. PMID: 32421363. Request Article

Department of Emergency Medicine, Yale University, New Haven, CT, USA.
Department of Emergency Medicine, Massachusetts General Hospital, Boston, MA, USA.
Department of Public Health Sciences, Henry Ford Hospital, Detroit, MI, USA.
School of Public Health, Yale Center for Analytical Sciences, Yale University, New Haven, CT, USA.

Objective: We previously demonstrated that plasma levels of F-actin and Thymosin Beta 4 differs among patients with septic shock, non-infectious systemic inflammatory syndrome and healthy controls and may serve as biomarkers for the diagnosis of sepsis. The current study aims to determine if these proteins are associated with or predictive of illness severity in patients at risk for sepsis in the Emergency Department (ED).Methods: Prospective, biomarker study enrolling patients (>18 years) who met the Shock Precautions on Triage Sepsis rule placing them at-risk for sepsis.Results: In this study of 203 ED patients, F-actin plasma levels had a linear trend of increase when the quick Sequential Organ Failure Assessment (qSOFA) score increased. F-actin was also increased in patients who were admitted to the Intensive Care Unit (ICU) from the ED, and in those with positive urine cultures. Thymosin Beta 4 was not associated with or predictive of any significant outcome measures.Conclusion: Increased levels of plasma F-actin measured in the ED were associated with incremental illness severity as measured by the qSOFA score and need for ICU admission. F-actin may have utility in risk stratification of undifferentiated patients in the ED presenting with signs and symptoms of sepsis.

Public Health Sciences

Brasky TM, Bethea TN, Wesselink AK, **Wegienka GR**, Baird DD, and Wise LA. Dietary Fat Intake and Risk of Uterine Leiomyomata: A Prospective Ultrasound Study. *Am J Epidemiol* 2020; Epub ahead of print. PMID: 32556077. Full Text

Division of Medical Oncology, The Ohio State University College of Medicine, Columbus, OH.
Department of Medicine, Boston University School of Medicine, Boston, MA.
Department of Epidemiology, Boston University School of Public Health, Boston, MA.
Department of Public Health Sciences, Henry Ford Health System, Detroit, MI.
Epidemiology Branch, Women's Health Group, National Institute for Environmental Health Sciences, Research Triangle, NC.

Uterine leiomyomata (UL) are associated with severe reproductive morbidity and are the primary indication for hysterectomy in the United States. A recent prospective cohort study of Black women reported positive associations between intakes of marine-sourced omega-3 fatty acids and UL risk. We examined whether intakes of dietary fat were associated with UL incidence in a 5-year prospective study of premenopausal Black women living in Detroit who underwent serial ultrasound. At baseline (2010-2012) and 20, 40, and 60 months of follow-up, participants underwent transvaginal ultrasound. Among 1,171 UL-free women at baseline, incident UL were detected in 277 women. Cox regression was used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for the association of dietary fat and UL incidence. Intakes of total fat and saturated, monounsaturated, polyunsaturated (PUFA), and trans-fat were not appreciably associated with UL incidence. Intake of the marine omega-3 PUFA, docosahexaenoic acid, was associated with 49% higher UL incidence (quartile 4 vs. 1: HR 1.49, 95% CI: 1.04, 2.14; P trend=0.01). Intakes of total marine omega-3 PUFAs were similarly associated with elevated UL incidence (HR 1.35, 95% CI: 0.94, 1.93; P trend=0.03). It remains unclear whether the fatty acids or persistent environmental pollutants drive the association.

Public Health Sciences

Frendl DM, Epstein MM, Fouayzi H, **Krajenta R**, **Rybicki BA**, and Sokoloff MH. Prostate-specific antigen testing after the US Preventive Services Task Force recommendation: a population-based analysis of electronic health data. *Cancer Causes Control* 2020; Epub ahead of print. PMID: 32556947. Full Text

Department of Urology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA.
Department of Population and Quantitative Health Sciences, University of Massachusetts Medical School, Worcester, MA, USA.
Department of Population and Quantitative Health Sciences, University of Massachusetts Medical School, Worcester, MA, USA. mara.epstein@umassmed.edu.
Department of Medicine, University of Massachusetts Medical School, Worcester, MA, USA. mara.epstein@umassmed.edu.
Meyers Primary Care Institute, A Joint Endeavor of University of Massachusetts Medical School, Fallon Health, and Reliant Medical Group, Worcester, MA, USA. mara.epstein@umassmed.edu.
Meyers Primary Care Institute, A Joint Endeavor of University of Massachusetts Medical School, Fallon Health, and Reliant Medical Group, Worcester, MA, USA.
Department of Public Health Sciences, Henry Ford Hospital, Detroit, MI, USA.
Department of Urology, University of Massachusetts Medical School, Worcester, MA, USA.

PURPOSE: This study describes longitudinal trends in the use of prostate-specific antigen (PSA)-based testing in two geographically distinct healthcare systems following the 2011 US Preventive Services Task Force (USPSTF) recommendations against routine PSA screening. METHODS: We analyzed population-based health claims data from 253,139 men aged 40-80 who were enrolled at two US healthcare systems. We assessed trends in the percentage of eligible men receiving ≥ 1 PSA test per year by time period (2000-2008, 2009-2011, 2012-2014), age

(40-54, 55-69, 70-80), and race (white, black, other, unknown), and conducted a joinpoint regression analysis. RESULTS: Men aged 55-69 and 70-80 years of all races had similar use of PSA testing between 2000 and 2011, ranging between 47 and 56% of eligible men by year, while only 22-26% of men aged 40-54 had a PSA test per year during this period. Overall, the percentage of men receiving at least one PSA test per year decreased by 26% between 2009-2011 and 2012-2014, with similar trends across race and age groups. PSA testing declined significantly after 2011 (annual percent change = - 11.28). CONCLUSIONS: Following the 2011 USPSTF recommendations against routine PSA screening, declines in PSA testing were observed among men of all races and across all age groups in two large US healthcare systems.

Public Health Sciences

Selitsky L, **Markowitz N**, **Baxa DM**, **Kaljee L**, **Miree CA**, **Islam N**, **Burse C**, **Newaz R**, **Dankerlui D**, **Jacobsen G**, and **Joseph C**. Self-report of domestic violence and forced sex are related to sexual risk behaviors in a sample of juvenile detainees. *Health Justice* 2020; 8(1):15. PMID: 32577955. Full Text

Internal Medicine, Johns Hopkins Hospital, Baltimore, USA.
Division of Infectious Diseases, Henry Ford Health System and School of Medicine, Wayne State University, Detroit, USA.
William Beaumont School of Medicine, Oakland University, Rochester, USA.
Division of Infectious Diseases, Henry Ford Health System, Detroit, USA.
Global Health Initiative, Henry Ford Health System, Detroit, USA.
Department of Public Health Sciences, Henry Ford Health System, 1 Ford Place, Detroit, Michigan, USA.
Department of Public Health Sciences, Henry Ford Health System, 1 Ford Place, Detroit, Michigan, USA.
cjoseph1@hfhs.org.

BACKGROUND: Justice-involved youth have higher rates of sexually transmitted infections (STIs), and a higher prevalence of the associated sexual risk behaviors. Sexual risk behaviors are also associated with alcohol and drug use. Research suggests that a history of trauma is an important predictor of alcohol and drug use in youth offenders, and therefore is a likely contributor to sexual risk behavior in this population. The objective of this analysis is to determine the association of trauma, specifically, domestic violence and forced sex, to six sexual risk behaviors and a history of chlamydia among detained youth. METHODS: The analysis uses data from a convenience sample of detainees assenting to HIV testing conducted December 2016 - August 2017 using the state-certified Voluntary Counseling Testing and Referral (VCTR) process. RESULTS: Of the 379 youth that received VCTR at the facility, 308 (81.3%) were used in this analysis. Report of domestic violence was significantly associated with sex under the influence of alcohol and was also significantly associated with sex under the influence of marijuana. Forced sex was associated with a sexual partner of unknown HIV status. CONCLUSIONS: Traumatic experiences were related to sexual risk behaviors in this analysis, and substance use was strongly implicated in the association. Trauma is known to be a catalyst to sexual risk behaviors, substance use, and delinquency in adolescence. Results support the findings of other investigators and re-iterate the need for trauma-informed interventions that can improve the life trajectories of detained youth.

Public Health Sciences

Zhou L, **Adrianto I**, **Wang J**, **Wu X**, **Datta I**, and **Mi QS**. Single-Cell RNA-Seq Analysis Uncovers Distinct Functional Human NKT Cell Sub-Populations in Peripheral Blood. *Frontiers in Cell and Developmental Biology* 2020; 8. PMID: Not assigned. Full Text

L. Zhou, Center for Cutaneous Biology and Immunology Research, Department of Dermatology, Henry Ford Health System, Detroit, MI, United States
Q.-S. Mi, Center for Cutaneous Biology and Immunology Research, Department of Dermatology, Henry Ford Health System, Detroit, MI, United States
L. Zhou, Immunology Research Program, Henry Ford Cancer Institute, Henry Ford Health System, Detroit, MI, United States
Q.-S. Mi, Immunology Research Program, Henry Ford Cancer Institute, Henry Ford Health System, Detroit, MI, United States

Vα24-invariant human natural killer T (NKT) cells comprise a unique subset of CD1d-restricted T cells with potent immune regulatory function and are involved in the development of a variety of human diseases. However, the lack of comprehensive molecular subset identities limits their objective classification and clinical application. Using unbiased single-cell RNA sequencing (scRNA-seq) of over 4000 unstimulated and 7000 stimulated human peripheral blood NKT cells, we identified four and five clusters of NKT cells from each NKT group, respectively. Our study uncovers multiple previously unrecognized NKT subsets with potential functional specificities, including a cluster of NKT cells with regulatory T cell property. Flow cytometry and Ingenuity Pathway Analysis confirmed the existence of these NKT populations and indicated the related functional capacities. Our study provides the unbiased and more

comprehensive molecular identities of human NKT subsets, which will eventually lead the way to tailored therapies targeting selected NKT subsets.

Pulmonary and Critical Care
Awdish RLA. The Liminal Space. *N Engl J Med* 2020; Epub ahead of print. PMID: 32492299. Full Text

From Henry Ford Hospital, Detroit.

Pulmonary and Critical Care
Lamb CR, Desai NR, Angel L, Chaddha U, Sachdeva A, Sethi S, Bencheqroun H, Mehta H, Akulian J, Argento AC, **Diaz-Mendoza J**, Musani A, and Murgu S. Use of Tracheostomy During the COVID-19 Pandemic: CHEST/AABIP/AIPPD: Expert Panel Report. *Chest* 2020; Epub ahead of print. PMID: 32512006. Full Text

Author Affiliations: Department of Medicine, Division of Pulmonary and Critical Care, Lahey Hospital and Medical Center, Burlington, MA.
Chicago Chest Center, AMITA Health, Lisle, Illinois and Department of Medicine, Division of Pulmonary, Critical Care, Sleep and Allergy, University of Illinois at Chicago.
Department of Medicine, Division of Pulmonary and Critical Care, New York University Langone Health.
Division of Pulmonary, Critical Care and Sleep Medicine, Icahn School of Medicine at Mount Sinai, New York.
Department of Medicine, Division of Pulmonary and Critical Care, University of Maryland School of Medicine, Baltimore, Maryland.
Respiratory Institute, Division of Pulmonary and Critical Care, Cleveland Clinic, Cleveland, OH.
Department of Medicine, Division of Pulmonary and Critical Care, University of California Riverside.
Division of Pulmonary and Critical Care and Sleep Medicine, University of Florida.
Division of Pulmonary and Critical Care, UNC Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill.
Department of Medicine, Division of Pulmonary and Critical Care, Northwestern University, Feinberg School of Medicine.
Division of Pulmonary and Critical Care, Henry Ford Hospital and Department of Medicine, Wayne State University, Detroit, MI.
Division of Pulmonary Sciences and Critical Care Medicine, University of Colorado, Denver.
Division of Pulmonary and Critical Care Medicine,The University of Chicago. Electronic address: smurgu@medicine.bsd.uchicago.edu.

BACKGROUND: The role of tracheostomy during the COVID-19 pandemic remains unknown. The goal of this consensus statement is to examine the current evidence for performing tracheostomy in patients with respiratory failure from COVID-19 and offer guidance to physicians on the preparation, timing and technique while minimizing the risk of infection to health care workers (HCW). METHODS: A panel comprised of intensivists and interventional pulmonologists from three professional societies representing 13 institutions with experience in managing COVID-19 patients across a spectrum of healthcare environments developed key clinical questions addressing specific topics on tracheostomy in COVID-19. A systematic review of the literature and an established modified Delphi consensus methodology were applied to provide a reliable evidenced based consensus statement and expert panel report. RESULTS: Eight key questions, corresponding to 14 decision points, were rated by the panel. The results were aggregated, resulting in eight main recommendations and five additional remarks intended to guide health care providers in the decision-making process pertinent to tracheostomy in patients with COVID-19 related respiratory failure. CONCLUSION: This panel suggests performing tracheostomy in patients expected to require prolonged mechanical ventilation. A specific timing of tracheostomy cannot be recommended. There is no evidence for routine repeat RT- PCR testing in patients with confirmed Covid-19 evaluated for tracheostomy. To reduce the risk of infection in HCW, we recommend performing the procedure using techniques that minimize aerosolization while wearing enhanced personal protective equipment (PPE). The recommendations presented in this statement may change as more experience is gained during this pandemic.

Pulmonary and Critical Care
Martirosov AL, **Smith ZR**, **Hencken L**, **MacDonald NC**, **Griebe K**, **Fantuz P**, **Grafton G**, **Hegab S**, **Ismail R**, **Jackson B**, **Kelly B**, **Miller M**, and **Awdish R**. Improving transitions of care for critically ill adult patients on pulmonary arterial hypertension medications. *Am J Health Syst Pharm* 2020; 77(12):958-965. PMID: 32495842. Full Text

Wayne State University, Detroit, MI, and Henry Ford Hospital, Detroit, MI.
Henry Ford Hospital, Detroit, MI.
Henry Ford Hospital, Detroit, MI, and Wayne State University School of Medicine, Detroit, MI.

PURPOSE: The purpose of this report is to describe the activities of critical care and ambulatory care pharmacists in a multidisciplinary transitions-of-care (TOC) service for critically ill patients with pulmonary arterial hypertension (PAH) receiving PAH medications. SUMMARY: Initiation of medications for treatment of PAH involves complex medication access steps. In the ambulatory care setting, multidisciplinary teams often have a process for completing these steps to ensure access to PAH medications. Patients with PAH are frequently admitted to an intensive care unit (ICU), and their home PAH medications are continued and/or new medications are initiated in the ICU setting. Inpatient multidisciplinary teams are often unfamiliar with the medication access steps unique to PAH medications. The coordination and completion of medication access steps in the inpatient setting is critical to ensure access to medications at discharge and prevent delays in care. A PAH-specific TOC bundle for patients prescribed a PAH medication who are admitted to the ICU was developed by a multidisciplinary team at an academic teaching hospital. The service involves a critical care pharmacist completing a PAH medication history, assessing for PAH medication access barriers, and referring patients to an ambulatory care pharmacist for postdischarge telephone follow-up. In collaboration with the PAH multidisciplinary team, a standardized workflow to be initiated by the critical care pharmacist was developed to streamline completion of PAH medication access steps. Within 3 days of hospital discharge, the ambulatory care pharmacist calls referred patients to ensure access to PAH medications, provide disease state and medication education, and request that the patient schedule a follow-up office visit to take place within 14 days of discharge. CONCLUSION: Collaboration by a PAH multidisciplinary team, critical care pharmacist, and ambulatory care pharmacist can improve TOC related to PAH medication access for patients with PAH. The PAH TOC bundle serves as a model that may be transferable to other health centers.

Pulmonary and Critical Care

Matar R, Alrahmani L, Monzer N, **Debiane LG**, Berbari E, Fares J, Fitzpatrick F, and Murad MH. Clinical Presentation and Outcomes of Pregnant Women with COVID-19: A Systematic Review and Meta-Analysis. *Clin Infect Dis* 2020; Epub ahead of print. PMID: 32575114. Full Text

Department of Internal Medicine, Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester MN, USA.
Department of Obstetrics and Gynecology, Division of Maternal-Fetal Medicine, Mayo Clinic, Rochester MN, USA.
Department of Obstetrics and Gynecology, Division of Maternal Fetal Medicine, Loyola University Medical Center, Chicago, IL, USA.
Department of Medicine, The Royal College of Surgeons in Ireland, Dublin, Ireland.
Department of Internal Medicine, Division of Pulmonary and Critical Care, Henry Ford, Detroit MI, USA.
Department of Internal Medicine, Division of Infectious Diseases, Mayo Clinic, Rochester MN, USA.
Department of Neurological Surgery, Northwestern University, Chicago IL, USA.
Department of Microbiology, Beaumont Hospital, Dublin, Ireland.
Department of Clinical Microbiology, The Royal College of Surgeons in Ireland, Dublin, Ireland.
The Mayo Clinic Robert D. and Patricia E. Kern Center for the Science of Health Care Delivery, Rochester MN, USA.

INTRODUCTION: Descriptions of coronavirus disease-2019 (COVID-19) have focused on the non-pregnant adult population. This study aims to describe the clinical characteristics and perinatal outcomes of COVID-19 in pregnancy. METHODS: We searched databases from December 2019 to April 30th, 2020. Eligible studies reported clinical characteristics, radiological findings and/or laboratory testing of pregnant women during infection. Data were pooled across studies using random-effects model. RESULTS: Twenty-four studies (136 women) were included. Most common symptoms were fever (62.9%) and cough (36.8%). Laboratory findings included elevated C-Reactive Protein (57%) and lymphocytopenia (50%). Ground-glass opacity was the most common radiological finding (81.7%). Preterm birth rate was 37.7% and cesarean delivery rate was 76%. There was one maternal death. There were two fetal COVID-19 cases. CONCLUSION: The clinical picture in pregnant women with COVID-19 did not differ from the non-pregnant population, however, the rate of preterm birth and cesarean delivery are considerably higher than international averages.

Radiation Oncology

Kumar S, Nahum AE, and **Chetty IJ**. Monte-Carlo-computed dose, kerma and fluence distributions in heterogeneous slab geometries irradiated by small megavoltage photon fields. *Phys Med Biol* 2020; Epub ahead of print. PMID: 32485691. Request Article

Radiological Physics & AD, Bhabha Atomic Research Centre, Mumbai, Maharashtra, INDIA.
Physics Department, Until retirement (October 2015): Head of Physics Research, Clatterbridge Cancer Centre, Bebington, Wirral, Merseyside CH63 4JY, UK, UNITED KINGDOM OF GREAT BRITAIN AND NORTHERN IRELAND.
Dept of Radiation Oncology, Henry Ford Hospital, 2799 West Grand Blvd, Detroit, MI 48202-2689, USA, Detroit, Michigan, UNITED STATES.

Small-field dosimetry is central to the planning and delivery of radiotherapy to patients with cancer. Small-field dosimetry is beset by complex issues, such as loss of charged-particle equilibrium (CPE), source occlusion and electron scattering effects in low-density tissues. The purpose of the present research was to elucidate the fundamental physics of small fields through the computation of absorbed dose, kerma and fluence distributions in heterogeneous media using the Monte-Carlo method. Absorbed dose and kerma were computed using the DOSRZnrc Monte-Carlo (MC) user-code for beams with square field sizes ranging from 0.25 × 0.25 to 7× 7 cm2 (for 6 MV 'full linac' geometry) and 0.25 × 0.25 to 16 × 16 cm2 (for 15 MV 'full linac' geometry). In the bone inhomogeneity the dose increases (vs. homogeneous water) for field sizes < 1 × 1 cm2 at 6 MV and ≤ 3 × 3 cm2 at 15 MV and decreases (vs. homogeneous water) for field sizes ≥ 3 × 3 cm2 at 6 MV and ≥ 5 × 5 cm2 at 15 MV. In the lung inhomogeneity there is negligible decrease in dose compared to in uniform water for field sizes > 5 × 5 cm2 at 6 MV and ≥ 16 × 16 cm2 at 15 MV, consistent with the Fano theorem. The near-unity value of the absorbed-dose to collision-kerma ratio, D/Kcol, at the centre of the bone and lung slabs in the heterogeneous phantom demonstrated that CPE is achieved in bone for field sizes > 1 × 1 cm2 at 6 MV and > 5 × 5 cm2 at 15 MV; CPE is achieved in lung at field sizes > 5 × 5 cm2 at 6 MV and ≥ 16 × 16 cm2 at 15 MV. Electron-fluence perturbation factors for the 0.25 × 0.25 cm2 field were 1.231 and 1.403 for bone-to-water and 0.454 and 0.333 for lung-to-water were at 6 and 15 MV respectively. For field sizes large enough for quasi-CPE, the MC-derived dose-perturbation factors, lung-to-water, were close to unity; electron-fluence perturbation factors, lung-to-water, were ~1.0, consistent with the 'Fano' theorem. At 15 MV in the lung inhomogeneity the magnitude and also the 'shape' of the primary electron-fluence spectrum differed significantly from that in water. Beam penumbrae relative to water were narrower in the bone inhomogeneity and broader in the lung inhomogeneity for all field sizes.

Radiation Oncology

Pugh SL, Rodgers JP, Yeager KA, Chen RC, **Movsas B**, Bonanni R, Dignam J, and Bruner DW. Characteristics of Participation in Patient-Reported Outcomes and Electronic Data Capture Components of NRG Oncology Clinical Trials. *Int J Radiat Oncol Biol Phys* 2020; Epub ahead of print. PMID: 32590048. Full Text

NRG Oncology Statistics and Data Management Center. Electronic address: PughS@NRGOncology.org.
NRG Oncology Statistics and Data Management Center.
Emory University Hospital/Winship Cancer Institute.
UNC Hospitals Radiation Oncology Clinic-N.C. Cancer Hospital.
Henry Ford Cancer Institute, Henry Ford Health System.

PURPOSE: To assess reasons patients do not consent to patient-report outcome (PRO) and electronic PRO data capture components of clinical trials and potential selection bias by having a separate consent. METHODS: Selected XXXX trials were included based on disease site and inclusion of PROs and electronic PRO data capture via VisionTree Optimal Care (VTOC; VisionTree Software, Inc, San Diego, CA), as separate consent questions. Reasons for not participating were assessed. Pretreatment characteristics between patients who did and did not consent were tested using chi-square and t-tests for univariate comparisons and logistic regression for multivariable analyses. RESULTS: 10 trials were selected in head and neck (HN), prostate, gynecological, breast, lung, and gastrointestinal cancers with 4 of these trials having electronic PRO data capture. Most patients consented to the PRO component (75.3%) but not electronic PRO data capture (37.8%). More white patients consented to PROs than non-whites across all trials (odds ratio [OR]=0.53, 95% confidence interval [CI]: 0.45-0.63, p<0.001) and more patients with education after high school consented compared to those with less education (OR=1.71, 95% CI: 1.46-2.02, p<0.001). Patients who are younger, white and a never or former smoker are more likely to participate in electronic PRO data capture (OR=0.63, 95% CI: 0.47-0.85, p=0.002; OR=0.60, 95% CI: 0.44-0.82, p=0.001; OR=0.57, 95% CI: 0.41-0.78, p=0.001, respectively). CONCLUSIONS: These results suggest that a patient's race, age, and education may impact whether a patient chooses to consent or is offered to participate in PRO and/or electronic PRO data capture components. More investigation is needed but this analysis provides support for making PROs integrated in the trial.

Sleep Medicine

Heggeness LF, Bean CAL, **Kalmbach DA**, and Ciesla JA. Cognitive risk, coping-oriented substance use, and increased avoidance tendencies among depressed outpatients: A prospective investigation. *J Clin Psychol* 2020; Epub ahead of print. PMID: 32478424. Full Text

Department of Psychological Sciences, Kent State University, Kent, Ohio.
Thomas Roth Sleep Disorders & Research Center, Henry Ford Health System, Detroit, Michigan.

OBJECTIVE: The present study was designed to assess the interplay between depressive cognition, coping-oriented substance use, and future behavioral disengagement tendencies. Cognitive risk subtypes examined include brooding rumination, attributional bias (internal/stable/global), and dysfunctional attitudes. METHOD: Individuals were recruited from outpatient treatment settings and met criteria for a unipolar depressive disorder (N = 70; 66% female; 81%

White; M(age) = 31; SD(age) = 13.2). Participants completed self-report measures of brooding rumination, attributional style, dysfunctional attitudes, coping-oriented substance use, and behavioral disengagement tendencies following a 3-week period. RESULTS: Brooding rumination, stable attributional style, and dysfunctional attitudes were positively associated with later behavioral disengagement tendencies. Coping-oriented substance use moderated associations between both internal attributional style, as well as dysfunctional attitudes onto later behavioral disengagement. CONCLUSIONS: With regard to stress-related avoidance, subsyndromal substance use may play a detrimental role among cognitively vulnerable, depressed outpatients when said drug or alcohol use serves as a means of coping.

Sleep Medicine
Roehrs TA, Auciello J, Tseng J, and Whiteside G. Current and potential pharmacological treatment options for insomnia in patients with alcohol use disorder in recovery. *Neuropsychopharmacol Rep* 2020; Epub ahead of print. PMID: 32543111. Full Text

Henry Ford Health System, Sleep Disorders and Research Center, Detroit, MI, USA.
Department of Psychiatry and Behavioral Neuroscience, School of Medicine, Wayne State University, Detroit, MI, USA.
Purdue Pharma L.P., Stamford, CT, USA.
Imbrium Therapeutics L.P., Stamford, CT, USA.

Alcohol use disorder (AUD) is characterized by dysfunction in motivational, mood-stress regulation, and sleep systems that interact in complex ways to heighten the risk of relapse during abstinence. Emerging data suggest that excessive and chronic alcohol use disrupts sleep homeostasis and, in abstinence, subjects with AUD are known to experience insomnia that may persist for weeks to years, which we propose to refer to as insomnia associated with alcohol cessation (IAAC). The purpose of this review is to provide an update of pharmacological approaches to therapy including compounds in development, to raise awareness of the prevalence of and unmet need in IAAC and highlight differences in treatment consideration for IAAC as compared to insomnia disorder. We performed a search of select electronic databases to identify studies of pharmacological agents used to treat sleep disturbances in abstinent or treatment-seeking patients with alcohol use disorder. The search, conducted in June 2019 and updated in December 2019, yielded 1,188 abstracts after duplicates were removed, of which 36 full-text articles were assessed for eligibility. Eighteen studies were included, 15 randomized controlled trials and three open-label studies. Several classes of medications including antidepressants, anticonvulsants, and antipsychotics have been evaluated for their effectiveness in treating sleep disturbances in abstinent or treatment-seeking patients with AUD. None of these medications are approved by the FDA for the treatment of IAAC, and the currently available evidence for these agents is limited. Randomized, controlled clinical trials are warranted to evaluate the efficacy and safety of medications in the treatment of IAAC.

Surgery
Collins KM, and Doyle MBM. Revisiting the organ procurement organization-based organ procurement center in the COVID era. *Am J Transplant* 2020; Epub ahead of print. PMID: 32503083. Full Text

Division of Transplant and Hepatobiliary Surgery, Henry Ford Hospital, Detroit, Michigan, USA.
Division of Abdominal Organ Transplantation, Department of Surgery, Washington University School of Medicine, St. Louis, Missouri, USA.

Surgery
Kitajima T, Hibi T, **Moonka D**, Sapisochin G, **Abouljoud MS**, and **Nagai S**. Center Experience Affects Liver Transplant Outcomes in Patients with Hilar Cholangiocarcinoma. *Ann Surg Oncol* 2020; Epub ahead of print. PMID: 32495286. Full Text

Division of Transplant and Hepatobiliary Surgery, Henry Ford Hospital, Detroit, MI, USA.
Department of Pediatric Surgery and Transplantation, Kumamoto University Hospital, Kumamoto, Japan.
Gastroenterology and Hepatology, Henry Ford Hospital, Detroit, MI, USA.
Multi-Organ Transplant and Hepato-Pancreato-Biliary Surgical Oncology, University Health Network, University of Toronto, Toronto, ON, Canada.
Division of Transplant and Hepatobiliary Surgery, Henry Ford Hospital, Detroit, MI, USA. snagai1@hfhs.org.

BACKGROUND: Based on favorable outcomes reported by experienced centers, perihilar cholangiocarcinoma (Ph-CCA) has become an accepted indication for liver transplantation (LT). What is less clear is if the reported outcomes have been reproduced nationwide in the US. OBJECTIVE: The aim of this study was to evaluate post-transplant outcomes in patients with Ph-CCA and to determine prognostic factors. METHODS: Patients who underwent LT with Model for End-stage Liver Disease exception scores for Ph-CCA between 2010 and 2017 were evaluated. Transplant

centers were classified into well- and less-experienced groups: Group 1 [well-experienced (≥ 6 LTs), 7 centers]; Group 2 [less-experienced (< 6 LTs), 23 centers]. Post-transplant mortality due to all-cause and recurrence of Ph-CCA were set as endpoints. RESULTS: Post-transplant outcomes were significantly better in Group 1 than in Group 2, with 1-, 3-, and 5-year patient survival rates of 91.8%, 56.9%, and 45.8%, versus 65.6%, 48.8%, and 26.0%, respectively. Group 2 showed a significantly higher risk of 1-, 3-, and 5-year all-cause mortality and 1-year mortality associated with Ph-CCA recurrence. Center experience was an independent risk factor for post-transplant mortality. In intention-to-treat analysis, a positive prognostic effect of LT was significant and LT decreased the mortality risk by 86% in the well-experienced group [hazard ratio (HR) 0.14, $p < 0.001$], whereas this effect was not observed in the less-experienced group (HR 1.35, $p = 0.47$). CONCLUSIONS: Risk of recurrence of malignancy and mortality was significantly higher in the less-experienced center group. Center effects on post-transplant outcomes in patients with Ph-CCA should be recognized, and the introduction of center approval for LT for Ph-CCA may be justified to achieve comparable outcomes between centers.

Surgery

Nasser H, **Ivanics T**, Varban OA, Finks JF, Bonham A, Ghaferi AA, and **Carlin AM**. Comparison of early outcomes between Roux-en-Y gastric bypass and sleeve gastrectomy among patients with body mass index ≥ 60 kg/m(2). *Surg Endosc* 2020; Epub ahead of print. PMID: 32572625. Full Text

Department of Surgery, Henry Ford Hospital, 2799 W Grand Blvd, Detroit, MI, 48202, USA. hnasser2@hfhs.org.
Department of Surgery, Henry Ford Hospital, 2799 W Grand Blvd, Detroit, MI, 48202, USA.
Department of Surgery, University of Michigan, Ann Arbor, MI, USA.

BACKGROUND: There is no consensus on the ideal bariatric operation to choose for patients with extremely high body mass index (BMI). The aim of this study was to compare the perioperative complications, weight loss, and comorbidity remission between laparoscopic Roux-en-Y gastric bypass (LRYGB) and laparoscopic sleeve gastrectomy (LSG) among patients with BMI ≥ 60 kg/m(2). METHODS: Data from a statewide bariatric surgery registry were used to identify all patients with BMI ≥ 60 kg/m(2) undergoing LRYGB or LSG between January 2006 and June 2019. Risk and reliability adjustment were used to compare outcomes between the two groups. RESULTS: A total of 6015 patients were identified and 2505 (41.6%) underwent LRYGB and 3510 (58.4%) underwent LSG. The overall mean age was 43.1 ± 11.2 years with a mean preoperative BMI of 66.7 ± 6.4 kg/m(2). Females accounted for 69.3% and the majority were either white (68.5%) or black (21.2%). LRYGB was associated with a higher rate of adjusted 30-day postoperative serious complications (4.0% vs 2.2%; $p < 0.01$) including anastomotic leak, obstruction, and bleeding. Resource utilization was also higher with LRYGB (23.7% vs 14.8%; $p < 0.01$) and included more emergency department visits, readmissions, reoperations, and length of stay ≥ 4 days. The overall 1-year follow-up rate was 38.8%. The adjusted percent total weight loss at 1 year was significantly higher following LRYGB compared to LSG (36.6 ± 9.3 vs 31.3 ± 9.3%; $p < 0.01$). LRYGB was associated with a higher rate of treatment discontinuation for diabetes mellitus, hyperlipidemia, and obstructive sleep apnea. CONCLUSIONS: In patients with BMI ≥ 60 kg/m(2), LRYGB was associated with better weight loss and medication discontinuation 1 year following surgery at the expense of an increase in perioperative complications and resource utilization compared to LSG.

Urology

Cheng PJ, Keihani S, Roth JD, Pariser JJ, Elliott SP, Bose S, Khavari R, Crescenze I, Stoffel JT, Velaer KN, Elliott CS, **Raffee SM**, **Atiemo HO**, Kennelly MJ, Lenherr SM, and Myers JB. Contemporary multicenter outcomes of continent cutaneous ileocecocystoplasty in the adult population over a 10-year period: A Neurogenic Bladder Research Group study. *Neurourol Urodyn* 2020; Epub ahead of print. PMID: 32506711. Full Text

Division of Urology, University of Utah, Salt Lake City, Utah.
Department of Urology, Indiana University School of Medicine, Indianapolis, Indiana.
Department of Urology, University of Minnesota, Minneapolis, Minnesota.
Department of Urology, Houston Methodist Hospital, Houston, Texas.
Department of Urology, University of Michigan, Ann Arbor, Michigan.
Department of Urology, Stanford University, Stanford, California.
Division of Urology, Santa Clara Valley Medical Center, San Jose, California.
Vattikuti Urology Institute, Henry Ford Hospital, Detroit, Michigan.
McKay Urology, Carolinas Rehabilitation, Charlotte, North Carolina.

AIMS: Evidence is sparse on the long-term outcomes of continent cutaneous ileocecocystoplasty (CCIC). We hypothesized that obesity, laparoscopic/robotic approach, and concomitant surgeries would affect morbidity after CCIC and aimed to evaluate the outcomes of CCIC in adults in a multicenter contemporary study. METHODS: We retrospectively reviewed the charts of adult patients from sites in the Neurogenic Bladder Research Group undergoing CCIC (2007-2017) who had at least 6 months of follow-up. We evaluated patient demographics, surgical details, 90-day complications, and follow-up surgeries. the Mann-Whitney U test was used to compare continuous

variables and χ^2 and Fisher's Exact tests were used to compare categorical variables. RESULTS: We included 114 patients with a median age of 41 years. The median postoperative length of stay was 8 days. At 3 months postoperatively, major complications occurred in 18 (15.8%), and 24 patients (21.1%) were readmitted. During a median follow-up of 40 months, 48 patients (42.1%) underwent 80 additional related surgeries. Twenty-three patients (20.2%) underwent at least one channel revision, most often due to obstruction (15, 13.2%) or incontinence (4, 3.5%). Of the channel revisions, 10 (8.8%) were major and 14 (12.3%) were minor. Eleven patients (9.6%) abandoned the catheterizable channel during the follow-up period. Obesity and laparoscopic/robotic surgical approach did not affect outcomes, though concomitant surgery was associated with a higher rate of follow-up surgeries. CONCLUSIONS: In this contemporary multicenter series evaluating CCIC, we found that the short-term major complication rate was low, but many patients require follow-up surgeries, mostly related to the catheterizable channel.

Urology

Palanisamy N, Yang J, Shepherd PDA, Li-Ning-Tapia EM, Labanca E, Manyam G, Ravoori M, Kundra V, Araujo JC, Efstathiou E, Pisters LL, Wan X, Wang X, Vazquez ES, Aparicio AM, **Carskadon S**, Tomlins SA, Kunju LP, Chinnaiyan AM, Broom BM, Logothetis C, Troncoso P, and Navone NM. The MD Anderson prostate cancer patient-derived xenograft series (MDA PCa PDX) captures the molecular landscape of prostate cancer and facilitates marker-driven therapy development. *Clin Cancer Res* 2020; Epub ahead of print. PMID: 32576626. Full Text

Urology, Henry Ford Health System.
Molecular and Cellular Oncology, University of Texas MD Anderson Cancer Center.
Department of Genitourinary Medical Oncology and the David H. Koch Center for Applied Research of Genitourinary Cancers, The University of Texas MD Anderson Cancer Center.
Department of Genitourinary Medical Oncology and David H. Koch Center for Applied Research of Genitourinary Cancers, University of Texas MD Anderson Cancer Center.
Department of Genitourinary Medical Oncology, University of Texas MD Anderson Cancer Center.
Bioinformatics and Computational Biology, University of Texas MD Anderson Cancer Center.
Cancer Systems Imaging, The University of Texas MD Anderson Cancer Center.
Abdominal Imaging Department, The University of Texas MD Anderson Cancer Center.
Genitourinary Medical Oncology, University of Texas MD Anderson Cancer Center.
geniturinary medical oncology, University of Texas MD Anderson Cancer Center.
Stem Cell Transplantation Rsch, The University of Texas MD Anderson Cancer Center.
Biostatistics, University of Texas MD Anderson Cancer Center.
Laboratorio de Inflamación y Cáncer, UBA. FCEN. QB / CONICET - UBA. IQUIBICEN.
Genitourinary Medical Oncology, The University of Texas MD Anderson Cancer Center.
Henry Ford Health System.
Department of Pathology, Department of Urology, Michigan Center for Translational Pathology, Comprehensive Cancer Center, University of Michigan-Ann Arbor.
Pathology, University of Michigan-Ann Arbor.
Bioinformatics & Computational Biology, University of Texas MD Anderson Cancer Center.
Pathology, The University of Texas MD Anderson Cancer Center.
Department of Genitourinary Medical Oncology and the David H. Koch Center for Applied Research of Genitourinary Cancers, The University of Texas MD Anderson Cancer Center nnavone@mdanderson.org.

BACKGROUND: Advances in prostate cancer (PCa) lag behind other tumor types partly due to the paucity of models reflecting key milestones in PCa progression. OBJECTIVE: To develop clinically relevant PCa models. DESIGN: Since 1996 we have generated clinically annotated patient-derived xenografts (PDXs) (the MDA PCa PDX series) linked to specific phenotypes reflecting all aspects of clinical PCa. RESULTS: We studied two cell line-derived xenografts and the first 80 PDXs derived from 47 human PCa donors. Of these, 47 PDXs derived from 22 donors are working models and can be expanded either as cell lines (MDA PCa 2a and 2b) or PDXs. The histopathologic, genomic, and molecular characteristics (AR, ERG, and PTEN loss) maintain fidelity with the human tumor and correlate with published findings. PDX growth response to mouse castration and targeted therapy illustrate their clinical utility. Comparative genomic hybridization and sequencing show significant differences in oncogenic pathways in pairs of PDXs derived from different areas of the same tumor. We also identified a recurrent focal deletion in an area that includes the SPOPL gene in PDXs derived from 7 human donors out of 28 studied (25%). SPOPL is a SPOP paralog, and SPOP mutations define a molecular subclass of PCa. SPOPL deletions are found in 7% of TCGA PCas, which suggests that our cohort is a reliable platform for targeted drug development. CONCLUSIONS: The MDA PCa PDX series is a dynamic resource that captures the molecular landscape of PCas progressing under novel treatments and enables optimization of PCa-specific, marker-driven therapy.

Urology
Rakic N, **Keeley J**, and **Abdollah F**. Re: Radical Prostatectomy or Observation for Clinically Localized Prostate Cancer: Extended Follow-up of the Prostate Cancer Intervention Versus Observation Trial (PIVOT). *Eur Urol Oncol* 2020; Epub ahead of print. PMID: 32546347. Full Text

Vattikuti Urology Institute, Henry Ford Hospital, Detroit, MI, USA.
Vattikuti Urology Institute, Henry Ford Hospital, Detroit, MI, USA. Electronic address: firas.abdollah@gmail.com.

Urology
Rambhatla A. Editorial Comment. *J Urol* 2020; Epub ahead of print. PMID: 32574513. Full Text

Vattikuti Urology Institute, Henry Ford Health System, Detroit, Michigan.

Conference Abstracts

Behavioral Health Services/Psychiatry
Williams A, Miller MK, and **Olex M**. The missing link: Health literacy and cognitive function in treatment adherence in head and neck cancer. *Psycho-Oncology* 2020; 29:69.

A. Williams, Henry Ford Health System

Background/Purpose: Health literacy is the degree to which a person has the capacity to obtain, process, and understand basic information and services needed to make decisions about their health care. Poor health literacy has been associated with difficulties managing medications, assessing and evaluating health information, completing medical and financial forms, and comparing nutritional information of foods. As such, health literacy is closely related to adherence to medical treatment. Cognitive function contributes to one's health literacy, though also independently contributes to adherence. Patients with head and neck cancers require complex, often multimodal care, and both health literacy and cognitive function have been found to be lower than the general population. However, no study has examined the interaction between cognitive function and health literacy in the vulnerable patient population. Methods: 200 consecutive patients presenting for pretreatment evaluation with an embedded health psychologist received standardized assessment protocol of cognitive assessment (Montreal Cognitive Assessment), health literacy (REALM-SF), understanding of medical recommendations, and education history. Treatment adherence was obtained via chart review and was defined as having completed the treatment recommended by the Multi-Disciplinary Tumor Board. Results: Patients were predominantly male (83%), white (80%) with an average age of 67 years (SD = 9.87 years.). The average years of education was 13 years (equivalent to "some college"). The mean health literacy score was 5 (SD = 1, range 0-7), indicating an average level of reading equivalent to seventh-eighth grade. The mean cognitive function score was 21 (SD = 5, range 10-30). Health literacy and cognitive function were correlated ($P < .05$). Treatment adherence data was available for the 200 patients included, with 95% adhering to Tumor Board recommendations. Lower health literacy and lower cognitive function were associated with non-adherence to treatment recommendations ($P < .05$). Conclusions and Implications: Health literacy and cognitive function are rarely studied in head and neck cancer. These important contributors to treatment understanding and adherence are even less frequently clinically evaluated in this vulnerable population. The current study demonstrates the need for assessment of both health literacy and cognitive function in patients with head and neck cancer to aid in identification and intervention to improve treatment adherence, survival outcomes, and quality of life.

Gastroenterology
Bhurwal A, Mutneja HR, **Haq KF**, Solanki S, Chandra Chakinala R, Bartel MJ, and Brahmbhatt B. Thirty-day incidence of post-ERCP complications: Incidence, risk factors and outcomes. *Gastrointestinal Endoscopy* 2020; 91(6):AB355.

Introduction: Endoscopic Retrograde Cholangiopancreatography often leads to mortality and morbidity with complications such as post procedure bleeding, post procedure laceration and post procedure hematoma. Currently, there are no national studies to determine the incidence of these complications and impact on health care utilization in terms of readmissions. Therefore, we aim to assess the national incidence of post ERCP hemorrhage, laceration and hematoma. The secondary aims of the study were to identify the readmissions associated with such complications and evaluate differences in the index admissions in terms of demographics, procedural differences. Methods: This was a retrospective cohort study using the National Readmission Database for the year 2016. Discharges with International Classification of Diseases,10th Revision, Clinical Modification (ICD-10-CM) procedures codes for ERCP were included. Post ERCP complications such as post procedure laceration, hematoma and hemorrhage were defined as an ICD-10-CM code for the same. Subsequently, 30-day readmissions were then

calculated for readmissions focusing on post ERCP fever and post ERCP bacteremia. Primary aims were to evaluate the incidence of complications during index admission and readmission. We also aimed to analyze demographic and procedure differences leading to complications. All statistical analysis was performed using STATA software. Results: We analyzed a total of 135,905 discharges undergoing ERCPs for diagnostic and therapeutic purposes. Out of these, 8 cases of post procedure hematoma per 1,000 ERCP were noticed during index admission. Similarly, incidence of post procedure laceration was 3.5/1,000 ERCP cases and post procedure bleeding was 6 per 1,000 ERCPs during the index admission. Approximately, 11.35% of these discharges were readmitted within 30 days of discharge indicating early readmission. However, complications of ERCP leading to readmissions were infrequent. Out of the discharges, post procedure hematoma was reported in 1.4 per 1,000 ERCPs, post procedure laceration in 1.07 per 1,000 ERCPs and post procedure hematoma in 1.07 per 1,000 ERCPs. The occurrence of post procedure complications had higher frequency of PTC or bile duct exploration. As expected, the length of stay and total hospitalization charges were also higher. Discussion: In a retrospective study, the occurrence of post ERCP complications such as post procedure hematoma, post procedure laceration and post procedure hemorrhage were less than 1%. Majority of the complications were noticed during the index admission. Early readmissions after index admission with ERCP for the complications are also infrequent. These suggest that the adverse effects with ERCP are relatively low with low effect on health care utilization. Further studies are warranted to determine the specific risk factors for the complications.

Gastroenterology

Bhurwal A, Mutneja HR, Shah I, Solanki S, Chakinala RC, **Haq KF**, Bartel MJ, and Brahmbhatt B. De novo post-ERCP fever and de novo post-ERCP bacteremia in patients with history of bariatric surgery– incidence, risk factors and outcomes. *Gastrointestinal Endoscopy* 2020; 91(6):AB520.

Background: History of bariatric surgery adds to the technical challenge of performing Endoscopic Retrograde cholangio-pancreatoscopy (ERCP) leading to complications. However, there are limited studies analyzing the complications in patients with bariatric surgery especially in a national cohort. The aim of the study was to assess the (1) incidence of post ERCP fever and bacteremia in discharges with history of bariatric surgery utilizing the national cohort (2) risk factors for post ERCP fever (3) effects on outcomes. Methods: This was a retrospective cohort study using 2016 Nationwide Inpatient Sample (NIS) including all patients undergoing ERCP. ICD 10-CM codes were used to identify patients with history of bariatric surgery and ERCP procedure. Post-ERCP bacteremia was defined as an ICD-10 CM code for a secondary diagnosis of infection or septic shock or fever in patients who received an ERCP. Patients were excluded from the study if they had an ICD-10 CM code for a principal diagnosis of acute cholangitis. Primary outcome was incidence of post-ERCP fever and bacteremia in patients with altered anatomy. The secondary aims were to evaluate the risk factors leading to complications and effects on outcomes. Proportions were compared using fisher's exact test and continuous variables using student t-test. Multivariable and Poisson regression was performed. Results: We included a total of 133,764 ERCP procedures out of which 1.27% (n=1,969) were performed in patients who had bariatric surgery in past. Fever with no signs of bacteremia or sepsis after ERCP was not significantly higher in patients with altered anatomy (1.8% vs 1.2%, p=0.96). Post ERCP bacteremia was significantly lower in patients with history of bariatric surgery (2.65% vs 5.26%, p=0.03). Bariatric surgery cohort had significantly higher frequency of percutaneous cholecystectomy (PTC) (1.18% vs 0.42%,p=0.03). After adjustment of confounders, biliary sphincterotomy increased odds of post ERCP bacteremia upto 5 times (OR 5.66,95% CI 1.1-28.9,p=0.03). Altered anatomy did not significantly increase the odds of mortality in ERCP cohort (0.43, 95% CI 0.06-3.07, p=0.4). The cohort had significantly lower length of stay (4.77 days vs 5.6 days, p<0.001). History of bariatric surgery did not independently increase hospitalization charges (68,729 $ vs 72,061 $,p=0.22). Conclusion: The study shows that occurrence of fever and post ERCP sepsis in altered anatomy is 1.8% and 2.65% respectively. Higher frequency of PTC in the cohort or use of antibiotics would be plausible reasons which might explain less frequent progression to bacteremia. Biliary sphincterotomy increased odds of post ERCP bacteremia upto five times. Further prospective studies are needed to evaluate specific risk factors which might explain reason behind post ERCP bacteremia in altered anatomy patients after sphincterotomy. [Formula presented] [Formula presented]

Gastroenterology

Columbus Morales IM, **Kaur R**, **Ashraf T**, **Nimri FM**, **Bhatti S**, and **Kutait A**. A time performance comparison between moderate and deep sedation for screening colonoscopies in obese patients with obstructive sleep apnea. *Gastrointestinal Endoscopy* 2020; 91(6):AB278.

Introduction: Colonoscopy is currently one of the preferred screening modalities for colon cancer in the US being advantageous due to allowing direct visualization, ability to perform polypectomy and biopsies. Different sedation modalities are available to perform the procedure but there has been a shift to the use of deep sedation for the past decade due to its association to higher patient satisfaction; the evidence is lacking in terms of other benefits. In special patient populations, such as morbid obese and obstructive sleep apnea (OSA), there is an indication to use deep sedation, however, there is little evidence to support its practice over other modalities, such as moderate sedation. The use of deep sedation may not be the safer choice in comparison to moderate sedation while adding

unnecessary expenses. The purpose of this study is to determine if moderate sedation can be as efficient as deep sedation for screening colonoscopies in obese patients with OSA. Methods: A retrospective cohort study of obese patients with OSA undergoing screening colonoscopy from 2014 to 2018 was performed. Patients with a colonoscopy performed for non-screening purposes were excluded. Examined time metrics were sedation to scope, cecum time, duration of procedure and recovery time. Other clinical data obtained included age, sex, social history, ASA classification, Mallampati score, procedural complications, and peri-procedural vital signs. Moderate sedation was supervised by the endoscopist using midazolam with fentanyl or meperidine. Deep sedation was done with anesthesia staff using propofol. Results: A total of 458 patients with OSA and obesity who underwent screening colonoscopy were identified. The mean age was 59.2 years, 46.5% were male and the mean BMI was 42.8 (Table 1). From the study population, 225 (49.1%) underwent moderate sedation (Table 2). The mean sedation to scope time was 4.5 minutes and 7 minutes in the moderate and deep sedation groups, respectively ($p < 0.001$). The mean duration of the procedure was 18.4 vs 21.7 minutes, in the moderate sedation and deep sedation, respectively ($p < 0.001$). The recovery time was 45.1 and 57.6 minutes in moderate sedation and deep sedation, respectively ($p < 0.001$). The most common complication was hypotension found on 11.6% of patients on the deep sedation group ($p < 0.001$). Conclusion: This study found that all evaluated time metrics were lower in the moderate sedation group. This can be interpreted as moderate sedation being a less time-consuming modality than deep sedation for screening colonoscopies in obese patients with OSA. This could potentially decrease health care costs and increase productivity by the number of patients that can be seen in a day while maintaining equivalent patient safety. [Formula presented] [Formula presented]

Gastroenterology

Iqbal U, **Haq KF**, Khara HS, Shah RN, Khan MA, **Siddiqui MA**, Hu Y, **Abu Ghanimeh MK**, **Sadiq O**, **Watson A**, **Salgia R**, and **Zuchelli T**. Safety and efficacy of endoscopic transpapillary gallbladder stenting for symptomatic gallbladder disease in cirrhosis: A systematic review and meta-analysis. *Gastrointestinal Endoscopy* 2020; 91(6):AB380.

Background: Symptomatic gallbladder disease is common in patients with cirrhosis and cholecystectomy has been the preferred method for treatment. Nevertheless, these patients are at high risk for complications and an alternate, less invasive, approach could decrease morbidity and mortality. Endoscopic insertion of cystic duct (transpapillary gallbladder) stent has been shown to be effective in treatment of symptomatic gallbladder disease. However, evidence is limited at this time, more so in patients with underlying cirrhosis. Methods: A comprehensive literature review was conducted by searching databases including Embase, Cochrane Central and PubMed from inception to August 2019 to identify all studies that evaluated outcomes of endoscopic transpapillary gallbladder stenting (ETGS) for symptomatic gallbladder disease in patients with cirrhosis. Our primary outcome was technical success defined as successful stent placement and clinical success defined as resolution of gallbladder disease symptoms. Proportions and 95% confidence intervals (CIs) were initially calculated for each of the event outcomes. Pooled estimates and measures of variability from each included study were used to generate forest plots. Publication bias was evaluated by Egger's test. Variability between studies was assessed by heterogeneity tests using I2 statistic. All analyses were conducted using RStudio (Version 1.0.136) using the 'Meta' and 'Metafor' package. Results: Seven studies including 109 patients met our inclusion criteria. At least, 94 patients (86%) had a Child-Turcotte-Pugh score of B or C. Most common indiciation for ETGS was recurrent biliary colic (51.3%) followed by acute cholecystitis (33.9%), and biliary pancreatitis (11.9%). ETGS was techinically successful in 104 patients with pooled technical success of 95% (95% CI: 89%-98%) with no statistical hetereogeniety as calculated by I2=0. In patients with successful ETGS, clinical success was achieved in 99 patients with pooled clinical success of 97% (95% CI: 82%-99%) with statistical heterogeniety I2=33%. Adverse events were reported in 15.6% with most common being pancreatitis (4.6%) followed by cholangitis (3.7%), and duodenal ulceration (1.8%). Technical failure resulted due to inability to cannulate the cystic duct (1.8%), impacted cystic duct stone (1.8%), and tortuous inflammed cystic duct complicated by perforation requiring cholecystostomy tube (0.9%). Overall mortality was found to be less than 1% as one patient with acute cholecystitis ultimately required open cholecystectomy complicated by sepsis and death. Conclusion: ETGS is a relatively safe and effective therapeutic modality for symptomatic gallbladder disease in patients with end-stage liver disease. Larger prospective trials are needed to better evaluate the safety and efficacy of ETGS for symptomatic gallbladder disease in patients with cirrhosis. [Formula presented] [Formula presented]

Gastroenterology

Iqbal U, Siddique O, Khara HS, Khan MA, **Haq KF**, Solanki S, **Siddiqui MA**, **Zuchelli T**, Shellenberger MJ, and Birk J. Post endoscopic retrograde cholangiopancreatography pancreatitis prevention using topical epinephrine: A systematic review and meta-analysis. *Gastrointestinal Endoscopy* 2020; 91(6):AB387.

Introduction: Post-endoscopic retrograde cholangiopancreatography pancreatitis (PEP) is a common complication of endoscopic retrograde cholangiopancreatography (ERCP). Multiple drugs and techniques have been studied for the prevention of PEP. Topical epinephrine has recently been studied for the prevention of PEP and theoretically should work similarly as a PD stent. Topical epinephrine sprayed on the ampulla can reduce edema by arteriolar

vasoconstriction and therefore improve pancreatic outflow. Evidence regarding the use of topical epinephrine in the prevention of PEP is inconsistent with some studies favoring their use while other studies did not show any benefit. We, therefore, conducted a systematic review and meta-analysis to delineate if topical epinephrine is useful in the prevention of PEP. Methods: A comprehensive literature review was conducted by searching multiple databases until August 2019, to identify all studies that evaluated the use of topical epinephrine alone or in conjunction with other agents for the prevention of PEP. The characteristics of the participants and outcome measurements (incidence of PEP) were analyzed. All analysis was conducted using Revman 5.3. Results: Eight studies, including 6 randomized controlled trials (RCTs) and 2 observational studies with 4123 patients, were included in the meta-analysis. Our overall results included two types of studies. Some studies evaluated both topical epinephrine and rectal indomethacin therapy together and some studies compared topical epinephrine with placebo therapy. Five RCTs are of good quality while one was of fair quality. Both the observational studies were of good quality. Overall, there was no difference in the incidence of PEP in patients who underwent ERCP and were treated with epinephrine spray versus those who were not, OR=0.62 (CI 0.30-1.25) with heterogeneity (I2=72%). In a subgroup analysis, topical epinephrine, when compared to placebo significantly decreases the risk of PEP, OR=0.30 (0.16-0.55). However, in a subgroup analysis, addition of topical epinephrine to rectal indomethacin did not provide any additional advantage in decreasing the incidence of PEP, when compared to rectal indomethacin alone OR=1.15 (0.58-2.28). Conclusion: Topical epinephrine does not provide any additional advantage in combination with rectal indomethacin in the prevention of PEP in patients who underwent ERCP. However, topical epinephrine alone is associated with lower odds of PEP compared to placebo and can be considered if rectal indomethacin is unavailable or there is any contraindication to its use. It may also be considered as a suitable alternative to prophylactic pancreatic stenting. Future studies comparing topical epinephrine versus PD stenting can be considered to evaluate if topical epinephrine provides a similar advantage in decreasing PEP as compared to PD stenting.

Gastroenterology
Kamal F, Khan MA, Bayoumi M, Marella HK, Khan S, Khan Z, **Haq KF**, Howden CW, Tombazzi C, and Ismail MK. Comparison of per-oral endoscopic myotomy and pneumatic dilation in the management of achalasia: Systematic review and meta-analysis. *Gastrointestinal Endoscopy* 2020; 91(6):AB135-AB136.

Background: Pneumatic dilation (PD) is a commonly used endoscopic treatment for achalasia but its efficacy is limited by high rate of recurrence of symptoms. PD is also associated with a small but significant risk of esophageal perforation. Per-oral endoscopic myotomy (POEM) is a relatively newer treatment option. POEM has been compared with PD in the management of achalasia. Aims: To compare the efficacy and safety of POEM and PD in the management of achalasia by systematic review and meta-analysis Methods: We reviewed Medline, Scopus, Web of Science and Cochrane databases from inception to September 2019 to identify observational studies and randomized controlled trials (RCTs) comparing POEM with PD in the management of achalasia. Our primary outcome of interest was clinical success defined by post-treatment Eckardt score ≤3. Secondary outcomes were adverse events, difference in post-treatment mean Eckardt score, integrated relaxation pressure (IRP) and basal lower esophageal sphincter pressure (LESP) between groups. Data were analyzed using a random effects model and summarized as pooled odds ratio (OR) with 95% CI for categorical variables and pooled standardized mean difference (SMD) with 95% CI for continuous variables. Heterogeneity was assessed by I2 statistic. Results: We included 6 observational studies and 1 RCT with 619 patients; 255 underwent POEM and 364 underwent PD. Main results are summarized in Table 1 and depicted graphically in Figure 1. POEM demonstrated better clinical success at 3 and 6 months and at 1, 2 and 3 years post-treatment compared to PD. Pooled OR (95% CI) for clinical success was 0.12 (0.06, 0.24) at 1 year and 0.15 (0.08, 0.28) at 2 years post-treatment (Figures 1A, 1B). Esophageal perforation occurred in 0/255 patients who received POEM and 4/364 who had PD. The most common adverse events with POEM were subcutaneous emphysema and new onset gastroesophageal reflux disease (GERD). Subcutaneous emphysema resolved spontaneously in all cases and did not require treatment. Risk of GERD was significantly higher with POEM; pooled OR 1.66 (1.20, 2.29). Mean pre-treatment Eckardt score was slightly higher in patients undergoing PD. Post-treatment Eckardt was lower with POEM; pooled SMD (95% CI) -0.312 (-0.488, -0.136). There was no difference in pre-treatment IRP or LESP between groups. Post-treatment IRP was lower with POEM than PD; pooled SMD -0.418 (-0.640, -0.195). Post-treatment LESP was also lower with POEM; pooled SMD -0.613 (-0.830, -0.395). All outcomes of interest had low heterogeneity except for post-treatment LESP (I2=90%), although this was reduced to 66% after excluding one study of patients aged 65 or older. Conclusions: POEM has better long-term outcomes than PD in the treatment of achalasia. PD is associated with a small risk of perforation. However, risk of new onset GERD is much higher with POEM than PD. [Formula presented] [Formula presented]

Gastroenterology
Kamal F, Khan MA, Marella HK, Reddy YK, **Haq KF**, Bayoumi M, Akbar H, Heda RP, and Tombazzi C. Urgent vs. Elective colonoscopy for lower gastrointestinal bleeding: Meta-analysis of randomized controlled trials. *Gastrointestinal Endoscopy* 2020; 91(6):AB494.

Background: Acute lower gastrointestinal (GI) bleeding (LGIB) is a common cause for hospitalization; colonoscopy is recommended for diagnostic evaluation and possible treatment. However, the optimal timing of colonoscopy is controversial. Urgent colonoscopy (i.e., within 24 hours) is often performed but its benefits are unclear. There is limited evidence to support the use of urgent colonoscopy in acute LGIB. Some studies have compared the role of urgent vs. elective colonoscopy in management. Aim: To compare urgent vs. elective colonoscopy in the management of acute LGIB by meta-analysis of mrandomized controlled trials (RCTs) Methods: To identify RCTs comparing urgent vs. elective colonoscopy in LGIB, we searched databases including Pubmed, Scopus, Cochrane library and web of science from inception to October 2019. The outcomes we evaluated included rate of rebleeding, stigmata of recent hemorrhage (SRH), identification of bleeding source, mortality, need for surgery and length of hospital stay. For categorical variables, pooled odds ratios (OR) with 95% confidence intervals (CI) were calculated using random effects model. For continuous variables, standard mean differences (SMD) with 95% CI were calculated. Quality was assessed using Cochrane tool for assessing risk of bias for RCTs. Results: We included 4 RCTs with 460 patients; 228 underwent urgent colonoscopy and 235 underwent elective colonoscopy. Results are summarized in Table 1 and depicted graphically in Figure 1. There were no significant differences in detection of SRH, mortality, need for surgery or endoscopic intervention. There were no significant differences in identification of a source of bleeding; pooled OR (95% CI): 1.88 (0.87, 4.05), I2= 43% (Figure 1A) or rates of rebleeding between groups; pooled OR: 1.68 (0.79, 3.59) I2= 44% (Figure 1B). There were low levels of heterogeneity in analysis of these outcomes. There was no significant difference in length of hospital stay between groups; SMD (95%) CI= 0.12 (-0.23, 0.46), I2= 60%. This analysis was limited by moderate heterogeneity probably due to differences in discharge criteria in different countries. All RCTs had high risk of performance bias and low risk of selection, detection, attrition and reporting bias. Conclusions: There is no evidence that urgent colonoscopy decreases rates of rebleeding, mortality or need for surgery in patients with LGIB or that it increases the rates of detection of sources of bleeding or SRH.

Gastroenterology
Kamal F, Khan MA, Reddy YK, **Haq KF**, Heda RP, Tariq R, Ismail MK, Tombazzi C, and Howden CW. Risk factors for delayed post-polypectomy bleeding: Systematic review and meta-analysis. *Gastrointestinal Endoscopy* 2020; 91(6):AB508-AB509.

Background: Delayed post-polypectomy bleeding (DPPB) is an important complication of colonoscopic polypectomy that can be associated with substantial morbidity and may require hospitalization, blood transfusion, repeat colonoscopy and, rarely, angiographic embolization or surgery. Studies have evaluated and reported different risk factors for DPPB. Aim: To identify risk factors for DPPB by systematic review and meta-analysis of observational studies Methods: We conducted a systematic search of databases including Pubmed, Scopus, Web of science and Cochrane library from inception to November 2019 for studies reporting risk factors for DPPB. Adjusted odds ratios (OR) with 95% confidence intervals (CI) for individual risk factors were pooled using random effects model. I2statistics were used to assess heterogeneity. Publication bias was assessed by Egger's test. Results: We included 21 observational studies with 48,990 patients. Results are summarized in Table 1. Factors that were associated with increased risk of DPPB included polyp size >10mm (OR 3.05; Figure 1A), right-sided colon polyps (OR 2.56; Figure 1B), immediate post-polypectomy bleeding (OR 2.86), hypertension (OR 1.68), use of anticoagulants/antiplatelet agents (OR 4.33), and heparin bridging (OR 10.61). Macroscopic form of polyps (pedunculated vs. sessile) was not associated with increased risk of DPPB; pooled OR (95% CI) = 1.36 (0.88, 2.11); I2= 57%. Heparin bridging was associated with the highest risk of DPPB (pooled OR (95% CI) = 10.61 (6.46, 17.43); I2= 17%). There were low levels of heterogeneity for all these risk factors except macroscopic form of polyps (I2= 57%). We found no evidence of publication bias. Conclusions: Polyp size >10mm, right colon polyp location, immediate post-polypectomy bleeding, hypertension, use of anticoagulants/antiplatelet agents and heparin bridging are associated with increased risks of DPPB. Heparin bridging is associated with a very high risk of DPPB;benefits of bridging should be carefully weighed against its risks in these patients. [Formula presented] [Formula presented]

Gastroenterology
Kamal F, Khan MA, Talat A, Gilman C, Arshad HMS, **Haq KF**, Khan S, Ahmad D, and Tombazzi C. Endoscopic vs. Surgical resection for gastric gastrointestinal stromal tumors <5cm in size: Systematic review and meta-analysis. *Gastrointestinal Endoscopy* 2020; 91(6):AB594.

Background: Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors of gastrointestinal (GI) tract. Stomach is the most common site of GISTs. Endoscopic resection of gastric GISTs is being increasingly performed. Some studies have compared outcomes of endoscopic vs surgical resection of gastric GISTs. Aim: To compare outcomes of endoscopic vs surgical resection of gastric GISTs by systematic review and meta-analysis. Methods: We reviewed Pubmed, Scopus, Cochrane and Web of Science from inception to November 2019 to identify studies comparing endoscopic and surgical resection in the management of gastric GISTs <5cm in size. The outcomes assessed included; complications, recurrence rate, rate of R0 resection (defined by removal of entire tumor with negative margins), length of hospital stay and operative time. Pooled odds ratios (OR) with 95% confidence

intervals (CI) were calculated for categorical variables and Standardized mean difference (SMD) with 95% CI were calculated for continuous variables. Data were analyzed using random effects model. Heterogeneity was assessed using I2 statistic. Results: We included 7 studies with 963 patients. 578 patients underwent endoscopic resection and 385 patients underwent surgical resection of gastric GISTs. Results are summarized in table 1. There was no difference in rate of complications between two groups; pooled OR (95% CI): 0.65 (0.29, 1.46). 2 studies reported data on R0 resection rate, and it was better with surgical resection; pooled OR (95% CI): 0.03 (0, 0.21). Length of hospital stay and operative times were significantly shorter in endoscopy group (Figure 1A and B). There was no difference in tumor recurrence rate between two groups; pooled OR (95% CI): 0.66 (0.13, 3.20). Conclusions: Length of hospital stay and operative times are shorter with endoscopic resection of gastric GISTs <5cm in size without increased risk of complications compared to surgical resection. Limited amount of data showed better R0 resection rate with surgical resection. Further studies are required to confirm these findings.

Gastroenterology

Kaur R, **morales IMC**, **Ashraf T**, **Bhatti S**, **Nimri FM**, and **Kutait A**. Assessing respiratory complications in patients with obesity and obstructive sleep apnea undergoing a screening colonoscopy with moderate and deep sedation. *Gastrointestinal Endoscopy* 2020; 91(6):AB530.

Introduction: Millions of screening colonoscopies are performed annually which means there is a substantial health cost for insurances. There has been more utilization of deep sedation requiring costly anesthesia services compared to moderate sedation given severity of systemic diseases, increased comfort, satisfaction, and ease of scoping for the endoscopist. Typically, obese patients with obstructive sleep apnea (OSA) have required deep sedation, however many are able to utilize moderate more safely. Here we assess respiratory complications in deep and moderate sedation in high risk patients who have obesity and OSA undergoing a screening colonoscopy. Methods: A retrospective cohort study was done in patients with obesity and OSA who have undergone a screening colonoscopy between 2014 and 2018 with either moderate or deep sedation. Background history included age, sex, race, BMI, alcohol, tobacco and marijuana use. Complexity and airway was measured by ASA and Mallampati score (MS). OSA severity was assessed by the AHI score. Moderate sedation was supervised by the endoscopist using midazolam with fentanyl or meperidine. Deep sedation was done with anesthesia staff using propofol. Intra-procedure respiratory complications were assessed by apneic episodes as determined by the end tidal CO2. Results: 458 patients with OSA and obesity, with 49.1% undergoing moderate sedation, were analyzed. There were no major background differences in sex, age or BMI (table 1). A significant race difference was noted between the two groups with majority African American (59.6%) for deep and Caucasian (59.1%) for moderate sedation (p<.001, table 1). Overall, the mean diagnostic AHI was 48.0 and recent AHI 5.3. The majority ASA class in moderate sedation was ASA II compared to ASA III in deep sedation (p<.001, table 1). MS II was most prevalent in both sedation groups with more MS III in deep sedation compared to moderate sedation (p<.001, table 1). Intra-procedural respiratory depression was significantly noted in deep sedation (5.2% vs 0.9%, p=0.008). Interventions solely for deep sedation included 1 oral airway insertion and 3.4% needing intubation (p=0.007, table 2). Discussion: There is a notable increased respiratory risk in deep sedation. Patient's requiring intra-procedural intubation can go on to have further post-procedure complications. Traditionally, ASA III and MS III are done with anesthesia, however this study showed that patients with similar ASA and MS were able to undergo moderate sedation with little to no complications. These findings go on to advocate that while close airway monitoring with anesthesia is common in obese patients with OSA, moderate sedation carries much less risk and should be the preferred modality. It is also certainly more cost effective without the need for anesthesia services cutting down a sizeable amount of healthcare costs.

Gastroenterology

Khan MA, Saumoy M, Iqbal U, **Haq KF**, Khan A, Kamal F, **Zuchelli T**, Anwar H, Mohammed Abdul MK, and Sharaiha RZ. Efficacy and safety of self-expandable metal stents for management of bariatric surgery leaks. A systematic review and meta-analysis. *Gastrointestinal Endoscopy* 2020; 91(6):AB231-AB232.

Background: Post bariatric surgery leaks can be difficult to manage, and surgical re-exploration is associated with significant morbidity and mortality. Endoscopic deployment of self-expandable metal stents (SEMS) is a less invasive modality and has been utilized for management of such leaks avoiding the need for re-exploration surgery in selected patients. Aim: Conduct a systematic review and meta-analysis to evaluate the efficacy and safety of endoscopically placed SEMS for management of post bariatric surgery leaks. Methods: We searched Medline, Embase and Cochrane library from inception through November 26, 2019 to identify studies evaluating the efficacy of SEMS for treatment of post bariatric surgery leaks. The primary outcome of interest was rate of successful closure of leaks determined radiologically after removal of SEMS. Secondary outcomes included rates of successful stent removal and adverse events including rate of stent migration. These outcomes were presented as weighted pooled rates WPR and analyzed using random effects model of meta-analysis. Publication bias was calculated with funnel plots and Beg Mazumdar test. Duval and Tweedie's trim and fill test was used to adjust for publication bias. To avoid inherent bias associated with case reports and small case series only studies with at least 10 patients were included. NIH tool was used for single arm before-after studies for quality assessment of individual studies. Results: A total of

19 observational studies with 539 patients with post-surgery leaks were included in this systematic review and meta-analysis. Among the patients, 58% were females. 22% of patients had undergone Roux-en-Y bypass surgery, 73% % had laparoscopic sleeve gastrectomy 2% had duodenal switch surgery while the remaining 3% had laparoscopic gastric banding. Fourteen studies were rated as good quality, while 5 studies were rated as fair quality as per NIH tool for quality assessment. Pooled WPR with 95% confidence interval (CI) was 83.2% (79.6%, 86.3%), I2=0%. Funnel plot appeared asymmetric and publication bias was detected by Beg Mazumdar test (P=0.05). After adjusting for publication bias pooled WPR was 82.6% (78%, 86.4%). Pooled WPR for successful removal of stents was 94.9% (90.7%, 97.3%), I2=0%. Pooled WPR with 95% CI for rate of stent migration was 18.8% (13.3%, 25.9%) with significant heterogeneity. Conclusions: SEMS appear to be a favorable option for management of majority of patients with post bariatric surgery leaks. However, they have a significant risk of stent migration thus necessitating multiple endoscopies. Prospective studies evaluating the timing of stent placement and comparison with re-exploration surgery are needed.

Gastroenterology

Shinn B, Boortalary T, Raijman I, Nieto J, Khara HS, Kumar SV, Confer B, Diehl DL, El Halabi MAAN, Ichkhanian Y, Runge TM, Kumbhari V, Khashab MA, Tyberg A, Shahid HM, Sarkar A, Gaidhane M, Bareket R, Kahaleh M, **Piraka C**, **Zuchelli T**, Law R, Sondhi AR, Kedia P, Robbins JS, Calogero C, Bakhit M, Chiang AL, Schlachterman A, Kowalski TE, and Loren DE. 960 Maximizing success in single-session edge - predictive factors of stent migration. *Gastrointestinal Endoscopy* 2020; 91(6):AB80.

Background: Roux-en-Y gastric bypass anatomy poses a challenge in performing ERCP due to the inability to access the excluded stomach and duodenum. EUS-directed gastro-gastric ERCP (EDGE) uses a lumen apposing metal stent (LAMS) to access the excluded stomach and is most often performed in two-stages with initial placement of the LAMS followed by ERCP weeks later. The need for urgent ERCP in this patient population has led to the advent of single-session EDGE with LAMS and ERCP on the same day. The most serious and common complication of this procedure is intra-procedural migration of the LAMS. The purpose of this study was to identify predictive factors of LAMS complications during single-session EDGE in a large multicenter cohort. Methods: A multi-centered, retrospective chart review was conducted at nine tertiary medical centers. Single-session EDGE procedures were identified and data including age, gender, LAMS diameter, dilation, route of LAMS placement (gastric or jejunal), stent fixation and procedure complications were collected. The primary outcome was intra-procedural LAMS migration. Groups were compared using Fisher's exact test for univariate analysis and binary logistic regression analysis to predict independent factors associated with stent migration. Results: 131 patients were included in the study who underwent single-session EDGE. Median age=58 y, 74.8% were female. LAMS migration occurred in 12 patients (9.1%). In univariate analysis, statistically fewer LAMS migrations occurred in patients with a 20mm diameter LAMS (2/84) vs 15mm (7/42), p=0.006, those with suture fixation, p=0.032, and those who underwent LAMS dilation, p=0.026. Location of LAMS placement did not affect the rate of stent migration (2/40 jejunal vs 10/91 gastric, p=0.343) although a trend towards more migration in the trans-gastric route was observed. The use of electrocautery-enhanced stents did not influence the rate of migration. Double pigtail stents for anchoring did not reduce the rate of migration. Binary logistic regression analysis of stent diameter, dilation, suture fixation, access route and electrocautery identified that 15mm stents were significantly more likely to migrate than 20mm (OR=7.9; 95% CI:1.3-47; p=0.024). Of the patients that experienced LAMS migration, 3 required surgery, 2 were rescued with esophageal stent bridging and 2 with a second LAMS. Bleeding occurred in 2 patients and was managed endoscopically at the time of the procedure. No deaths occurred in the cohort. Conclusions: Same day EDGE procedures can be performed safely with an acceptable complication rate. Larger diameter 20mm stents are the strongest predictor of a non-migrated LAMS, whereas stent fixation and dilation after deployment may also improve procedural success. Expanding on this cohort will offer further insights into the optimal technique for single-session EDGE.

Gastroenterology

Zhang J, **Suresh S**, Ahmed A, **Piraka C**, **Abu Ghanimeh MK**, **Pompa R**, **Singla S**, **Dang D**, **Isseh M**, **Elbanna A**, **Kaur R**, and **Zuchelli T**. Recurrence rate and risk factors following cold snare endoscopic mucosal resection of polyps ≥20 mm in size. *Gastrointestinal Endoscopy* 2020; 91(6):AB483-AB484.

Introduction: Traditionally, endoscopic mucosal resection (EMR) for polyps ≥20mm has been performed with snare cautery. Due to adverse events (AE) associated with cautery, such as bleeding and perforation, the use of cold snare EMR has increased. These AE are not routinely seen with cold EMR, due to the lack of cautery. Data evaluating adenoma/sessile polyp recurrence rates (ARR) and risk factors for recurrence after cold snare EMR of polyps ≥20mm has not been fully assessed. The aim of this study is to define ARR for polyps ≥20mm removed via cold snare EMR and risk factors for recurrence. Methods: A retrospective chart review was conducted from 1/2015 to 7/2019 at a single tertiary care center. In this period, 469 patients underwent piecemeal cold snare EMR of polyps ≥20mm by 5 endoscopists. Complete resection of the polyp was documented in all cases. Of these, 310 had a surveillance colonoscopy and were included in the study, however, 159 were lost to follow up. Data including age, gender, race, history of predisposal to colon cancer, smoking and alcohol history, polyp location, histology, dysplasia at index, and

size of the polyp were collected. Results: 108 (34.8%) patients had evidence of recurrence on pathology at follow up colonoscopy. The average time for follow in the ARR group was 5.7 months. There was no association between recurrence and gender, personal history of polyposis syndrome, family history of colon cancer, smoking, alcohol use, number of polyps removed at index colonoscopy, and the polyp location. Patients with recurrence were found to be older (p=0.008), Asian or African American compared to Caucasian (p=0.02); and required the use of endoscopic clips (p=0.017) at index procedure. Recurrence rates were higher in larger polyps (34 vs 27 mm, p=<0.001). Also, ARR increased with polyps >30mm (26.7% in polyps 20-30mm vs 76.9% in polyps >50mm). There was a significant association between polyp histology and ARR; tubulovillious adenomas (p=<0.001) and high-grade dysplasia (p=0.003) more likely to recur while tubular adenomas and sessile serrated polyps had lower ARR. Among patients with follow-up procedures, there was no interval cancer found. Conclusion: To our knowledge this is the largest, if not only, cohort looking at ARR for polyps ≥20mm removed via piecemeal cold snare EMR. Surprisingly, the ARR in the cold EMR group was 34.8%, which is higher than the average ARR commonly seen with hot EMR (~20%). Factors that influenced the ARR were older age, Asian or African American race, endoclip use, polyp size and histology. Cold snare EMR has been shown to be a safe procedure but the ARR and factors that affect this rate must be considered when managing these patients. Prospective trials are needed to further validate these findings.

Hematology/Oncology

Ahsan B, **Thanikachalam K**, **Robison A**, **Li J**, **Datta I**, **Onwubiko I**, **Khan G**, and **Raoufi M**. Molecular characteristics of pancreatic neuroendocrine tumors, do they correlate with metastases? *Modern Pathology* 2020; 33(3):1687-1688.

B. Ahsan, Henry Ford Health System, Detroit, MI, United States

Background: Pancreatic neuroendocrine tumors (PNET) have an unpredictable biological behavior that cannot be reliably predicted by histological and clinical manifestations. We performed next generation sequencing (NGS) on PNET to understand the molecular pathogenesis and to identify potential biomarkers correlating with metastases and survival. Design: Hybrid capture-based comprehensive genomic profiling was performed on both primary and metastatic PNET from 28 patients. Metastatic sites were grouped as lymph nodes and distant metastases (consisted of liver followed by bone). NGS was performed on genomic DNA & RNA isolated from formalin-fixed paraffin embedded tissue using the whole exome NGS assay covering 20,000 genes. Average number of DNA reads was 52 million at 3:1 somatic to germline. All variants were detected with >99% confidence based on allele frequency and amplicon coverage, with an average sequencing depth of coverage >500x and an analytical sensitivity of 5%. Tumor mutation burden and MSI status were compared using the two-sample t-test between tumor types. Frequency of mutations in each gene was compared between tumor types using the Fisher's exact test. To account for multiple comparisons, the False Discovery Rate was estimated using Benjamini-Hochberg procedure. R package "maftools" was used to summarize and visualize the findings. Results: Mutation burden was higher in primary tumors with metastases versus primary tumors without metastases (p=0.034) while no significance was found in MSI status between these two groups. Among the 20 mutated genes, MUC4 and MEN1 were the most frequently mutated genes in both primary and metastatic tumors (fig1&2). At a p-value threshold of 0.2, two distant metastatic tumors had mutation on PCNX3 gene, while none were found in lymph node metastases (p=0.057). In addition, more mutations on TGFBR1 in distant metastases compared to lymph node metastases (p=0.154). We also found that three primary tumors with metastases had mutations on E2F4, HRNR, LRP1B genes while none were found in primary tumors with no metastases (p=0.2). (Figure presented) Conclusions: Decoding the complexity and unpredictable nature of PNET has been perplexing and the subject of many several research projects. The current project, the first ever done on the subject, with an attempt to distinguish the metastatic vs non-metastatic tumors try to underlie the difference of molecular signature between the two. Further studies are needed to consolidate the findings and bring them to clinical practice.

Internal Medicine

Columbus Morales IM, **Kaur R**, **Ashraf T**, **Nimri FM**, **Bhatti S**, and **Kutait A**. A time performance comparison between moderate and deep sedation for screening colonoscopies in obese patients with obstructive sleep apnea. *Gastrointestinal Endoscopy* 2020; 91(6):AB278.

Introduction: Colonoscopy is currently one of the preferred screening modalities for colon cancer in the US being advantageous due to allowing direct visualization, ability to perform polypectomy and biopsies. Different sedation modalities are available to perform the procedure but there has been a shift to the use of deep sedation for the past decade due to its association to higher patient satisfaction; the evidence is lacking in terms of other benefits. In special patient populations, such as morbid obese and obstructive sleep apnea (OSA), there is an indication to use deep sedation, however, there is little evidence to support its practice over other modalities, such as moderate sedation. The use of deep sedation may not be the safer choice in comparison to moderate sedation while adding unnecessary expenses. The purpose of this study is to determine if moderate sedation can be as efficient as deep sedation for screening colonoscopies in obese patients with OSA. Methods: A retrospective cohort study of obese

patients with OSA undergoing screening colonoscopy from 2014 to 2018 was performed. Patients with a colonoscopy performed for non-screening purposes were excluded. Examined time metrics were sedation to scope, cecum time, duration of procedure and recovery time. Other clinical data obtained included age, sex, social history, ASA classification, Mallampati score, procedural complications, and peri-procedural vital signs. Moderate sedation was supervised by the endoscopist using midazolam with fentanyl or meperidine. Deep sedation was done with anesthesia staff using propofol. Results: A total of 458 patients with OSA and obesity who underwent screening colonoscopy were identified. The mean age was 59.2 years, 46.5% were male and the mean BMI was 42.8 (Table 1). From the study population, 225 (49.1%) underwent moderate sedation (Table 2). The mean sedation to scope time was 4.5 minutes and 7 minutes in the moderate and deep sedation groups, respectively ($p < 0.001$). The mean duration of the procedure was 18.4 vs 21.7 minutes, in the moderate sedation and deep sedation, respectively ($p < 0.001$). The recovery time was 45.1 and 57.6 minutes in moderate sedation and deep sedation, respectively ($p < 0.001$). The most common complication was hypotension found on 11.6% of patients on the deep sedation group ($p < 0.001$). Conclusion: This study found that all evaluated time metrics were lower in the moderate sedation group. This can be interpreted as moderate sedation being a less time-consuming modality than deep sedation for screening colonoscopies in obese patients with OSA. This could potentially decrease health care costs and increase productivity by the number of patients that can be seen in a day while maintaining equivalent patient safety.

Internal Medicine

Kaur R, **Morales IMC**, **Ashraf T**, **Bhatti S**, **Nimri FM**, and **Kutait A**. Assessing respiratory complications in patients with obesity and obstructive sleep apnea undergoing a screening colonoscopy with moderate and deep sedation. *Gastrointestinal Endoscopy* 2020; 91(6):AB530.

Introduction: Millions of screening colonoscopies are performed annually which means there is a substantial health cost for insurances. There has been more utilization of deep sedation requiring costly anesthesia services compared to moderate sedation given severity of systemic diseases, increased comfort, satisfaction, and ease of scoping for the endoscopist. Typically, obese patients with obstructive sleep apnea (OSA) have required deep sedation, however many are able to utilize moderate more safely. Here we assess respiratory complications in deep and moderate sedation in high risk patients who have obesity and OSA undergoing a screening colonoscopy. Methods: A retrospective cohort study was done in patients with obesity and OSA who have undergone a screening colonoscopy between 2014 and 2018 with either moderate or deep sedation. Background history included age, sex, race, BMI, alcohol, tobacco and marijuana use. Complexity and airway was measured by ASA and Mallampati score (MS). OSA severity was assessed by the AHI score. Moderate sedation was supervised by the endoscopist using midazolam with fentanyl or meperidine. Deep sedation was done with anesthesia staff using propofol. Intra-procedure respiratory complications were assessed by apneic episodes as determined by the end tidal CO_2. Results: 458 patients with OSA and obesity, with 49.1% undergoing moderate sedation, were analyzed. There were no major background differences in sex, age or BMI (table 1). A significant race difference was noted between the two groups with majority African American (59.6%) for deep and Caucasian (59.1%) for moderate sedation ($p<.001$, table 1). Overall, the mean diagnostic AHI was 48.0 and recent AHI 5.3. The majority ASA class in moderate sedation was ASA II compared to ASA III in deep sedation ($p<.001$, table 1). MS II was most prevalent in both sedation groups with more MS III in deep sedation compared to moderate sedation ($p<.001$, table 1). Intra-procedural respiratory depression was significantly noted in deep sedation (5.2% vs 0.9%, $p=0.008$). Interventions solely for deep sedation included 1 oral airway insertion and 3.4% needing intubation ($p=0.007$, table 2). Discussion: There is a notable increased respiratory risk in deep sedation. Patient's requiring intra-procedural intubation can go on to have further post-procedure complications. Traditionally, ASA III and MS III are done with anesthesia, however this study showed that patients with similar ASA and MS were able to undergo moderate sedation with little to no complications. These findings go on to advocate that while close airway monitoring with anesthesia is common in obese patients with OSA, moderate sedation carries much less risk and should be the preferred modality. It is also certainly more cost effective without the need for anesthesia services cutting down a sizeable amount of healthcare costs.

Internal Medicine

Zhang J, **Suresh S**, Ahmed A, **Piraka C**, **Abu Ghanimeh MK**, **Pompa R**, **Singla S**, **Dang D**, **Isseh M**, **Elbanna A**, **Kaur R**, and **Zuchelli T**. Recurrence rate and risk factors following cold snare endoscopic mucosal resection of polyps ≥20 mm in size. *Gastrointestinal Endoscopy* 2020; 91(6):AB483-AB484.

Introduction: Traditionally, endoscopic mucosal resection (EMR) for polyps ≥20mm has been performed with snare cautery. Due to adverse events (AE) associated with cautery, such as bleeding and perforation, the use of cold snare EMR has increased. These AE are not routinely seen with cold EMR, due to the lack of cautery. Data evaluating adenoma/sessile polyp recurrence rates (ARR) and risk factors for recurrence after cold snare EMR of polyps ≥20mm has not been fully assessed. The aim of this study is to define ARR for polyps ≥20mm removed via cold snare EMR and risk factors for recurrence. Methods: A retrospective chart review was conducted from 1/2015 to 7/2019 at a single tertiary care center. In this period, 469 patients underwent piecemeal cold snare EMR of polyps ≥20mm by 5 endoscopists. Complete resection of the polyp was documented in all cases. Of these, 310 had a surveillance

colonoscopy and were included in the study, however, 159 were lost to follow up. Data including age, gender, race, history of predisposal to colon cancer, smoking and alcohol history, polyp location, histology, dysplasia at index, and size of the polyp were collected. Results: 108 (34.8%) patients had evidence of recurrence on pathology at follow up colonoscopy. The average time for follow in the ARR group was 5.7 months. There was no association between recurrence and gender, personal history of polyposis syndrome, family history of colon cancer, smoking, alcohol use, number of polyps removed at index colonoscopy, and the polyp location. Patients with recurrence were found to be older (p=0.008), Asian or African American compared to Caucasian (p=0.02); and required the use of endoscopic clips (p=0.017) at index procedure. Recurrence rates were higher in larger polyps (34 vs 27 mm, p=<0.001). Also, ARR increased with polyps >30mm (26.7% in polyps 20-30mm vs 76.9% in polyps >50mm). There was a significant association between polyp histology and ARR; tubulovillious adenomas (p=<0.001) and high-grade dysplasia (p=0.003) more likely to recur while tubular adenomas and sessile serrated polyps had lower ARR. Among patients with follow-up procedures, there was no interval cancer found. Conclusion: To our knowledge this is the largest, if not only, cohort looking at ARR for polyps ≥20mm removed via piecemeal cold snare EMR. Surprisingly, the ARR in the cold EMR group was 34.8%, which is higher than the average ARR commonly seen with hot EMR (~20%). Factors that influenced the ARR were older age, Asian or African American race, endoclip use, polyp size and histology. Cold snare EMR has been shown to be a safe procedure but the ARR and factors that affect this rate must be considered when managing these patients. Prospective trials are needed to further validate these findings.

Pathology

Ahsan B, **Thanikachalam K**, **Robison A**, **Li J**, **Datta I**, **Onwubiko I**, **Khan G**, and **Raoufi M**. Molecular characteristics of pancreatic neuroendocrine tumors, do they correlate with metastases? *Modern Pathology* 2020; 33(3):1687-1688.

B. Ahsan, Henry Ford Health System, Detroit, MI, United States

Background: Pancreatic neuroendocrine tumors (PNET) have an unpredictable biological behavior that cannot be reliably predicted by histological and clinical manifestations. We performed next generation sequencing (NGS) on PNET to understand the molecular pathogenesis and to identify potential biomarkers correlating with metastases and survival. Design: Hybrid capture-based comprehensive genomic profiling was performed on both primary and metastatic PNET from 28 patients. Metastatic sites were grouped as lymph nodes and distant metastases (consisted of liver followed by bone). NGS was performed on genomic DNA & RNA isolated from formalin-fixed paraffin embedded tissue using the whole exome NGS assay covering 20,000 genes. Average number of DNA reads was 52 million at 3:1 somatic to germline. All variants were detected with >99% confidence based on allele frequency and amplicon coverage, with an average sequencing depth of coverage >500x and an analytical sensitivity of 5%. Tumor mutation burden and MSI status were compared using the two-sample t-test between tumor types. Frequency of mutations in each gene was compared between tumor types using the Fisher's exact test. To account for multiple comparisons, the False Discovery Rate was estimated using Benjamini-Hochberg procedure. R package "maftools" was used to summarize and visualize the findings. Results: Mutation burden was higher in primary tumors with metastases versus primary tumors without metastases (p=0.034) while no significance was found in MSI status between these two groups. Among the 20 mutated genes, MUC4 and MEN1 were the most frequently mutated genes in both primary and metastatic tumors (fig1&2). At a p-value threshold of 0.2, two distant metastatic tumors had mutation on PCNX3 gene, while none were found in lymph node metastases (p=0.057). In addition, more mutations on TGFBR1 in distant metastases compared to lymph node metastases (p=0.154). We also found that three primary tumors with metastases had mutations on E2F4, HRNR, LRP1B genes while none were found in primary tumors with no metastases (p=0.2). (Figure presented) Conclusions: Decoding the complexity and unpredictable nature of PNET has been perplexing and the subject of many several research projects. The current project, the first ever done on the subject, with an attempt to distinguish the metastatic vs non-metastatic tumors try to underlie the difference of molecular signature between the two. Further studies are needed to consolidate the findings and bring them to clinical practice.

Pathology

Alhamar M, **Alkamachi B**, **Mehrotra H**, **Sanchez J**, **Schultz D**, and **Chitale D**. Prognosis and categorization of HER2 fluorescent in-situ hybridization (FISH) results in patients with invasive breast cancer who received HER2 targeted agents: Analysis of 226 patients. *Modern Pathology* 2020; 33(3):100-101.

M. Alhamar, Henry Ford Health System, Detroit, MI, United States

Background: In management of invasive breast cancers (IBC), status of HER2 (ERBB2) gene serves as a strong prognostic predictor & predictive marker of response to HER2 Targeted Agents (HTA). There is significant heterogeneity in response to these agents in HER2- positive cases. Our aim was to determine the distribution of the status of HER2 by FISH in IBC along with its predictive implications. Design: IBC cases that were tested for HER2FISH & received HTA from 2006-2017 were identified. HER2FISH was interpreted using the ASCO/CAP

guidelines at the time of reporting. Cases were grouped as follows: 1) Monosomy (ratio ≥2.0, mean HER2/cell<4.0) 2) Co- Amplified (ratio<2.0, mean HER2/cell ≥6.0) 3) Low amplified (ratio ≥2.0, mean HER2/cell 4.0-5.9) 4) Amplified (ratio ≥2.0-2.99, mean HER2/cell >6) 5) Excessive Amplification (ratio ≥3.0) 6) 2013 Equivocal (ratio<2.0, mean HER2/cell 4.0-5.9) 7) Negative. Outcomes studied were recurrence, metastasis, second breast primary, disease specific survival (DSS) & overall survival (OS). Results: There were 226 cases, with median age 65 (range 26-98), 58% Caucasians, 24% African Americans, 1.5% others & 16.5% unknown. The median HER2FISH ratio was 2.47 (1.18-21) & HER2 signal/cell 5.71 (2.09-21). Table 1 shows categoric distribution of cases. 60/226-27% patients received neoadjuvant chemotherapy, 139/226-62% hormonal therapy, 187/226-83% adjuvant & 146/226-65% radiotherapy. The median follow up was 207 weeks (4.3-708). Overall, 165/226-73% patients were alive without disease, 17/226-7% alive with disease, 33/226-15% died of IBC & 11/226-5% died due to other causes. 31/226-14% patients developed metastasis, 7/226-3% local recurrence & 4/226-2% second breast primary. The category of HER2FISH status was significantly associated with OS (p<0.05-Figure1), higher HER2 amplification was associated with fewer deaths, possibly reflecting a better response to HTA. Her2FISH status also statistically significantly relates to metastasis (p=0.04-Figure 2) & second primary (p<0.05) but not with recurrence (p=0.09) or DSS (p=0.5) in our cohort. (Table presented) Conclusions: The current HER2FISH interpretation does not stratify as high or low amplification based on FISH results. In our study, we demonstrate that high HER2 amplification is significantly associated with longer OS; these patients seem to benefit more from HTA. We recommend reporting these categories when assessing HER2FISH in IBC. Larger, prospective longitudinal studies are needed to validate our findings.

Pathology

Alhamar M, **Gupta N**, **Oyedeji O**, **Hogan K**, **Sood A**, **Arora S**, **Schultz D**, **Jeong W**, **Williamson S**, **Menon M**, and **Hassan O**. Precision prostatectomy: Analysis of surgical pathology findings of a promising and novel surgical approach for patients with low to intermediate-risk prostate cancer. *Modern Pathology* 2020; 33(3):850-852.

M. Alhamar, Henry Ford Health System, Detroit, MI, United States

Background: Precision Prostatectomy (PP) is a novel surgical approach introduced at our institution to treat low to intermediate-risk prostate cancer. It includes radical resection of the dominant nodule (DN) side, with preservation of neurovascular bundle, capsule, & 5-10 mm of prostatic tissue on the contralateral side. Here we report on the surgical pathology findings and outcome data on PP. Design: Detailed pathological findings were studied from PP patients. Post-operative erectile function & biochemical recurrence (BCR) were studied. Clinical selection criteria for PP included: (1) PSA ≤15 ng/mL (2) clinical stage ≤cT2 (3) a dominant unilateral lesion with grade group (GG) ≤3 (4) no primary Gleason score ≥4 contralaterally. Results: A total of 77 patients were studied, with median age 59 (range 47-75). Median pre-operative PSA was 5.5 (1.4 -23) and median number of positive biopsies was 3 (1-9). A second mapping biopsy was performed in 35/77 (45%). Most (64/77, 83%) had frozen section evaluation of the precision side. Of the PP specimens, median GG was 2 (1-5), median tumor percentage was 6% (1-32%). Almost all (75/77, 97%) had a DN, whereas 2/77 (3%) showed scattered microscopic tumor foci. Median DN size was 20 mm (4-35) & most (60/77, 78%) had secondary nodule(s) (SN). Median number of SN was 2 (1-6) & median size was 8 mm (1-30). Positive resection margin was present in 33/77 (43%) with a median linear extent of 3 mm (0.5 - 48). This was at the DN in 16/33 (49%), SN in 10/33 (30%), & both in 7/33 (21%). The DN was incompletely excised in the PP side in 4 cases (3 of these were midline, whereas the diagnostic biopsy missed the DN in the 4th). For the remainder, positive margin was present on the radical side, which would render the same results as a radical prostatectomy (RP) approach. Overall 20/77 had positive margin at the PP side (See Table 1). Only one patient (1%) had a positive lymph node. Median follow up was 8 months (1-24). All patients had excellent results with post-op erectile function & 3 had BCR. BCR was not significantly correlated with the status of DN excision (p= 0.8) (Table & Figure1). (Table presented) Conclusions: PP promises excellent post-op erectile function compared to RP. Pre-op saturation biopsy to map the tumor may aid in optimizing cancer control in these patients. Although initial results are promising, longer follow up is needed to assess long-term outcomes.

Pathology

Alhamar M, **Hassan O**, **Sood A**, **Arora S**, **Jeong W**, **Williamson S**, **Menon M**, and **Gupta N**. Histopathologic features of prostate cancer in patients who underwent seminal vesicle-sparing radical prostatectomy: A novel surgical approach. *Modern Pathology* 2020; 33(3):849-850.

M. Alhamar, Henry Ford Health System, Detroit, MI, United States

Background: Incontinence and erectile dysfunction are common complications of radical prostatectomy (RP). Seminal vesicle (SV) involvement is found in 5-23% of RP, frequently with grade group (GG) 3-5. At our institution a novel seminal vesicle-sparing approach (SVSRP) has been introduced, with preservation of either one or both seminal SVs in a select group of patients to improve functional outcomes. Here we report on the surgical pathology findings on SVSRP. Design: All SVSRP were reported by a specialist genitourinary pathologist. Detailed pathologic findings

including grade, tumor size, number of tumor nodules, margin status, and pathologic stage were studied. Results: Specimens from 33 patients were studied with median age of 63 (range 51-80). In the diagnostic biopsy, 7 were Grade Group (GG) 1, 16 GG2, 6 GG3, 2 GG4, 1 GG5, and 1 not applicable (post hormonal therapy). Median number of biopsies taken was 12 (6-36) and median number positive biopsies was 3 (1-11). Half (16/33, 48%) had frozen section (FS) evaluation of the SV. Almost all (32/33) had bilateral sparing of SV, whereas in one FS of the SV base was positive and unilateral sparing of SV was performed. Median tumor percentage was 6% (1-30%). A dominant tumor nodule (DN) was identified in 31/33 (94%), whereas 2 had scattered microscopic tumor foci. Median size of the DN was 21 mm (11-30) and median number of secondary nodule(s) was 1 (1-6). Median GG of the DN was 2 (1-5). Positive margin was present in 20/33 (60%). However, only one (3%) had positive margin at the site of SVSRP. Median linear extent of positive margin was 3.5 mm (1-20 mm). Lymphovascular invasion was present in 2/33 (6%), 1/33 (3%) had bladder neck invasion, 1/33 (3%) had lymph node metastasis, 15/33 (45%) had extraprostatic extension, and 4/33 (12%) showed intraductal carcinoma. The case with positive margin at the SVSRP site was the case with unilateral (left) SV sparing. (Table). (Table presented) Conclusions: SVSRP is a promising surgical approach which may offer early return of continence compared to RP while allowing resection of clinically significant tumor. Although 60% of our cases had positive margins, only one case with aggressive disease had positive margin at the SVSRP site. The rest would have had positive margins with a conventional RP. Further refinement of selection criteria with additional pre-op or intra-op biopsies of the seminal vesicles may help to improve oncologic control in this surgical approach.

Pathology

Alkamachi B, **Alhamar M**, **Mehrotra H**, **Sanchez J**, **Schultz D**, and **Chitale D**. Evaluation of HER2 fluorescent in-situ hybridization (FISH) status in 274 patients with invasive breast cancer: Comparison of the last 3 ASCO/CAP guidelines for fish interpretation and its effect on HER2 status classification. *Modern Pathology* 2020; 33(3):102.

B. Alkamachi, Henry Ford Health System, Detroit, MI, United States

Background: HER2 gene status as a primary predictor of responsiveness to HER2-targeted therapies in invasive breast carcinomas (IBC), is assessed by in situ hybridization (ISH) for HER2 gene amplification or protein overexpression assessed by immunohistochemistry (IHC). We sought to access the influence of changes in HER2 FISH ASCO /CAP reporting guidelines from 2007, 2013 and 2018 on HER2 status. Design: This is a retrospective study of patients with IBC, who underwent HER2FISH testing between 2006 and 2017. At our institution, HER2 status is first determined by HER2IHC staining. All the HER2IHC equivocal (2+) cases are reflexed to HER2FISH. HER2FISH status was assessed by using Vysis dual FISH probe (Abbott Molecular, Inc., FDA Approved PathVysion HER-2 DNA Probe Kit). A comparative analysis was made based on 2007, 2013 and 2018 ASCO/CAP guidelines to assess HER2 status reclassification. Results: Complete data were available on 274 patients with equivocal HER2IHC results, 104 (38%) Caucasians, 52 (19%) African American, 4(1%) other, and 114 (42%) unknown. The results are summarized in tables 1-3 below. (Table presented) Conclusions: We observed 27.2% reclassification rate by using 2013 guidelines compared to 2007, lower threshold for positive (from equivocal, 20.7% of patients re-classified to positive and 6.5% to negative HER2 status). In contrast, the 2018 updates eliminated the FISH equivocal category with concomitant Her2IHC correlation and additional scoring of tumor nuclei. Implementing 2018 CAP guidelines led to 100% reclassification of 2007 equivocal cases into in 81.7% negative cases and 18.3% positive for HER2 status. Prospective data on survival is necessary to evaluate impact of 2018 guidelines on outcomes.

Pathology

Alkamachi B, **Zhu S**, **Elshaikh M**, and **Allo G**. Prognostic significance of depth and pattern of cervical stromal invasion in type 1 endometrial carcinoma. *Modern Pathology* 2020; 33(3):1005-1006.

B. Alkamachi, Henry Ford Health System, Detroit, MI, United States

Background: The prognostic significance of cervical stromal invasion (CSI) by endometrial carcinoma is well established, and patients with this form of invasion are offered similar adjuvant therapy. It is not clear whether characteristics of this form of invasion have prognostic implications. We aim in this study to investigate the prognostic significance of depth and pattern of cervical stromal invasion in patients with type 1 endometrial carcinoma. Design: This is a retrospective study of patients with type 1, FIGO stage 2 endometrial cancer, who were treated at our institution between 1991 and 2019. After IRB approval, we assessed microscopic depth of CSI (measured as distance from cervical surface to deepest point of invasion within cervical stroma), cervical stromal thickness, and pattern of invasion (based on endocervical adenocarcinoma previously described patterns A, B, and C). Clinical data were collected from the medical records. Descriptive analysis and Cox regression models were produced. Results: Material and data were available on 50 patients. Median age at diagnosis was 65(41-91) years, of which 30 patients had FIGO grade 1, 23 showed <50% myometrial invasion, 11 had angioinvasion, 40 had underwent lymph node dissection, and 42 received adjuvant radiation. Median depth of CSI was 3.5(0.5-20.0) mm, with median percentage invasion to cervical stromal thickness of 33.3(6.7-100)%. CSI to >2/3 of cervical stroma was found in 8 (16%) of

patients, and was associated with worse overall survival (OS) in univariable analysis (HR, 0.22; 95% CI, 0.06-0.75), and after controlling for age, race, grade, depth of myometrial invasion, angioinvasion, peritoneal washings, and adjuvant radiotherapy (HR, 0.08; 95% CI, 0.01-0.53). CSI of 5.0 mm or more, found in 16(32%) patients, was associated with tendency towards worse OS (HR, 3.1; 95% CI, 0.96 - 10.2), while CSI of 50% cervical stroma or more (n=17, 34%) or patterns of invasion were not associated with different OS on univariable analysis. Recurrence was present in 5(10%) of patients, significantly higher in those with >1/3 CSI (LH, 7.1; 0=0.008). (Figure presented) Conclusions: A small subset of type 1, FIGO stage 2 endometrial cancers shows extension to more than 2/3 of cervical stroma and exhibits worse overall survival. Subcategorization of stage 2 and therapy tailoring may be indicated in these patients. Further studies are needed.

Pathology

Al-Obaidy K, Eble J, Cheng L, Nassiri M, **Williamson S**, Idrees M, and Grignon D. Recurrent kras mutation is an early event in the development of papillary renal neoplasm with reverse polarity. *Modern Pathology* 2020; 33(3):846.

K. Al-Obaidy, Indiana University, School of Medicine, Indianapolis, IN, United States

Background: Papillary renal neoplasm with reverse polarity is a recently proposed distinct renal tumor. In addition to its unique morphologic and immunohistochemical features, a recent study showed that these tumors represent the only kidney tumor with recurrent KRAS mutation. Design: We reviewed a series of 177 previously retrieved cases of end stage kidneys at Indiana University for incidentally found non-mass forming papillary renal neoplasms with reverse polarity, using the same criteria suggested by Al-Obaidy et al. The tumors were composed of papillary or tubulopapillary architecture covered by a single layer of eosinophilic cells with finely granular eosinophilic cytoplasm and apically located round nuclei with inconspicuous nucleoli. No intracellular hemosiderin, psammoma bodies, mitotic figures, necrosis, or clusters of foamy macrophages should be present. Immunohistochemical staining (GATA-3, AMACR and vimentin) and polymerase chain reaction (PCR) for KRAS mutations was performed. Results: The cohort consisted of 8 cases from 7 patients, 4 were males and 4 were females, with an age range of 42-75 years (mean, 57 years, median 60 years) and a size range of 1-3 mm. All cases were positive for GATA-3 immunostain. AMACR and vimentin immunostains were performed on one and both were negative (Figure 1). Of the 8 cases identified, only 3 had successful PCR analysis (neoplasm sizes 3 mm). These were identified in 2 patients (one with bilateral neoplasms). KRAS mutations were present in all 3 neoplasms and were clustered in exon 2-codon 12: C.35 G>T (n = 2) or c.34 G>T (n = 1) resulting in p.Gly12Val and p.Gly12Cys alterations, respectively. An attempt to analyze the remaining 5 cases failed to detect any mutations, most likely due to the small size (1 mm), and a high likelihood of tissue loss with deeper sectioning despite microdissection attempts. One lesion with a KRAS mutation had an associated acquired cystic diseases associated renal cell carcinoma; that was negative for KRAS mutation. (Figure presented) Conclusions: The presence of KRAS mutations in small, clinically undetectable lesions provides a unique supportive finding to this proposed entity. In contrast to the size criteria used to define the clinical course of papillary adenoma vs carcinoma, the terminology "papillary renal neoplasms with reverse polarity" is recommended for all lesions identified regardless of the size as this study finds KRAS mutation to be an early event in their pathogenesis.

Pathology

Al-Obaidy K, **Williamson S**, Alruwaii F, Idrees M, and Ulbright T. Hepatoid yolk sac tumor (HYST), hepatocellular carcinoma (HCC) and hepatocytic teratoma (HT): A morphologic and immunohistochemical (IHC) study of 31 cases. *Modern Pathology* 2020; 33(3):847-848.

K. Al-Obaidy, Indiana University, School of Medicine, Indianapolis, IN, United States

Background: YST is known for its multiple patterns, which assist in its diagnosis. Purely hepatoid differentiation is rare, consisting of nests and cords of cells with abundant, eosinophilic to clear cytoplasm, well-defined cell borders, and round nuclei with prominent nucleoli. It is usually seen in metastases of patients with late recurrence, often years after orchiectomy, which complicates its recognition. Additionally, hepatocytic differentiation is a rare aspect of teratoma; it requires separation from HYST, and both should be distinguished from de novo HCC. We therefore investigated the morphologic and IHC features of these entities. Design: We retrieved 12 metastatic HYSTs (representing >90% of the tumor), 17 HCCs and 2 HTs (Figures 1-3, respectively) from tissue archives. Hematoxylin and eosin stained slides were reviewed to confirm each diagnosis. 4 µm-thick sections were stained with antibodies against SALL4, CK7, CK19, CDX2, glypican-3, arginase, HepPar-1, and villin in a Dako automated instrument. Results: The median and mean age of patients with HYST was 36 years (range, 20-63). 3 presented with metastatic disease and 9 recurred at a median of 10 years (range, 2-24) after initial diagnosis. The tumors formed trabeculae and cords, occasional gland-like structures, and had frequent basement membrane deposits. SALL4 (100%), glypican-3 (100%), CK19 (85%), CDX2 (85%) and villin (75%) were prominently positive; HepPar-1 stained rare single tumor cells (70%) and arginase was infrequently reactive (26%) (patchy in 1 and rare cells in 4). In HCC, HepPar-1 (94%) and arginase (82%) were diffusely positive, whereas glypican-3 (35%) and villin (12%) were less

common. SALL4, CK19 and CDX2 were negative. HTs formed sheets of hepatocytes with abortive ducts and portal triads (Figure 1). The hepatocytes stained positively for glypican-3, arginase, and HepPar-1 (2/2). Villin was positive in 1. CK7 (1/2) and CK19 (2/2) highlighted ductular formation. SALL4 and CDX-2 were negative (0/2). (Figure presented) Conclusions: In summary, SALL4, glypican-3, CDX2, and CK19 are sensitive markers for HYST, as is widely scattered single cell reactivity with HepPar-1. SALL4, CK19 and CDX2 positivity are specific in the differential with HCC, as are prominent intercellular basement membrane deposits. HTs show more consistent staining for arginase and HepPar-1 than HYST; they lack SALL4, contrasting with HYST.

Pathology

Dhillon J, **Williamson S**, Desai S, Menon S, Shah R, Sirohi D, Balzer B, Varma M, Luthringer D, Nigam L, Roy P, Kaushal S, Midha D, Aron M, Jain K, Naik S, Baisakh M, Kini L, Sharma S, Sable M, Jain E, Samra S, Ro J, Osunkoya AO, Vankalakunti M, Parwani A, Gopalan A, Magi-Galluzzi C, and Mohanty S. Reporting trends, practices, and resource utilization in neuroendocrine tumors of the prostate gland: A survey of genitourinary (GU) pathologists. *Modern Pathology* 2020; 33(3):880.

J. Dhillon, Moffitt Cancer Center, Tampa, FL, United States

Background: Neuroendocrine tumors of the prostate gland were recently classified in the WHO. Despite increasing experience in this area, the specifics and the new clinical and molecular emerging data from prostate cancers treated by contemporary androgen deprivation therapies, as well as primary lesions, need refinement of the diagnostic terminology to encompass the full spectrum of neuroendocrine differentiation. Use of immunohistochemistry (IHC) as a diagnostic, prognostic, and/or predictive tool remains unclear. This study aims at questionnaire- and scenario-based survey among the GU pathologists. Although some of the questions may appear superfluous, this topic based on discussions at multiple levels has evoked surprisingly passionate responses from some who have adopted a "more objective approach" using IHC, citing that recommendations imply that IHC is necessary to be certain. Design: An online survey containing 35 questions was undertaken by 39 GU pathologists (with 5 to 10 years, >10 years and >20 years experience) from four continents, focusing on ascertaining practice patterns in this area. Specific questions included whether, when, and how the respondents classify neuroendocrine differentiation/mixed carcinomas/Paneth cell change/neuroendocrine carcinoma (small, SCC/large cell, LCNEC) of the prostate gland. Additionally questions were posed regarding frequency and indications of IHC with respect to these issues. Some therapy and biomarker-related questions were added as well. De-identified respondent data was tabulated and analyzed by routine statistics. The responses were scored in percentage for each question. Results: 70% and 63% of the responders correctly diagnosed a SCC and mixed acinar adenocarcinoma-SCC, respectively. 37% pathologists felt the need of IHC in a SCC, even if the morphology is classical. A majority (87%) of the responders have the correct idea about the immunopanel and therapeutic options for a SCC. Most importantly, pathologists (85%) correctly mentioned that there is no role of TTF1 indifferentiating pulmonary from prostatic SCC, and determination of site of origin of a high-grade neuroendocrine carcinoma has no importance, as these are treated similarly. In the mixed carcinoma cases, exact quantitation of both the elements, grading of the acinar component as the therapy includes both androgen deprivation and platinum-based chemotherapy, and importance of androgen receptor immunoreactivity have been voted by 85% responders. 49% failed to diagnose Paneth cell-like differentiation, nor were they clear about its prognostic implications. Conclusions: 1. Awareness on morphological features and management of SCC across the pathologists was consistent and IHC work up was necessary for a subset of pathologists for confirmation. 2. Majority failed to recognize Paneth cell-like differentiation, nor were they clear about its prognostic implications, while a small subset failed to identify small cell-like PIN. 3. There still lies some confusion in recognizing Gleason 10 acinar adenocarcinoma and large cell neuroendocrine carcinoma. 4. In the mixed carcinoma cases, there seems to have a legitimate call for appropriate IHC work up, including prostatic and neuroendocrine markers and exact quantitation and grading of the acinar component as the therapy includes both androgen deprivation and platinum-based chemotherapy. 5. Based on the responses, practising trends are different between North America and Asia. Further study and consensus on best practice guidelines based on NCCN parameters are needed to provide guidance with regards to the appropriate indications for IHC use in the various scenarios and patterns of neuroendocrine features in the prostate gland.

Pathology

Fang H, Yabe M, Zhang X, Kim Y, **Shen Y**, Shao L, Ji Y, Wu X, Zheng G, Shen Q, Yuan Y, He R, Chen D, Medeiros LJ, and Hu S. Myelodysplastic syndrome with t(6;9)(p22;q34.1) categorized as acute myeloid leukemia: A large multicenter study of 105 cases. *Modern Pathology* 2020; 33(3):1281.

H. Fang, University of Texas, MD Anderson Cancer Center, Houston, TX, United States

Background: The t(6;9)(p23;q34.1)/DEK-NUP214 is a recurrent genetic abnormality that occurs in a subset of cases of acute myeloid subset leukemia (AML) and rarely in myelodysplastic syndrome (MDS). However, it is not known whether all cases with t(6;9) (p23;q34.1) should be categorized as AML when blast count is <20%. In this study, we

characterized and compared the clinicopathologic features of patients with MDS versus AML harboring t(6;9)(p23;q34.1). Design: Cases of AML or MDS carrying t(6;9)(p23;q34.1), diagnosed in 10 institutions, were collected and their clinicopathologic features were reviewed retrospectively. Results: The study cohort included 105 patients with t(6;9): 75 patients with AML and 30 with MDS. In all 98 patients with available data, the t(6;9) was detected at initial diagnosis of AML or MDS. There were 53 men and 52 women with a median age of 44 years (range, 10- 82) at initial diagnosis. Patients with AML were slightly younger than patients with MDS (median: 39 vs. 52 years) but this difference was not significant (P=0.08). As expected, patients with AML presented with leukocytosis and higher blast counts in peripheral blood and bone marrow (P=0.009, 0.004, <0.0001, respectively). However, no significant differences were observed in the hemoglobin level, platelet count, and basophil percentages in peripheral blood and bone marrow between patients with MDS versus AML. The median follow up time was 21.8 months. Of 30 patients with MDS, 17 (57%) developed AML after a median interval of 29 months (range, 1-94). There was no difference in overall survival between patients with MDS versus AML (median: 33.9 vs. 23.7 months, P=0.45). Fifty-seven patients received stem cell transplant during their clinical course. Patients who received transplant had longer overall survival than the non-transplant group (median: not reached vs. 17.3 months, P<.0001). After stratification by status of transplant, however, there were no significant differences between patients with MDS and patients with AML. Conclusions: Our data support the idea that myeloid neoplasms associated with t(6;9), irrespective of blast percentage, are best categorized as acute myeloid leukemia with recurrent genetic abnormalities, analogous to the WHO classification guidelines for myeloid neoplasms with t(8;21) and inv(16). Aggressive treatment strategies such as stem cell transplant might improve the survival of patients with myeloid neoplasms associated with t(6;9).

Pathology

Mehrotra H, Favazza L, Kezlarian B, Fowler R, Hanson N, and **Tibbetts R**. Resolution of a modified CDC definition for carbapenem resistant enterobacteriaceae (CRE) using a rapid multiplex, cartridge-based molecular assay for the confirmation of carbapenemase genes. *Modern Pathology* 2020; 33(3):1880-1881.

H. Mehrotra, Henry Ford Health System, Detroit, MI, United States

Background: CRE have emerged as a global threat due to their potential to cause invasive infections, often with high mortality rates and are primarily healthcare, associated, with a potential for spread to community settings. The CDC updated its definition of CRE as resistant to a carbapenem: MIC of ≥4 ug/ml for doripenem, meropenem, or imipenem, ≥2 ug/ml for ertapenem, OR documented to produce a carbapenemase. CRE are resistant to carbapenems primarily through the expression of carbapenemase genes (CP-CRE) carried on plasmids, which are easily transferrable hence the CDC recommendation to isolate patients with CP-CRE. However, production of AmpC/ESBL β-lactamases with a decrease of outer membrane proteins (OMP) (non-CP-CRE) can also lead to a higher ertapenem MIC, of which OMPs are not transferable but meet the CDC definition for CRE. The purpose of this study was to develop an algorithm to differentiate CP-CRE from non-CP-CRE using carbapenem MIC and confirmation by a rapid molecular assay. Design: Genetic and phenotypic testing was performed on 61 isolates of Enterobacteriaceae with MICs to ertapenem ranging from <0.25 ug/ml to >64 ug/ml using PCR to detect blaKPC, blaAmpC and blaESBL, and SDS-PAGE to determine OMP production. These data were used to create an algorithm to define CRE in our lab using MIC, the presence of resistance genes and/or OMP production. 40 isolates, including positive and negative controls, with known antibiotic susceptibilities were defined by this algorithm and confirmed by commercially available FDA approved rapid multiplex PCR for carbapenemase genes. Results: Using this algorithm, we observed 5 discordant PCR results giving us 85% concordance. However, we believe that 3 of these were due to loss of plasmids by repeated freeze-thaw cycles and intend to reanalyze MICs to confirm this. On eliminating these 3 isolates, we have 93% concordance.(Table presented) Conclusions: A combination of the CDC definition for CRE and lowered breakpoints to ertapenem led to overcalling non-CP-CRE as CPCRE may have resulted in inappropriate patient isolation, which is known to have negative patient outcomes and increase costs. Implementation of a multiplex PCR to rule out carbapenemases in isolates with elevated ertapenem but susceptible meropenem MICs resulted in a more sensitive and specific identification of CP-CRE.

Pathology

Onwubiko I, **Rodgers S**, **Oyedeji O**, **Taneja K**, **Hassan O**, **Gupta N**, and **Williamson S**. Metastatic carcinoma suggestive of urothelial carcinoma in the absence of known high-stage urothelial carcinoma: Analysis of clinical and pathologic parameters. *Modern Pathology* 2020; 33(3):950.

I. Onwubiko, Henry Ford Health System, Detroit, MI, United States

Background: Urothelial carcinoma that is pT2 or higher is known to be an aggressive disease. However, we have encountered occasional biopsies of metastatic carcinoma with features suggestive of urothelial carcinoma in patients who have no known high-stage primary tumor. Design: We searched our pathology database for reports indicating metastatic carcinoma with findings suggesting urothelial carcinoma. Clinical and pathologic data were reviewed to identify patients without a known high-stage primary tumor. Results: Search identified 272 specimens showing

metastatic carcinoma suggestive of urothelial carcinoma. Of these, 14 patients had no known primary tumor of pT2 or higher on comprehensive pathology and electronic medical record review, including 10 (71%) pT1, 3 (21%) carcinoma in situ, and 2 (14%) pTa. A substantial number (n=8, 57%) had tumors of the renal pelvis (n=5), ureter (n=1), or prostatic urethra (n=2). Metastatic sites included the lungs (n=4), liver (n=4), bone / soft tissue (n=3), brain (n=2), and lymph nodes (n=2). Unique patients included one with a renal pelvis high-grade papillary urothelial carcinoma concurrent with multiple sites of clear cell adenocarcinoma thought to be also of urinary tract origin. Another patient had prominent inflammatory / myxoid changes surrounding the ureter that was resected to relieve obstruction; however, no carcinoma was sampled in this specimen. Conclusions: A high proportion of patients with metastatic carcinoma suggestive of urothelial carcinoma in the absence of a high-stage primary tumor (pT2 or higher) have had a primary tumor in uncommon sites, including the renal pelvis, prostatic urethra, or ureter (57%). This raises the possibility that current staging parameters and pathologic evaluation for non-bladder primary tumors are not entirely adequate for assessing their risk.

Pathology

Smith S, McKenney J, Paner G, Al-Ahmadie H, Aron M, Berney D, Cheville J, Colecchia M, Compérat E, da Cunha I, Hansel D, Hes O, Hirsch M, Jimenez R, Kaushal S, Kuroda N, Kench J, Kryvenko O, Lopez-Beltran A, Luthringer D, Magi-Galluzzi C, Mehra R, Menon S, Rao P, Sangoi A, Schultz L, Simko J, Stohr B, Hoon Tan P, Tsuzuki T, Varma M, **Williamson S**, Zhou M, Zynger D, Moch H, Netto GJ, True L, Ro J, Trpkov K, Montironi R, Srigley J, Humphrey P, Epstein J, Reuter V, and Amin M. Urothelial dysplasia: Diagnostic value in clinical practice 20 years since the 1998 who/isup consensus. *Modern Pathology* 2020; 33(3):977-978.

S. Smith, Virginia Commonwealth University, School of Medicine, Richmond, VA, United States

Background: In the 1980-90s, flat neoplastic urothelial lesions were categorized as mild, moderate, and severe dysplasia, and urothelial carcinoma in situ (CIS). Three subsequent WHO classifications have condensed these lesions into urothelial dysplasia and CIS, with CIS including many lesions with moderate to severe dysplasia. Many suggest 'dysplasia' is infrequent in diagnostic specimens, but little is known of the use of this term in contemporary practice. Design: We surveyed 45 academic uropathologists practicing in 12 countries on their diagnostic practices regarding 'dysplasia'. Deidentified responses to both specific questions regarding diagnostic practice and opinions regarding dysplasia diagnosis in prior and future practice were tabulated. Results: Most respondents diagnosed dysplasia (82%) in the past 10 years, though many noted rarity of usage. Of those who have diagnosed dysplasia (N=37), 38% had done so in a de novo setting, although the majority (86%) made the diagnosis in the setting of antecedent urothelial neoplasm. Further, 31% have diagnosed dysplasia in the upper tract, 39% have diagnosed multifocal dysplasia, 56% diagnosed it with concurrent CIS or papillary neoplasm, and 33% used IHC to assess dysplasia versus CIS. Of those who did not diagnose dysplasia (N=8, 18%), all have reported the possibility of dysplasia in biopsies labeled 'atypical'. Most (83%) consider dysplasia a relevant concept in the pathogenesis of urothelial neoplasms and nearly all (91%) support greater study. Only a minority (11%) could identify any important work supporting dysplasia as a distinct entity in two decades. Overall, nearly half of the participants were for (56%) or against (44%) prospective use of 'dysplasia' in practice. Conclusions: Among academic uropathologists, there is striking variation in the use of 'urothelial dysplasia' across diagnostic settings. Most who use the term use it in biopsies with prior or concurrent urothelial neoplasia; some avoid the term, preferring 'atypia' for lesions falling short of CIS. This discrepancy confirms need for a diagnostic term for lesions with features believed neoplastic but insufficient to designate as CIS. The decrease in urologic pathologists who favor future use of 'dysplasia' diagnosis (56%) compared to those reporting prior use of the term (84%) may signal the opportunity to promulgate improved terminology to communicate diagnostic concern and uncertainty. Future study will be needed to inform recommended follow-up and management.

Pathology

Taneja K, and **Williamson S**. Persistent challenges in nuclear grading of clear cell renal cell carcinoma. *Modern Pathology* 2020; 33(3):980-981.

K. Taneja, Henry Ford Health System, Detroit, MI, United States

Background: The World Health Organization (WHO) and International Society of Urological Pathology (ISUP) grading system for renal cell carcinoma now focuses on nucleolar prominence as the main criterion. We aimed to investigate how this system is implemented in certain scenarios. Design: An online survey was circulated via e-mail to a group of genitourinary pathology specialists (GU) and shared publicly via social media (including via Twitter and 3 Facebook pathology groups, 2 focusing on urologic pathology and 1 large general surgical pathology group). The survey included a mixture of descriptive questions and images. Results: In total, 91 responses were received from non-trainee pathologists, 77 self-identified as GU and 14 as non-GU. The vast majority reported using the ISUP/WHO system rather than Fuhrman (92% GU, 79% non-GU). Most reported not requiring nucleoli to be eosinophilic when determining visibility (77% GU and 72% non-GU). Most indicated that nucleoli visualized at high magnification at all

(40×, composing an entire high-power field), would be considered grade 2, even if nucleoli are not eosinophilic / large (67% GU and 57% non- GU). Distinguishing grade 2 from 3 (10× magnification) yielded a similar response with 63% GU and 61% non-GU. When shown a photomicrograph taken at 40× magnification with visible but relatively small basophilic nucleoli (Figure A), most reported grade 2 (93% GU and 79% non-GU). For an image with more prominent nucleoli described as visible at 10×, 82% of GU and 71% non-GU reported grade 3. Respondents estimated using grade 1 in 5% or less of resection cases (73% GU, 57% non-GU, with one-third estimating 2% of cases or less). For multinucleated cells with bland individual nuclei (Figure B), most (84% GU, 86% non-GU) would not consider this grade 4. (Figure presented) Conclusions: The ISUP/WHO grading system for renal cell carcinoma has gained relatively widespread acceptance; however, some uncertainty remains regarding the degree of nucleolar prominence that warrants a higher grade. Despite the official descriptions requiring nucleoli to be eosinophilic, most pathologists do not require this in practice. Most respondents estimate that they use grade 1 very rarely. It is not entirely clear how tumor cells with multiple, non-bizarre nuclei should be handled, although most do not consider this inherently grade 4.

Pathology

Vijayanarayanan A, **Shaw B**, **Hogan K**, **Inamdar K**, and **Menon M**. The need for rapid cytogenetics in the era of vyxeos therapy for acute myeloid leukemia with myelodysplasia related changes (aml-mrc). *Modern Pathology* 2020; 33(3):1402.

A. Vijayanarayanan, Henry Ford Health System, Detroit, MI, United States

Background: AML-MRC criteria includes i) history of Myelodysplastic syndrome (MDS) or Myelodysplastic syndrome/Myeloproliferative neoplasm (MDS/MPN) or ii) MDS- related cytogenetic abnormality or iii) Multilineage dysplasia (>50 % dysplasia in at least 2 lineages). Recently, the drug Vyxeos was approved for the treatment of adults with newly diagnosed therapy related AML or AML-MRC and confers a significantly better survival than standard therapy. We aimed to identify the proportion of cases diagnosed as AML-MRC solely based on MDS associated cytogenetic abnormality (i.e. not meeting the morphologic criteria and/or not having history of MDS or MDS/MPN). Design: A cohort of 64 AML-MRC cases were re-examined morphologically to assess for and exactly quantify the degree of dysplasia. We examined bone marrow aspirate smears, touch preps, bone marrow biopsy and clot sections to assess for dysplasia. We categorized dysplasia into three categories; less than 10%, 10-50% and >50%. The other categories were normal/no dysplasia and not enough nonblast cells to accurately assess for dysplasia. Results: Out of 64 cases of AML- MRC, 53 had complex cytogenetics (83%), 5 had del (5q) or t (5q) (8%), 4 cases had -7 or del (7q) (6%) and 2 had other MDS associated abnormalities (3%). Only 30% of cases had more than 50% dysplasia in two or more lineages. 70% of cases required either a relevant clinical history (MDS or MDS/MPN) or MDS associated cytogenetic abnormalities for AML-MRC diagnosis. More than 50% dysplasia in two lineages was seen in 34% of cases with complex cytogenetics, 20% of del (5q)/ t(5q) cases and 0% of -7/ del (7q) cases. Most frequently reported dysplastic cell line was myeloid (45%) followed by megakaryocytic (38%) followed by erythroid (16%). 22% of cases had cytogenetic abnormalities other than those tested on a routine MDS or AML FISH panel. Conclusions: 63% of our cases needed an MDS associated cytogenetic abnormality to render a diagnosis of AML-MRC. 22% of cases had cytogenetic abnormalities which would have been missed on a routine MDS or AML FISH panel. In the absence of an AML-MRC diagnosis, patients are put on the standard 7+3 chemotherapy regimen and cannot be generally switched to Vyxeos at a later time. Considering the routine turnaround time of 7-21 days for conventional chromosomal analysis, it is imperative to have a preliminary cytogenetic result (generally 5 cell based) or a rapid chromosomal microarray analysis within 2-3 days of AML diagnosis to enable Vyxeos therapy.

Pathology

Williamson S, Al-Obaidy K, Smith S, Phillips C, Przybycin C, and Grignon D. Distal tubular hyperplasia: A novel form of renal tubular proliferation distinct from papillary adenoma. *Modern Pathology* 2020; 33(3):991-992.

S. Williamson, Henry Ford Health System, Detroit, MI, United States

Background: Papillary adenoma is the only established incipient or preneoplastic lesion in the current classification of renal cell neoplasms. However, we have occasionally encountered a more diffuse proliferation in the setting of chronic renal disease that appears different from papillary adenoma, warranting further study. Design: Renal specimens showing an unusual proliferation of tubules were retrieved from the authors' archives and studied for clinical and pathologic parameters and immunohistochemical profile. A series of end-stage renal disease specimens from one of the institutions was retrospectively reviewed to establish incidence. Results: In total, 12 specimens were retrieved showing this tubular proliferation diffusely (n=7) or focally (n=5). Eight were identified from a series of 177 end-stage renal disease specimens from one institution (5%), of which 5 were focal (3%) and 3 diffuse (2%). Eight patients had concurrent renal cell tumors including clear cell (n=4), papillary (n=3), clear cell papillary (n=1), or acquired cystic kidney disease (n=1) renal cell carcinoma (and papillary adenomas, n=5). Four occurred with no neoplasm. All patients had end-stage renal disease, 1 being an explanted allograft; however, there was no definite commonality to the patients' renal disease. In most (n=9), the predominant pattern was indentation of chronic

inflammation into renal tubules forming small polypoid structures (Figure A); however, 3 patients had predominantly hyperplastic epithelium with less conspicuous inflammation in the cores (Figure B). In 7 patients both patterns were appreciable at least focally, whereas the remainder (with focal, minimal lesions) had only the inflammatory pattern. Immunohistochemistry was consistently positive for cytokeratin 7, high molecular weight cytokeratin (sometimes weak), and GATA3. Staining for alpha-methylacyl-CoA racemase (AMACR) was negative or weak, dramatically less intense than that of papillary neoplasms or proximal tubules. CD3 and CD20 showed a mixture of B and T lymphocytes in the inflammatory areas. Figure 1 - 1035 Conclusions: We describe a novel form of renal tubular proliferation that differs from papillary adenoma in that it shows weak or negative AMACR immunoreaction and in some cases is widely dispersed in sampled renal parenchyma. Based on consistent staining for high molecular weight cytokeratin and GATA3, this appears to be a proliferation of distal tubules, with both inflammatory and hyperplastic patterns.

Pathology

Wu J, **Deebajah M**, Lai Z, Micale M, and Yu L. Utilization of deep neural network in recognition of bcr/abl gene rearrangements in fluorescence in situ hybridization images. *Modern Pathology* 2020; 33(3):1493-1494.

J. Wu, ZKShuangHe LLC, Beijing, China

Background: Interphase dual-color fluorescence in situ hybridization (iFISH) has been used for identification of BCR/ABL gene rearrangements in Chronic Myeloid Leukemia (CML). Artificial intelligence, particularly deep neural network (DNN), has achieved major breakthroughs in image analysis and classification. The purpose of this study is to see if DNN can be successfully trained to recognize of BCR/ABL gene rearrangements in FISH images. Database of single-cell images (101 positive, 278 negative), and original multi-cell images (33 positive, 118 negative). The classification model was built on single-cell images and use to test the end-to-end performance only on multi-cell images. The fully automatic analysis pipeline consists of single-cell detection and single-cell classification modules (Fig 1). The detection pipeline following systematic steps; starting with the RGB images are first converted into greyscale. After which we set an intensity threshold to remove the text and apply median blurring to de-noise the image. Referring to the topological structure, we detect the closing contours and generate a bounding box on the contour region. The small and overlapping regions are removed or merged. We crop and resize the original image in the bounding box regions into a dimension of 255 and rescale the RGB value into -1 to 1 as the input to the classification network. The deep neural network architecture for single-cell classification is based on VGG, which consists of 16 layers of convolution, max pooling and fully connected operations. The network outputs a binary vector indicating positive and negative. We use Adam optimizer and Cross-entropy loss to optimize the training process. During the training time, we apply flip operation as data augmentation. Results: Our end-to-end performance matrices showed a total f1-score of 98% and recall of 98%. (Table presented) Conclusions: Our study shows the deep neural network can be trained to reliably recognize BCR/ABL gene rearrangements in FISH images with pathologist-level of accuracy.

Pathology

Zarbo R, **Schmidt M**, **Althaver N**, **Whiteley L**, **Gupta N**, **Chitale D**, and **Goerke D**. Histomorphologic, immunohistochemical and molecular validation of 2.5-hour processed large specimens/tumor resections with tissue-tek xpress x120. *Modern Pathology* 2020; 33(3):1685.

R. Zarbo, Henry Ford Hospital, Detroit, MI, United States

Background: We seek to shorten histology preanalytic time to meet pathology reporting needs of 16 weekly specialty Tumor Boards in the precision medicine oncology program of the Henry Ford Cancer Institute. Design: We validated an extended 2.5-hour microwave and vacuum-assisted processing cycle (Tissue-Tek Xpress x120, Sakura Finetek USA, Torrance, CA) for large specimens/tumor resections compared to our 5.5-10 hour microwave process (Logos, Milestone, Kalamazoo, MI). Specimens were collected from operating rooms of Henry Ford Hospital, dissected fresh at 2-3mm thickness into mirror images and fixed in 10% neutral buffered formalin, minimum 6, maximum 72 hours. Xpress bench processing step post formalin fixation was 30 minutes of isopropranol-based pre-processing solution for water/formalin extraction followed by 2 hours of Xpress processor time composed of 2 x 30-minute microwave temperature controlled isopropyl alcohol and acetone based dehydration/xylene-free clearing retorts and 2 x 30-minute heated paraffin impregnation retorts using vacuum. Blocks from both Xpress and Logos pathways were cut and stained together to minimize inter-run variation. 3 pathologists assessed slides for histomorphology (188 tumor and 67 normal tissues), and 24 selected tumors in a tissue microarray (TMA) (2 cores from each tumor: 10 lung, 10 colon, 4 renal cell) for immunohistochemical (IHC) staining with 22 antibodies and molecular validation of DNA/RNA quality and next generation sequencing (NGS) assay using TruSeq Amplicon 48-gene Cancer Panel (Illumina, San Diego, CA). Results: All tissues were equivalent for histologic interpretation. There were no differences in IHC profiles of TMA tissues for PAX5, PAX8, CD45, CD3, CD10, CD20, TTF-1, Napsin A, CK5/6, CK7, cytokeratins AE1/AE3, CAM 5.2, p63, p40, EMA, vimentin, carbonic anhydrase IX, AMACR, CDX2, Ki67, and beta catenin. DNA/RNA quality

between the 2 processors was comparable (Table 1a, 1b) as was quality of DNA/RNA purity and amplicon fragment length (200, 300, 400 bp). There was good correlation between % uniformity of coverage, but poor for depth of coverage. All samples passed NGS quality matrix criteria for reporting variants and no differences in hot spot mutations were detected (Table 2). (Figure presented) Conclusions: This validated Xpress processor for large specimens/tumor resections will reduce current technical process time by 55-75% and promotes our goal of continuous laboratory production flow to meet the demand for faster surgical pathology diagnostic reporting.

Public Health Sciences

Ahsan B, **Thanikachalam K**, **Robison A**, **Li J**, **Datta I**, **Onwubiko I**, **Khan G**, and **Raoufi M**. Molecular characteristics of pancreatic neuroendocrine tumors, do they correlate with metastases? *Modern Pathology* 2020; 33(3):1687-1688.

B. Ahsan, Henry Ford Health System, Detroit, MI, United States

Background: Pancreatic neuroendocrine tumors (PNET) have an unpredictable biological behavior that cannot be reliably predicted by histological and clinical manifestations. We performed next generation sequencing (NGS) on PNET to understand the molecular pathogenesis and to identify potential biomarkers correlating with metastases and survival. Design: Hybrid capture-based comprehensive genomic profiling was performed on both primary and metastatic PNET from 28 patients. Metastatic sites were grouped as lymph nodes and distant metastases (consisted of liver followed by bone). NGS was performed on genomic DNA & RNA isolated from formalin-fixed paraffin embedded tissue using the whole exome NGS assay covering 20,000 genes. Average number of DNA reads was 52 million at 3:1 somatic to germline. All variants were detected with >99% confidence based on allele frequency and amplicon coverage, with an average sequencing depth of coverage >500x and an analytical sensitivity of 5%. Tumor mutation burden and MSI status were compared using the two-sample t-test between tumor types. Frequency of mutations in each gene was compared between tumor types using the Fisher's exact test. To account for multiple comparisons, the False Discovery Rate was estimated using Benjamini-Hochberg procedure. R package "maftools" was used to summarize and visualize the findings. Results: Mutation burden was higher in primary tumors with metastases versus primary tumors without metastases (p=0.034) while no significance was found in MSI status between these two groups. Among the 20 mutated genes, MUC4 and MEN1 were the most frequently mutated genes in both primary and metastatic tumors (fig1&2). At a p-value threshold of 0.2, two distant metastatic tumors had mutation on PCNX3 gene, while none were found in lymph node metastases (p=0.057). In addition, more mutations on TGFBR1 in distant metastases compared to lymph node metastases (p=0.154). We also found that three primary tumors with metastases had mutations on E2F4, HRNR, LRP1B genes while none were found in primary tumors with no metastases (p=0.2). (Figure presented) Conclusions: Decoding the complexity and unpredictable nature of PNET has been perplexing and the subject of many several research projects. The current project, the first ever done on the subject, with an attempt to distinguish the metastatic vs non-metastatic tumors try to underlie the difference of molecular signature between the two. Further studies are needed to consolidate the findings and bring them to clinical practice.

Radiation Oncology

Alkamachi B, **Zhu S**, **Elshaikh M**, and **Allo G**. Prognostic significance of depth and pattern of cervical stromal invasion in type 1 endometrial carcinoma. *Modern Pathology* 2020; 33(3):1005-1006.

B. Alkamachi, Henry Ford Health System, Detroit, MI, United States

Background: The prognostic significance of cervical stromal invasion (CSI) by endometrial carcinoma is well established, and patients with this form of invasion are offered similar adjuvant therapy. It is not clear whether characteristics of this form of invasion have prognostic implications. We aim in this study to investigate the prognostic significance of depth and pattern of cervical stromal invasion in patients with type 1 endometrial carcinoma. Design: This is a retrospective study of patients with type 1, FIGO stage 2 endometrial cancer, who were treated at our institution between 1991 and 2019. After IRB approval, we assessed microscopic depth of CSI (measured as distance from cervical surface to deepest point of invasion within cervical stroma), cervical stromal thickness, and pattern of invasion (based on endocervical adenocarcinoma previously described patterns A, B, and C). Clinical data were collected from the medical records. Descriptive analysis and Cox regression models were produced. Results: Material and data were available on 50 patients. Median age at diagnosis was 65(41-91) years, of which 30 patients had FIGO grade 1, 23 showed <50% myometrial invasion, 11 had angioinvasion, 40 had underwent lymph node dissection, and 42 received adjuvant radiation. Median depth of CSI was 3.5(0.5-20.0) mm, with median percentage invasion to cervical stromal thickness of 33.3(6.7-100)%. CSI to >2/3 of cervical stroma was found in 8 (16%) of patients, and was associated with worse overall survival (OS) in univariable analysis (HR, 0.22; 95% CI, 0.06-0.75), and after controlling for age, race, grade, depth of myometrial invasion, angioinvasion, peritoneal washings, and adjuvant radiotherapy (HR, 0.08; 95% CI, 0.01-0.53). CSI of 5.0 mm or more, found in 16(32%) patients, was associated with tendency towards worse OS (HR, 3.1; 95% CI, 0.96 - 10.2), while CSI of 50% cervical stroma or

more (n=17, 34%) or patterns of invasion were not associated with different OS on univariable analysis. Recurrence was present in 5(10%) of patients, significantly higher in those with >1/3 CSI (LH, 7.1; 0=0.008). (Figure presented) Conclusions: A small subset of type 1, FIGO stage 2 endometrial cancers shows extension to more than 2/3 of cervical stroma and exhibits worse overall survival. Subcategorization of stage 2 and therapy tailoring may be indicated in these patients. Further studies are needed.

Urology
Alhamar M, **Hassan O**, **Sood A**, **Arora S**, **Jeong W**, **Williamson S**, **Menon M**, and **Gupta N**. Histopathologic features of prostate cancer in patients who underwent seminal vesicle-sparing radical prostatectomy: A novel surgical approach. *Modern Pathology* 2020; 33(3):849-850.

M. Alhamar, Henry Ford Health System, Detroit, MI, United States

Background: Incontinence and erectile dysfunction are common complications of radical prostatectomy (RP). Seminal vesicle (SV) involvement is found in 5-23% of RP, frequently with grade group (GG) 3-5. At our institution a novel seminal vesicle-sparing approach (SVSRP) has been introduced, with preservation of either one or both seminal SVs in a select group of patients to improve functional outcomes. Here we report on the surgical pathology findings on SVSRP. Design: All SVSRP were reported by a specialist genitourinary pathologist. Detailed pathologic findings including grade, tumor size, number of tumor nodules, margin status, and pathologic stage were studied. Results: Specimens from 33 patients were studied with median age of 63 (range 51-80). In the diagnostic biopsy, 7 were Grade Group (GG) 1, 16 GG2, 6 GG3, 2 GG4, 1 GG5, and 1 not applicable (post hormonal therapy). Median number of biopsies taken was 12 (6-36) and median number positive biopsies was 3 (1-11). Half (16/33, 48%) had frozen section (FS) evaluation of the SV. Almost all (32/33) had bilateral sparing of SV, whereas in one FS of the SV base was positive and unilateral sparing of SV was performed. Median tumor percentage was 6% (1-30%). A dominant tumor nodule (DN) was identified in 31/33 (94%), whereas 2 had scattered microscopic tumor foci. Median size of the DN was 21 mm (11-30) and median number of secondary nodule(s) was 1 (1-6). Median GG of the DN was 2 (1-5). Positive margin was present in 20/33 (60%). However, only one (3%) had positive margin at the site of SVSRP. Median linear extent of positive margin was 3.5 mm (1-20 mm). Lymphovascular invasion was present in 2/33 (6%), 1/33 (3%) had bladder neck invasion, 1/33 (3%) had lymph node metastasis, 15/33 (45%) had extraprostatic extension, and 4/33 (12%) showed intraductal carcinoma. The case with positive margin at the SVSRP site was the case with unilateral (left) SV sparing. (Table). (Table presented) Conclusions: SVSRP is a promising surgical approach which may offer early return of continence compared to RP while allowing resection of clinically significant tumor. Although 60% of our cases had positive margins, only one case with aggressive disease had positive margin at the SVSRP site. The rest would have had positive margins with a conventional RP. Further refinement of selection criteria with additional pre-op or intra-op biopsies of the seminal vesicles may help to improve oncologic control in this surgical approach.

Books and Book Chapters

Surgery
Rountree KM, Barazi H, and Aulick NF. “Mondor Disease”. StatPearls. Treasure Island (FL), StatPearls Publishing Copyright © 2020, StatPearls Publishing LLC. 2020. PMID: 30855866. Full Text

Henry Ford Macomb
WVU School of Medicine
Ohio Valley medical Center

Initially described in 1939 by Henri Mondor, Mondor Disease classically describes a syndrome of sclerosing superficial thrombophlebitis of the veins of the anterior thoracic wall. The most commonly involved vessel is the superior epigastric vein producing a palpable cord in the inferior outer quadrant of the breast . Also known as Mondor's Cord, this rare clinical entity has also been reported as affecting the superficial penile veins . Fage is credited with first describing cording as a sign of superficial thrombophlebitis in 1870.

HFHS Publications on COVID-19

Behavioral Health Services/Psychiatry
Xiang X, **Ning Y**, and Kayser J. The Implications of COVID-19 for the Mental Health Care of Older Adults: Insights from Emergency Department Social Workers. *J Gerontol Soc Work* 2020; Epub ahead of print. PMID: 32543294. Request Article

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Shah PB, Welt FGP, Mahmud E, Phillips A, Kleiman NS, Young MN, Sherwood M, Batchelor W, **Wang DD**, Davidson L, **Wyman J**, Kadavath S, Szerlip M, Hermiller J, Fullerton D, and Anwaruddin S. Triage Considerations for Patients Referred for Structural Heart Disease Intervention During the COVID-19 Pandemic: An ACC/SCAI Position Statement. *JACC Cardiovasc Interv* 2020; 13(12):1484-1488. PMID: 32250751. Full Text

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Freeman EE, McMahon DE, Hruza GJ, Irvine AD, Spuls PI, Smith CH, Mahil SK, Castelo-Soccio L, Cordoro KM, Lara-Corrales I, Naik HB, Alhusayen R, Ingram JR, Feldman SR, Balogh EA, Kappelman MD, Wall D, Meah N, Sinclair R, Beylot-Barry M, Fitzgerald M, French LE, **Lim HW**, Griffiths CEM, and Flohr C. International Collaboration and Rapid Harmonization across Dermatologic COVID-19 Registries. *J Am Acad Dermatol* 2020; Epub ahead of print. PMID: 32562840. Full Text

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Pandey AS, Daou BJ, Tsai JP, Zaidi SF, Salahuddin H, Gemmete JJ, Oliver MJ, Singer J, Elder TA, Mbabuike N, Adel JG, Gujrati Y, Saleemi MA, Siddiqui FM, Elias AE, **Rehman MF**, **Marin H**, **Chebl AB**, **Kole M**, Wilseck JM, Kazmierczak CD, Mick JM, Majjhoo AQ, Naravetla BR, Rayes M, Luqman AW, Richards BF, Kelkar P, Burgess R, Thompson BG, Chaudhary N, Mazaris PA, Qahwash O, Razak MA, and Jumaa MA. Letter: COVID-19 Pandemic-The Bystander Effect on Stroke Care in Michigan. *Neurosurgery* 2020; Epub ahead of print. PMID: 32496518. Full Text

Emergency Medicine
Suleyman G, **Fadel RA**, **Malette KM**, **Hammond C**, **Abdulla H**, **Entz A**, **Demertzis Z**, **Hanna Z**, **Failla A**, **Dagher C**, **Chaudhry Z**, **Vahia A**, **Abreu Lanfranco O**, **Ramesh M**, **Zervos MJ**, **Alangaden G**, **Miller J**, and **Brar I**. Clinical Characteristics and Morbidity Associated With Coronavirus Disease 2019 in a Series of Patients in Metropolitan Detroit. *JAMA Netw Open* 2020; 3(6):e2012270. PMID: 32543702. Full Text

Infectious Diseases
Suleyman G, **Fadel RA**, **Malette KM**, **Hammond C**, **Abdulla H**, **Entz A**, **Demertzis Z**, **Hanna Z**, **Failla A**, **Dagher C**, **Chaudhry Z**, **Vahia A**, **Abreu Lanfranco O**, **Ramesh M**, **Zervos MJ**, **Alangaden G**, **Miller J**, and **Brar I**. Clinical Characteristics and Morbidity Associated With Coronavirus Disease 2019 in a Series of Patients in Metropolitan Detroit. *JAMA Netw Open* 2020; 3(6):e2012270. PMID: 32543702. Full Text

Internal Medicine
Suleyman G, **Fadel RA**, **Malette KM**, **Hammond C**, **Abdulla H**, **Entz A**, **Demertzis Z**, **Hanna Z**, **Failla A**, **Dagher C**, **Chaudhry Z**, **Vahia A**, **Abreu Lanfranco O**, **Ramesh M**, **Zervos MJ**, **Alangaden G**, **Miller J**, and **Brar I**. Clinical Characteristics and Morbidity Associated With Coronavirus Disease 2019 in a Series of Patients in Metropolitan Detroit. *JAMA Netw Open* 2020; 3(6):e2012270. PMID: 32543702. Full Text

Neurology
Pandey AS, Daou BJ, Tsai JP, Zaidi SF, Salahuddin H, Gemmete JJ, Oliver MJ, Singer J, Elder TA, Mbabuike N, Adel JG, Gujrati Y, Saleemi MA, Siddiqui FM, Elias AE, **Rehman MF**, **Marin H**, **Chebl AB**, **Kole M**, Wilseck JM, Kazmierczak CD, Mick JM, Majjhoo AQ, Naravetla BR, Rayes M, Luqman AW, Richards BF, Kelkar P, Burgess R, Thompson BG, Chaudhary N, Mazaris PA, Qahwash O, Razak MA, and Jumaa MA. Letter: COVID-19 Pandemic-The Bystander Effect on Stroke Care in Michigan. *Neurosurgery* 2020; Epub ahead of print. PMID: 32496518. Full Text

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Mohammad I, Berlie HD, Lipari M, **Martirosov AL**, Duong AA, Faraj M, **Bacon O**, and Garwood CL. Ambulatory Care Practice in the COVID-19 Era: Redesigning Clinical Services and Experiential Learning. *JACCP Journal of the American College of Clinical Pharmacy* 2020; Epub ahead of print. PMID: Not assigned. Full Text

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Lamb CR, Desai NR, Angel L, Chaddha U, Sachdeva A, Sethi S, Bencheqroun H, Mehta H, Akulian J, Argento AC, **Diaz-Mendoza J**, Musani A, and Murgu S. Use of Tracheostomy During the COVID-19 Pandemic: CHEST/AABIP/AIPPD: Expert Panel Report. *Chest* 2020; Epub ahead of print. PMID: 32512006. Full Text

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