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Henry Ford Health System

Henry Ford Health System Publication List – April 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 128 unique citations listed this month; articles are listed first, followed by conference abstracts and books and book chapters. 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

Berry R, **Brawner CA**, Kipa SG, **Stevens C**, **Bloom C**, and **Keteyian SJ**. Telemedicine Home-Based Cardiac Rehabilitation: A Case Series. *J Cardiopulm Rehabil Prev* 2020; Epub ahead of print. PMID: 32301763. Full Text

Division of Cardiovascular Medicine, Henry Ford Hospital, Detroit, Michigan (Mr Berry and Drs Brawner and Keteyian); Blue Cross Blue Shield of Michigan, Detroit, Michigan (Dr Kipa); Virtual Care, Henry Ford Health System, Detroit, Michigan (Ms Stevens); and Health Alliance Plan, Detroit, Michigan (Dr Bloom).

DETAILS OF THE CLINICAL CASE: In this case series report, we review 2 patients who were among the first to participate in the Henry Ford telemedicine home-based cardiac rehabilitation (TM-HBCR) program. These patients had barriers to full participation in a facility-based cardiac rehabilitation (CR) program due to return to work and access to transportation. However, they were willing and able to participate in the TM-HBCR program. DISCUSSION: The two cases discussed herein are examples of individuals who likely would not have fully participated in CR if the only option available was a facility-based program. While HBCR is not an option for all patients, it does address several barriers that are known to limit participation in facility-based CR for some individuals. SUMMARY: Technology has made it possible to provide the key components of a facility-based CR program through a TM-HBCR model using a secure connection to the patients via their personal mobile device.

Anesthesiology

Ladny M, Smereka J, **Ahuja S**, Szarpak L, Ruetzler K, and Ladny JR. Effect of 5 different cervical collars on optic nerve sheath diameter: A randomized crossover trial. *Medicine (Baltimore)* 2020; 99(16):e19740. PMID: 32311968. Full Text

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BACKGROUND: There is considerable evidence that prolonged use of cervical collars potentially cause detrimental effects including increase in optic nerve sheath diameter (ONSD) among healthy volunteers. Different types of cervical collars immobilize cervical spine variably well and may presumably differently influence the venous compression and hence the intracranial pressure. We therefore aimed to evaluate the influence of cervical spine immobilization with 5 different types of cervical collars on ONSD measured noninvasively by ultrasound on healthy volunteers. METHODS: We conducted a randomized crossover trial including 60 adult healthy volunteers. Control assessment of the optic nerve sheath thickness was performed in both sagittal and transverse planes. Patient was placed supine on a transport stretcher, cervical collar was placed, and ONSD measurement was performed after 5 and 20 minutes. During the next days, the procedure was repeated

with random allocation of participants and random cervical collar. RESULTS: Sixty healthy volunteers were included in our study. ONSD left diameter [mm] for the baseline was 3.8 [interquartile range (IQR): 3.65-3.93)] mm. Using AMBU after 5 min, ONSD was changed up to 4.505 (IQR 4.285-4.61; P < .001) mm. The largest change at 5 minutes and 20 minutes was using Philly 4.73 (IQR: 4.49-4.895; P < .001) and 4.925 (IQR: 4.65-5.06; P < .001), respectively. Necklite reported the lower change in ONSD: 3.92 (IQR: 3.795-4; P = 1.0) mm in 5 minutes and 3.995 (IQR: 3.875 - 4.1; P = 1.0) mm in 20 minutes. ONSD right diameter [mm] for the baseline was 3.8 (IQR 3.675-3.9) mm. Using AMBU after 5 minutes, ONSD was changed up to 4.5 (IQR 4.21-4.6) mm. The largest change at 5 minutes and 20 minutes was using Philly 4.705 (IQR 4.455-4.9) and 4.93 (IQR 4.645-5.075), respectively. Necklite reported the lower change in ONSD -33.9 (IQR 3.795-3.99) mm in 5 minutes and 3.995 (IQR 3.86-4.09) mm in 20 minutes. CONCLUSION: We report significant increase of ONSD from the baseline after cervical collar placement among healthy volunteers at 5 minutes and 20 minutes interval. In addition, no significant difference was noted between ONSD measurements at 5 and 20 minutes. Clinicians should take proactive steps to assess the actual need of cervical collar case by case basis. Nonetheless, when needed, Necklite moldable neck brace seems to be a reasonable option.Registration: ClinicalTrials database (www.clinicaltrials.gov, NCT03609879).

Anesthesiology

Ruetzler K, Smereka J, Abelairas-Gomez C, Frass M, Dabrowski M, Bialka S, Misiolek H, Plusa T, Robak O, Aniolek O, Ladny JR, Gorczyca D, **Ahuja S**, and Szarpak L. Comparison of the new flexible tip bougie catheter and standard bougie stylet for tracheal intubation by anesthesiologists in different difficult airway scenarios: a randomized crossover trial. *BMC Anesthesiol* 2020; 20(1):90. PMID: 32312225. Full Text

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Department of Emergency Medical Service, Wroclaw Medical University, Wroclaw, Poland.
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BACKGROUND: Incidence of difficult endotracheal intubation ranges between 3 and 10%. Bougies have been recommended as an airway adjunct for difficult intubation, but reported success rates are variable. A new generation flexible tip bougie appears promising but was not investigated so far. We therefore compared the new flexible tip with a standard bougie in simulated normal and difficult airway scenarios, and used by experienced anesthesiologists. METHODS: We conducted a observational, randomized, cross-over simulation study. Following standardized training, experienced anesthesiologists performed endotracheal intubation using a Macintosh blade and one of the bougies in six different airway scenarios in a randomized sequence: normal airway, tongue edema, pharyngeal obstruction, manual cervical inline stabilization, cervical collar stabilization, cervical collar stabilization and pharyngeal obstruction. Overall success rate with a maximum of 3 intubation attempts was the primary endpoint. Secondary endpoints included number of intubation attempts, time to intubation and dental compression. RESULTS: Thirty-two anesthesiologist participated in this study between January 2019 and May 2019. Overall success rate was similar for the flexible tip bougie and the standard bougie. The flexible tip bougie tended to need less intubation attempts in more difficult airway scenarios. Time to intubation was less if using the flexible tip bougie compared to the standard bougie. Reduced severity of dental compression was noted for the flexible tip bougie in difficult airway scenarios except cervical collar stabilization. CONCLUSION: In this simulation study of normal and difficult airways scenarios, overall success rate was similar for the flexible tip and standard bougie. Especially in more difficult airway scenarios, less intubation attempts, and less optimization maneuvers were needed if using the flexible tip bougie. TRIAL REGISTRATION: clinicaltrials.gov Identifier: NCT03733158. 7th November 2018.

Behavioral Health Services/Psychiatry

Clark-Sienkiewicz SM, and **Miller-Matero LR**. An Investigation of Racial Disparities in Weight Loss Outcomes: Roux-en-Y Gastric Bypass Versus Sleeve Gastrectomy. *J Racial Ethn Health Disparities* 2020; 7(2):234-237. PMID: 31667712. Request Article

Center for Health Policy and Health Services Research, Henry Ford Health System, One Ford Place, Detroit, MI, 48202, USA.
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OBJECTIVE: The current study aimed to test if racial disparities in weight loss outcomes between African American and Caucasian patients who underwent bariatric surgery were due to pre-surgical BMI differences. METHODS: Primary data was collected from pre-surgical evaluations conducted at a midwestern hospital. A retrospective chart review was conducted of 136 patients. Patient age and race, type of procedure, and pre- and 1-year post-surgical BMI were collected. RESULTS: African American patients were less likely to undergo bariatric surgery compared with Caucasian patients. Caucasian patients undergoing Roux-en-Y Gastric Bypass (RYGB) had a greater change in BMI compared with African American patients who underwent RYGB. Significant differences in weight loss outcomes were not found among patients who underwent the sleeve gastrectomy. Race was not related to pre-surgical BMI or procedure type. CONCLUSION: Despite pre-surgical BMI typically being higher among African American patients, this was not found in the current study. Pre-surgical BMI may not explain the racial disparities in weight loss post-bariatric surgery that are found between African American and Caucasian patients. Future studies should consider psychosocial, environmental, and cultural influences on racial disparities.

Behavioral Health Services/Psychiatry
Hecht LM, Schwartz N, **Miller-Matero LR**, **Braciszewski JM**, and Haedt-Matt A. Eating pathology and depressive symptoms as predictors of excessive weight gain during pregnancy. *J Health Psychol* 2020; Epub ahead of print. PMID: 32301343. Full Text

Illinois Institute of Technology, USA.
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Excessive gestational weight gain is associated with negative outcomes and the identification of contributing psychosocial factors may be useful in prevention and intervention. Pregnant women (N = 70) completed self-report measures of eating pathology, depressive symptomatology, and gestational weight gain. Global eating pathology was positively associated with overvaluation of shape and weight, dietary restraint, frequency of binge eating, and depressive symptoms. Depressive symptoms significantly predicted excessive gestational weight gain, while global eating pathology predicted excessive gestational weight gain at a trend level. Results suggest that depressive symptoms more strongly predict excessive gestational weight gain than eating pathology.

Behavioral Health Services/Psychiatry
Phillips JM, and **Longoria JN**. Addressing the neurodevelopmental needs of children and adolescents with congenital heart disease: A review of the existing intervention literature. *Child Neuropsychol* 2020; 26(4):433-459. PMID: 31672097. Request Article

Department of Behavioral Health, Henry Ford Health System, Detroit, MI, USA.

Congenital heart disease (CHD) is among the most prevalent birth defects in the United States. Given that children with CHD are at risk for differences with development, learning, and psychosocial functioning, effective intervention becomes a central tenant of recommendations following neuropsychological consultation and evaluation. The primary focus of this review is to summarize available interventions for children and adolescents with CHD. The existing CHD literature has concentrated on early developmental services, psychopharmacological treatment, and need for academic supports. The literature is limited with regard to intervention studies that target cognitive deficits and psychosocial difficulties. To address this discrepancy, efficacious interventions that have been used to mitigate these concerns within other medical groups are also discussed in an effort to provide options for alternative recommendations and services. The current paper is intended to facilitate comprehensive care for cardiac patients by providing clinicians with a review of the available intervention literature, as well as potential interventions that may serve as supplemental strategies in the interim.

Cardiology/Cardiovascular Research
Arora L, Krishnan S, Subramani S, Sharma A, Hanada S, **Villablanca PA**, Nunez-Gil IJ, and Ramakrishna H. Functional Tricuspid Regurgitation: Analysis of Percutaneous Transcatheter Techniques and Current Outcomes. *J Cardiothorac Vasc Anesth* 2020; Epub ahead of print. PMID: 32247538. Full Text

Division of Critical Care, Vascular and Organ Transplant Anesthesiology, Department of Anesthesia, University of Iowa Carver College of Medicine, Iowa City, IA.
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Division of Cardiothoracic Anesthesiology Solid Organ Transplant and Critical Care, Department of Anesthesia, University of Iowa Carver College of Medicine, Iowa City, IA.
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Interventional Cardiology, Hospital Clinico Universitario San Carlos, Madrid, Spain.
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Cardiology/Cardiovascular Research
Azzalini L, **Alaswad K**, Uretsky BF, Agostoni P, Galassi AR, Harada Ribeiro M, Filho EM, Morales-Victorino N, Attallah A, **Gupta A**, Zivelonghi C, Montorfano M, Bellini B, and Carlino M. Multicenter experience with the antegrade fenestration and reentry technique for chronic total occlusion recanalization. *Catheter Cardiovasc Interv* 2020; Epub ahead of print. PMID: 32320133. Full Text

The Zena and Michael A. Wiener Cardiovascular Institute, Icahn School of Medicine at Mount Sinai, New York, New York, USA.
Division of Interventional Cardiology, Cardio-Thoracic-Vascular Department, San Raffaele Scientific Institute, Milan, Italy.
Department of Cardiology, Henry Ford Hospital, Detroit, Michigan, USA.
Department of Cardiology, University of Arkansas for Medical Sciences (UAMS) and Central Arkansas Veterans Health System (CAVHS), Little Rock, Arkansas, USA.
Hartcentrum, Ziekenhuis Netwerk Antwerpen (ZNA) Middelheim, Antwerp, Belgium.
Department of PROMISE, University of Palermo, Palermo, Italy.
Department of Cardiology, Royal Brompton & Harefield Hospital, London, UK.
SOS CARDIO Hospital, Florianopolis, Santa Catarina, Brazil.
Heart Institute, Sao Paulo University School of Medicine, Sao Paulo, Sao Paulo, Brazil.
Interventional Cardiology, Santa Casa de Misericordia de Maceio, Maceio, Alagoas, Brazil.
Department of Cardiology, Adolfo Lopez Mateos, ISSSTE, Mexico City, Mexico.
Ascension St. John Hospital, Detroit, Michigan, USA.

OBJECTIVES: We aimed to evaluate the efficacy and safety of antegrade fenestration and reentry (AFR) for chronic total occlusion (CTO) recanalization in a multicenter registry. BACKGROUND: Adoption of antegrade dissection/reentry (ADR) for CTO recanalization has been limited, and novel ADR techniques are needed. METHODS: AFR involves the balloon-induced creation of multiple fenestrations between the false and true lumen. A targeted true lumen reentry is subsequently achieved with a low tip-load polymer-jacketed guidewire. Following the initial description and dissemination of AFR, patients undergoing AFR-based CTO recanalization at nine centers were included in the present registry. Study endpoints were AFR success, procedural success, and target-lesion failure (TLF) on follow-up. RESULTS: We included 41 patients. Mean J-CTO score was 2.5 +/- 1.4. In 80.5% of cases, AFR was performed after failed antegrade wire escalation. Another ADR technique was used before AFR in one-third of cases. AFR achieved distal true lumen reentry in n = 27/41 (65.9%) cases. In n = 14/41 (34.1%) cases with AFR failure, use of alternative techniques led to successful CTO recanalization in eight additional patients. The overall technical and procedural success rates were 85.4% and 82.9%, respectively. No AFR-related complications were observed. One-year TLF rate was 8.3% overall, with no differences between successful and failed AFR. CONCLUSIONS: We report on AFR feasibility in a multicenter registry of patients undergoing CTO recanalization. We observed a moderate success rate, coupled with the absence of complications. Moreover, even a failed AFR attempt did not preclude the use of alternative techniques to achieve recanalization. Further studies should confirm and extend our findings.

Cardiology/Cardiovascular Research
Azzalini L, Tzanis G, Mashayekhi K, Uretsky BF, Ojeda S, Pan M, Rinfret S, Avran A, **Alaswad K**, Yamane M, Karmpaliotis D, Brilakis ES, Carlino M, and Ybarra LF. Solving Challenging Situations and Complications in Everyday Percutaneous Coronary Intervention Using Chronic Total Occlusion Techniques. *J Invasive Cardiol* 2020; 32(3):E63-e72. PMID: 32123144. Request Article

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The field of chronic total occlusion (CTO) percutaneous coronary intervention (PCI) has witnessed a dramatic evolution in the last decade. The challenging nature of CTO interventions involves regularly dealing with support-related issues, uncrossable/undilatable lesions, manipulation of equipment in the subadventitial (also known as "subintimal") space, and the treatment of complications such as perforation and equipment loss or entrapment. The CTO experience has provided numerous techniques to the creative operator facing challenges in the non-CTO PCI setting. Herewith, we discuss an armamentarium of techniques routinely used in CTO-PCI, which can also be utilized in interventions for non-occlusive coronary artery disease and have the potential to improve the efficacy and safety of these procedures.

Cardiology/Cardiovascular Research
Bayes-Genis A, Liu PP, **Lanfear DE**, de Boer RA, Gonzalez A, Thum T, Emdin M, and Januzzi JL. Omics phenotyping in heart failure: the next frontier. *Eur Heart J* 2020; Epub ahead of print. PMID: 32337540. Full Text

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Department of Medicine, Universitat Autonoma Barcelona.
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Department of Cardiology, University of Groningen, University Medical Center, Groningen, The Netherlands.
Program of Cardiovascular Diseases, CIMA Universidad de Navarra and IdiSNA, Pamplona, Spain.
Institute of Molecular and Translational Therapeutic Strategies (IMTTS), Hannover Medical School, Hannover, Germany.
Institute of Life Sciences, Scuola Superiore Sant'Anna, Pisa, Italy.
Fondazione Toscana G. Monasterio, Pisa, Italy.
Cardiology Division, Department of Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA.

This state-of-the-art review aims to provide an up-to-date look at breakthrough omic technologies that are helping to unravel heart failure (HF) disease mechanisms and heterogeneity. Genomics, transcriptomics, proteomics, and metabolomics in HF are reviewed in depth. In addition, there is a thorough, expert discussion regarding the value of omics in identifying novel disease pathways, advancing understanding of disease mechanisms, differentiating HF phenotypes, yielding biomarkers for diagnosis or prognosis, or identifying new therapeutic targets in HF. The combination of multiple omics technologies may create a more comprehensive picture of the factors and physiology involved in HF than achieved by either one alone and provides a rich resource for predictive phenotype modelling. However, the successful translation of omics tools as solutions to clinical HF requires that the observations are robust and reproducible and can be validated across multiple independent populations to ensure confidence in clinical decision-making.

Cardiology/Cardiovascular Research
Berry R, **Brawner CA**, Kipa SG, **Stevens C**, **Bloom C**, and **Keteyian SJ**. Telemedicine Home-Based Cardiac Rehabilitation: A Case Series. *J Cardiopulm Rehabil Prev* 2020; Epub ahead of print. PMID: 32301763. Full Text

Division of Cardiovascular Medicine, Henry Ford Hospital, Detroit, Michigan (Mr Berry and Drs Brawner and Keteyian); Blue Cross Blue Shield of Michigan, Detroit, Michigan (Dr Kipa); Virtual Care, Henry Ford Health System, Detroit, Michigan (Ms Stevens); and Health Alliance Plan, Detroit, Michigan (Dr Bloom).

DETAILS OF THE CLINICAL CASE: In this case series report, we review 2 patients who were among the first to participate in the Henry Ford telemedicine home-based cardiac rehabilitation (TM-HBCR) program. These patients had barriers to full participation in a facility-based cardiac rehabilitation (CR) program due to return to work and access to transportation. However, they were willing and able to participate in the TM-HBCR program. DISCUSSION: The two cases discussed herein are examples of individuals who likely would not have fully participated in CR if the only option available was a facility-based program. While HBCR is not an option for all patients, it does address several barriers that are known to limit participation in facility-based CR for some individuals. SUMMARY: Technology has made it possible to provide the key components of a facility-based CR program through a TM-HBCR model using a secure connection to the patients via their personal mobile device.

Cardiology/Cardiovascular Research
Brener MI, Burkhoff D, **Basir MB**, and **Alqarqaz M**. Pressure-Volume Analysis Illustrating Left Ventricular Unloading by a Percutaneous Transvalvular Left Ventricular to Aortic Pump. *Circ Heart Fail* 2020; 13(4):e006788. PMID: 32295408. Full Text

Division of Cardiology, Columbia University Medical Center, New York, NY (M.I.B.).
Cardiovascular Research Foundation, New York, NY (D.B.).
Division of Cardiology, Henry Ford Hospital System, Detroit, MI (M.B.B., M.A.).

Cardiology/Cardiovascular Research
Choi AD, Geske JB, Lopez-Mattei JC, Parwani P, **Wang DD**, Winchester DE, Sengupta PP, Zoghbi WA, Shaw LJ, Chandrashekhar YS, and Blankstein R. Cardiovascular Imaging Through the Prism of Modern Metrics. *JACC: Cardiovascular Imaging* 2020; 13(5):1256-1269. PMID: Full Text

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Since its inception in 2008, JACC: Cardiovascular Imaging (iJACC) has served as an important publication for all contemporary aspects of cardiovascular imaging. Understanding the dissemination trends in cardiovascular imaging has traditionally been evaluated through citations that assess interest in the research community. Recently, social media, alternative metrics (Altmetrics), and other modern metrics have enabled a more broader understanding of the interests of clinical readership. Through the prism of Altmetrics, this review discusses the most impactful studies across the spectrum of cardiovascular imaging within and outside of iJACC during a 3-year period (2017 to 2019). The top 100 Altmetrics iJACC articles in this timeframe, included articles with the highest impact with the combination of high Altmetrics (median: 66; interquartile range [IQR]: 56 to 108), high citations (median: 26; IQR: 17 to 34), and high downloads (median: 9,626; IQR: 5,770 to 11,435). This review aims to provide a framework to understand how to incorporate these metrics for a modern approach to dissemination of knowledge in the field of cardiovascular imaging.

Cardiology/Cardiovascular Research
Dabbagh MF, **Aurora L**, **D'Souza P**, **Weinmann AJ**, **Bhargava P**, and **Basir MB**. Cardiac Tamponade Secondary to COVID-19. *JACC Case Rep* 2020; Epub ahead of print. PMID: 32328588. Request Article

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A 67-year-old female presented with upper respiratory symptoms and was diagnosed with COVID-19. She was found to have a large hemorrhagic pericardial effusion with echocardiographic signs of tamponade and mild left ventricular impairment. Clinical course was complicated by development of Takotsubo cardiomyopathy. She was treated with pericardiocentesis, colchicine, corticosteroids and hydroxychloroquine with improvement in symptoms.

Cardiology/Cardiovascular Research
Gupta A, **Fouad L**, **Basir M**, **Neupane S**, **Zaidan M**, **Koenig G**, **Alqarqaz M**, **Villablanca PA**, **O'Neill WW**, and **Alaswad K**. Safety and effectiveness of MANTA vascular closure device after large-bore mechanical circulatory support: Real-world experience. *Cardiovascular Revascularization Medicine* 2020; Epub ahead of print. PMID: Not assigned. Full Text

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Background: Real world safety and effectiveness of MANTA vascular closure device (VCD) for large bore arteriotomy closure after decannulation of mechanical circulatory support (MCS) devices is not known. Methods: All consecutive patients who underwent large bore arteriotomy closure with MANTA VCD following decannulation of MCS between February to October 2019 at a large tertiary care academic medical center were included. Safety and effectiveness of MANTA VCD was assessed on immediate post-closure angiogram for 23 access sites, and immediate post-closure duplex arterial ultrasound or manual vascular examination for 1 access site each. Technical success was defined as achievement of arteriotomy closure in absence of major bleeding or access site endovascular or surgical intervention. Results: A total of 25 MANTA VCD were placed in 22 unique patients by 7 different operators. A 14 Fr or 18 Fr MANTA VCD was used in 15 (60%) and 10 (40%) of deployments, respectively via transfemoral (n = 23, 92%) or transaxillary (n = 2, 8%) access. Technical success was achieved in 24 of 25 (96%) cases. Minor access site bleeding occurred in 3 patients (12%) and failure of MANTA VCD with major access site bleeding occurred in 1 patient (4%) requiring endovascular balloon tamponade. No cases of retroperitoneal bleeding, collagen plug embolization, covered stent placement, or surgical vascular repair were observed. Conclusion: In this single center experience, the use of MANTA VCD for large bore arteriotomy closure following percutaneous decannulation of MCS devices appears to be safe and effective. Larger multicenter studies of efficacy, safety, and cost-effectiveness are needed.

Cardiology/Cardiovascular Research
Kaafarani M, Saw J, Daniels M, Song T, **Rollet M**, Kesinovic S, Lamorgese T, **Kubiak K**, Qi Z, Pantelic M, **O'Neill W**, and **Wang DD**. Role of CT imaging in left atrial appendage occlusion for the WATCHMAN™ device. *Cardiovascular Diagnosis and Therapy* 2020; 10(1):45-58. PMID: Not assigned. Full Text

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Computed tomography (CT) plays a key role in the peri-procedural planning of left atrial appendage occlusion (LAAO) device placement and post-procedural evaluation. The geometric variability of the interatrial septum, left atrium, and the left atrial appendage morphology can be fully visualized and intuitively appreciated through CT-derived, patient-specific 3D model unique to each individual's anatomy. This review further defines the strengths and limitations of CT peri-procedural imaging in the planning of LAAO.

Cardiology/Cardiovascular Research
Neupane S, **Gupta A**, **Basir M**, and **Alaswad K**. Chronic total occlusion percutaneous coronary interventions: identifying patients at risk of complications. *Expert Rev Cardiovasc Ther* 2020; Epub ahead of print. PMID: 32345070. Request Article

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Introduction: Angina refractory to medical therapy and providing complete revascularization (after acute coronary syndrome or in patients with ischemic cardiomyopathy) are common indications for CTO PCI. Unfortunately, CTO PCI is associated with higher rates of complications when compared with non-CTO PCI.Areas covered: In this article, we review available studies on risk prediction in CTO PCI and outline strategies to avoid complications.Expert opinion: Identifying patients at increased risk of periprocedural major adverse cardiovascular events (MACE) is of great importance. It enhances the conversations about the risk and benefits of CTO PCI and it allows for shared decision making when deciding to undergo or forego such procedures.

Cardiology/Cardiovascular Research
Saxena A, Garan AR, Kapur NK, **O'Neill WW**, Lindenfeld J, Pinney SP, Uriel N, Burkhoff D, and Kern M. Value of Hemodynamic Monitoring in Patients With Cardiogenic Shock Undergoing Mechanical Circulatory Support. *Circulation* 2020; 141(14):1184-1197. PMID: 32250695. Full Text

Maimonides Medical Center, Brooklyn, NY (A.S.).
Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA (A.R.G.).
Tufts Medical Center, Boston, MA (N.K.K.).
Henry Ford Health System, Detroit, MI (W.W.O.).
Vanderbilt University Medical Center, Nashville, TN (J.L.).
Zena and Michael Wiener Cardiovascular Institute, Icahn School of Medicine at Mount Sinai, New York (S.P.P.).
Columbia University Irving Medical Center, Weill Cornell Medicine, New York (N.U.).
Cardiovascular Research Foundation, New York (D.B.).
University of California Irvine and VA Long Beach Healthcare System (M.K.).

The recent widespread availability and use of mechanical circulatory support is transforming the management and outcomes of cardiogenic shock (CS). Clinical decision-making regarding the optimization of therapies for patients with CS can be guided effectively by hemodynamic monitoring with a pulmonary artery catheter (PAC). Because several studies regarding the benefit of PACs are ambiguous, the use of PACs is variable among clinicians treating patients with CS. More notable is that PAC use has not been studied as part of a randomized, controlled trial in patients with CS with or without mechanical circulatory support. Standardized approaches to hemodynamic monitoring in these patients can improve decision-making and outcomes. In this review, we summarize the hemodynamics of CS and mechanical circulatory support with PAC-derived measurements, and provide a compelling rationale for the use of PAC monitoring in patients with CS receiving mechanical circulatory support.

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 Coronavirus Disease 2019 (COVID-19) Pandemic: An ACC /SCAI Consensus Statement. *Catheter Cardiovasc Interv* 2020; Epub ahead of print. PMID: 32251546. Full Text

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The COVID-19 pandemic has strained health care resources around the world causing many institutions to curtail or stop elective procedures. This has resulted in the inability to care for patients valvular and structural heart disease (SHD) in a timely fashion potentially placing these patients at increased risk for adverse cardiovascular complications including congestive heart failure 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 versus the risk of delaying a needed procedure. In this document, we suggest guidelines as to how to triage patients in need of SHD interventions and provide a framework of how to decide when it may be appropriate to proceed with intervention despite the ongoing pandemic. In particular, we address the triage of patients in need of trans-catheter aortic valve replacement and percutaneous mitral valve repair. We also address procedural issues and considerations for the function of structural heart disease teams during the COVID-19 pandemic. This article is protected by copyright. All rights reserved.

Cardiology/Cardiovascular Research
So CY, **Wang DD**, **Kang G**, **Villablanca PA**, **Frisoli T**, and **O'Neill WW**. Vacuuming the LAA: Left Atrial Appendage Thrombectomy Using AngioVac to Facilitate Percutaneous Mitral Balloon Valvuloplasty. *Structural Heart* 2020; Epub ahead of print. PMID: Not assigned. Full Text

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Cardiology/Cardiovascular Research
Villablanca PA, **Lee J**, **Wang DD**, **Frisoli T**, **So CY**, **Kang G**, **O'Neill WW**, and **Eng MH**. Transseptal puncture through an Amplatzer Atrial Septal Occluder for edge-to-edge repair with MitraClip NTr system. *Cardiovasc Revasc Med* 2020; Epub ahead of print. PMID: 32224042. Request Article

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Center for Health Policy and Health Services Research
Clark-Sienkiewicz SM, and **Miller-Matero LR**. An Investigation of Racial Disparities in Weight Loss Outcomes: Roux-en-Y Gastric Bypass Versus Sleeve Gastrectomy. *J Racial Ethn Health Disparities* 2020; 7(2):234-237. PMID: 31667712. Request Article

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OBJECTIVE: The current study aimed to test if racial disparities in weight loss outcomes between African American and Caucasian patients who underwent bariatric surgery were due to pre-surgical BMI differences. METHODS: Primary data was collected from pre-surgical evaluations conducted at a midwestern hospital. A retrospective chart review was conducted of 136 patients. Patient age and race, type of procedure, and pre- and 1-year post-surgical BMI were collected. RESULTS: African American patients were less likely to undergo bariatric surgery compared with Caucasian patients. Caucasian patients undergoing Roux-en-Y Gastric Bypass (RYGB) had a greater change in BMI compared with African American patients who underwent RYGB. Significant differences in weight loss outcomes were not found among patients who underwent the sleeve gastrectomy. Race was not related to pre-surgical BMI or procedure type. CONCLUSION: Despite pre-surgical BMI typically being higher among African American patients, this was not found in the current study. Pre-surgical BMI may not explain the racial disparities in weight loss post-bariatric surgery that are found between African American and Caucasian patients. Future studies should consider psychosocial, environmental, and cultural influences on racial disparities.

Center for Health Policy and Health Services Research
Hecht LM, Schwartz N, **Miller-Matero LR**, **Braciszewski JM**, and Haedt-Matt A. Eating pathology and depressive symptoms as predictors of excessive weight gain during pregnancy. *J Health Psychol* 2020; Epub ahead of print. PMID: 32301343. Full Text

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Excessive gestational weight gain is associated with negative outcomes and the identification of contributing psychosocial factors may be useful in prevention and intervention. Pregnant women (N = 70) completed self-report measures of eating pathology, depressive symptomatology, and gestational weight gain. Global eating pathology was positively associated with overvaluation of shape and weight, dietary restraint, frequency of binge eating, and depressive symptoms. Depressive symptoms significantly predicted excessive gestational weight gain, while global eating pathology predicted excessive

gestational weight gain at a trend level. Results suggest that depressive symptoms more strongly predict excessive gestational weight gain than eating pathology.

Center for Health Policy and Health Services Research
Merced K, Imel ZE, Baldwin SA, Fischer H, Yoon T, Stewart C, Simon G, **Ahmedani B**, Beck A, Daida Y, Hubley S, Rossom R, Waitzfelder B, Zeber JE, and Coleman KJ. Provider Contributions to Disparities in Mental Health Care. *Psychiatr Serv* 2020; Epub ahead of print. PMID: 32340593. Full Text

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OBJECTIVE: Disparities in diagnosis of mental health problems and in access to treatment among racial-ethnic groups are apparent across different behavioral conditions, particularly in the quality of treatment for depression. This study aimed to determine how much disparities differ across providers. METHODS: Bayesian mixed-effects models were used to estimate whether disparities in patient adherence to antidepressant medication (N=331,776) or psychotherapy (N=275,095) were associated with specific providers. Models also tested whether providers who achieved greater adherence to treatment, on average, among non-Hispanic white patients than among patients from racial-ethnic minority groups attained lower disparities and whether the percentage of patients from racial-ethnic minority groups in a provider caseload was associated with disparities. RESULTS: Disparities in adherence to both antidepressant medication and psychotherapy were associated with the provider. Provider performance with non-Hispanic white patients was negatively correlated with provider-specific disparities in adherence to psychotherapy but not to antidepressants. A higher proportion of patients from racial-ethnic minority groups in a provider's caseload was associated with lower adherence among non-Hispanic white patients, lower disparities in adherence to psychotherapy, and greater disparities in adherence to antidepressant medication. CONCLUSIONS: Adherence to depression treatment among a provider's patients from racial-ethnic minority groups was related to adherence among that provider's non-Hispanic white patients, but evidence also suggested provider-specific disparities. Efforts among providers to decrease disparities might focus on improving the general skill of providers who treat more patients from racial-ethnic minority groups as well as offering culturally based training to providers with notable disparities.

Center for Health Policy and Health Services Research
Nerenz DR, Cella D, Fabian L, Nuccio E, Bott J, Austin JM, Simon S, Needleman J, and Johnson K. The NQF Scientific Methods Panel: Enhancing the Review and Endorsement Process for Performance Measures. *Am J Med Qual* 2020; Epub ahead of print.:1062860620914026. PMID: 32223651. Full Text

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In the summer of 2017, the National Quality Forum (NQF) announced the formation of a Scientific Methods Panel (hereafter referred to as "the Panel") as part of a redesign of its endorsement process. NQF created the Panel in response to stakeholder request during a Kaizen improvement event held in May 2017. Given the Panel's role in the endorsement of performance measures used in national payment programs, the objective of this article is to describe the work of the Panel, and to describe its function in the larger context of the NQF measure endorsement process and in the measurement enterprise writ large. This article also serves as an introduction to a series of planned white papers being authored by the panel on specific technical issues in the area of health care performance measurement.

Center for Health Policy and Health Services Research
Spradling PR, Xing J, **Rupp LB**, Moorman AC, **Gordon SC**, **Lu M**, Teshale EH, Boscarino JA, Schmidt MA, Daida YG, and Holmberg SD. Low Uptake of Direct-acting Antiviral Therapy Among Hepatitis C Patients With Advanced Liver Disease and Access to Care, 2014-2017. *J Clin Gastroenterol* 2020; Epub ahead of print. PMID: 32250999. Full Text

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GOALS: To determine the proportion and characteristics of adults with hepatitis C at health care organizations in 4 US states who initiated direct-acting antivirals (DAAs). BACKGROUND: There are almost no data to assess the penetrance of treatment of the hepatitis C population in general US health care settings. STUDY: We conducted a prospective observational study using electronic clinical, pharmacy, and mortality data to determine the fraction of patients who initiated DAAs between January 2014 and December 2017, by start date and regimen. We used stepwise multivariate logistic regression analysis to identify sociodemographic and clinical characteristics associated with receipt of DAAs. RESULTS: Of 8823 patients, 2887 (32.7%) received DAAs. Quarterly (Q) uptake ranged from 1.1% in Q3 2014 to a high of 5.6% in Q2 2015. Characteristics associated with receipt of DAAs included age 51 to 70 years, higher income, pre-2014 treatment failure, and higher noninvasive fibrosis score (FIB4); however, over one half of patients with FIB4 scores >3.25, consistent with severe liver disease, were not treated. A lower likelihood of initiation was associated with Medicaid coverage. Of 5936 patients who did not initiate treatment, 911 (15.3%) had died and 2774 (46.7%) had not had a clinical encounter in >/=12 months by the end of the study. Fewer than 1% of DAA prescriptions originated from nonspecialty providers. CONCLUSIONS: During 4 calendar years of follow-up, one third of patients initiated DAAs. Large fractions of untreated patients had advanced liver disease, died, or were lost to follow-up. Even among patients in integrated health care systems, receipt of DAAs was limited.

Center for Individualized and Genomic Medicine Research
Mak ACY, Sajuthi S, Joo J, **Xiao S**, Sleiman PM, White MJ, Lee EY, Saef B, Hu D, **Gui H**, Keys KL, Lurmann F, Jain D, Abecasis G, Kang HM, Nickerson DA, Germer S, Zody MC, Winterkorn L, Reeves C, Huntsman S, Eng C, Salazar S, Oh SS, Gilliland FD, Chen Z, Kumar R, Martinez FD, Wu AC, Ziv E, Hakonarson H, Himes BE, Williams LK, Seibold MA, and Burchard EG. Novel KITLG/SCF Regulatory Variants Are Associated with Lung Function in African American Children with Asthma. *Genetics* 2020; Epub ahead of print. PMID: 32327564. Request Article

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Baseline lung function, quantified as forced expiratory volume in the first second of exhalation (FEV1), is a standard diagnostic criterion used by clinicians to identify and classify lung diseases. Using whole genome sequencing data from the National Heart, Lung, and Blood Institute TOPMed project, we identified a novel genetic association with FEV1 on chromosome 12 in 867 African American children with asthma (p = 1.26 x 10(-8), beta = 0.302). Conditional analysis within 1 Mb of the tag signal (rs73429450) yielded one major and two other weaker independent signals within this peak. We explored statistical and functional evidence for all variants in linkage disequilibrium with the three independent signals and yielded 9 variants as the most likely candidates responsible for the association with FEV1 Hi-C data and eQTL analysis demonstrated that these variants physically interacted with KITLG (aka SCF) and their minor alleles were associated with increased expression of KITLG gene in nasal epithelial cells. Gene-by-air-pollution interaction analysis found that the candidate variant rs58475486 interacted with past-year SO2 exposure (p = 0.003, beta = 0.32). This study identified a novel protective genetic association with FEV1, possibly mediated through KITLG, in African American children with asthma. This is the first study that identified genetic association between lung function and KITLG, which has established role in orchestrating allergic inflammation in asthma.

Dermatology
Cohen L, Brodsky MA, **Zubair R**, **Kohli I**, **Hamzavi IH**, and Sadeghpour M. Cutaneous Interaction with Visible Light: What Do We Know. *J Am Acad Dermatol* 2020; Epub ahead of print. PMID: 32289393. Full Text

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Visible light has been used therapeutically in dermatology for years for a variety of cosmetic and medical indications, including skin rejuvenation and the treatment of inflammatory and neoplastic conditions, among others. Until recently, visible light was thought to be relatively inert compared to its spectral neighbors, ultraviolet and infrared radiation. However, recent literature has described the ability of visible light to cause erythema in light skin and pigmentary changes in individuals with darker skin types. Concern surrounding its potentially damaging cutaneous effects has been raised in both the medical community as well as in social media outlets. In this article, we provide an evidenced-based review describing what is currently known about visible light, focusing on its role in dermatologic diseases including disorders of hyperpigmentation such as melasma and post-inflammatory hyperpigmentation.

Dermatology
Del Rosso JQ, Kircik LH, **Gold LS**, and Thiboutot D. Androgens, Androgen Receptors, and the Skin: From the Laboratory to the Clinic With Emphasis on Clinical and Therapeutic Implications. *Journal of Drugs in Dermatology* 2020; 19(3):S30-S35. PMID: Not assigned. Request Article

The effects of androgens on human skin include growth and differentiation of sebaceous glands, terminal hair growth, epidermal barrier function, wound healing, and modification of the cutaneous microbiome. Androgens exert their activities via ligand formation with intracytoplasmic androgen receptors which can then translocate to the nucleus and interact with genetic androgen response elements to influence signaling cascades. Differences in tissue distribution and activities of enzymes that modify androgen synthesis and catabolism, variations related to gender and ethnicity/race, and genetic polymorphisms that affect androgen receptor functionality directly impact androgen physiology and the pathophysiology associated with a variety of disease states. This manuscript reviews the fundamentals of androgen physiology, androgen synthesis and catabolism in local skin tissue, androgen receptor activity, as well as the impact of genetic polymorphisms and gender. Emphasis is placed on the roles of androgenic activity in sebaceous gland development, sebum production, and the pathophysiology of acne vulgaris.

Dermatology
Ellis MM, **Jones LR**, **Siddiqui F**, **Sunkara PR**, and **Ozog DM**. The Efficacy of Surgical Excision Plus Adjuvant Multimodal Therapies in the Treatment of Keloids: A Systematic Review and Meta-Analysis. *Dermatol Surg* 2020; Epub ahead of print. PMID: 32224709. Full Text

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BACKGROUND: Research evaluating the efficacy of multimodal therapy for the treatment of keloids has reported combination regimens are most effective. OBJECTIVE: To compare recurrence rates for keloids treated with surgery plus one adjuvant intervention (dual therapy) versus surgery plus 2 or more adjuvant interventions (triple therapy). MATERIALS AND METHODS: Systematic literature review and meta-analysis of combination treatment for keloids. RESULTS: After full-text review, we included 60 articles representing 5,547 keloids: 5,243 received dual therapy, 259 received triple therapy, and 45 received quadruple therapy (the latter 2 groups were combined for analysis). The difference in recurrence rates between dual (19%) and triple therapy (11.2%) was not significant (p = .343). However, the difference in recurrence rates between dual therapy using surgery and radiation (18.7%) and triple therapy using surgery, radiation, and a third intervention (7.7%) was significant (p = .002). The differences for surgery and intralesional triamcinolone (TAC) showed trends toward significance, because keloids treated with dual therapy (21.7%) had a higher recurrence rate than those treated with triple therapy comprised of surgery, TAC, and another intervention (13.7%; p = .099). CONCLUSION: Triple therapy using surgery plus radiation and/or TAC as one of the adjuvant treatment modalities may achieve the lowest recurrence rates for keloids.

Dermatology
Hamzavi IH, **Lyons AB**, **Kohli I**, **Narla S**, **Parks-Miller A**, Gelfand JM, **Lim HW**, and **Ozog D**. Ultraviolet germicidal irradiation: possible method for respirator disinfection to facilitate reuse during COVID-19 pandemic. *J Am Acad Dermatol* 2020; Epub ahead of print. PMID: 32246972. Full Text

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Dermatology
Hebert A, Thiboutot D, **Stein Gold L**, Cartwright M, Gerloni M, Fragasso E, and Mazzetti A. Efficacy and Safety of Topical Clascoterone Cream, 1%, for Treatment in Patients With Facial Acne: Two Phase 3 Randomized Clinical Trials. *JAMA Dermatol* 2020; Epub ahead of print. PMID: 32320027. Full Text

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Importance: Acne is a common, multifactorial skin condition, and treatments with novel mechanisms have been elusive. Objective: To assess the safety and efficacy of clascoterone cream, 1%, a novel topical androgen receptor inhibitor, in 2 phase 3 randomized clinical trials (CB-03-01/25 and CB-03-01/26). Design, Setting, and Participants: Two identical, multicenter, randomized, vehicle-controlled, double-blind, phase 3 studies conducted from November 2015 to April 2018 evaluated the efficacy and safety of use of clascoterone cream, 1%, in males and nonpregnant females 9 years and older with moderate or severe facial acne as scored on the Investigator's Global Assessment scale. Participants were enrolled if they had 30 to 75 inflammatory lesions and 30 to 100 noninflammatory lesions. Interventions: Patients were randomized to treatment with clascoterone cream, 1%, or vehicle cream and applied approximately 1 g to the whole face twice daily for 12 weeks. Main Outcomes and Measures: Treatment success was defined as an Investigator's Global Assessment score of 0 (clear) or 1 (almost clear), and a 2-grade or greater improvement from baseline and absolute change from baseline in noninflammatory and inflammatory lesion counts at week 12. Safety measures included adverse event frequency and severity. Results: A total of 1440 patients were randomzied in 2 studies. In CB-03-01/25, 353 participants were randomized to treatment with clascoterone cream, 1% (median [range] age, 18.0 [10-58] years; 221 [62.6%] female), and 355 participants were randomized to treatment with vehicle cream (median [range] age, 18.0 [9-50] years; 215 (60.6%) female); in CB-03-01/26, 369 participants were randomized to treatment with clascoterone cream, 1% (median [range] age, 18.0 [10-50] years; 243 [65.9%] female), and 363 participants were randomized to treatment with vehicle cream (median [range] age, 18.0 [range, 11-42] years; 221 [60.9%] female). At week 12, treatment success rates in CB-03-01/25 and CB-03-01/26 with clascoterone cream, 1%, were 18.4% (point estimate, 2.3; 95% CI, 1.4-3.8; P < .001) and 20.3% (point estimate, 3.7; 95% CI, 2.2-6.3; P < .001) vs 9.0% and 6.5% with vehicle, respectively. At week 12, in both CB-03-01/25 and CB-03-01/26, treatment with clascoterone cream, 1%, resulted in a significant reduction in absolute noninflammatory lesions from baseline to -19.4 (point estimate difference, -6.4; 95% CI, -10.3 to -2.6; P < .001) and -19.4 (point estimate difference, -8.6; 95% CI, -12.3 to -4.9; P < .001) vs -13.0 and -10.8 with vehicle, respectively, as well as a reduction in inflammatory lesions from baseline to -19.3 (point estimate difference, -3.8; 95% CI, -6.4 to -1.3; P < .001) and -20.0 (point estimate difference, -7.4; 95% CI, -9.8 to -5.1; P < .001) vs -15.5 and -12.6 with vehicle, respectively. Adverse events rates were low and mostly mild; the predominant local skin reaction was trace or mild erythema. Conclusions and Relevance: Use of clascoterone cream, 1%, for acne treatment appears to demonstrate favorable efficacy and safety with low adverse event rates. Trial Registration: ClinicalTrials.gov Identifiers: NCT02608450 and NCT02608476.

Dermatology
Kohli I, Kastner S, Thomas M, Nahhas AF, **Braunberger TL**, **Mohammad TF**, Nicholson CL, Canfield D, Kollias N, **Lim HW**, **Hamzavi IH**, and Patwardhan SV. Quantitative measurement of skin surface oiliness and shine using differential polarized images. *Arch Dermatol Res* 2020. PMID: 32270323. Full Text

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Excess amounts of skin surface oil can lead to adverse psychological consequences. Grease-spot photometry-based techniques measure sebum production rate. However, besides being tedious, these measurements are influenced by contact area, applied pressure, and time of application. Image analysis of polarized images has the potential to provide objective, quantitative information of skin oiliness. This study was designed to set up an imaging device for capturing and enhancing the changes in skin surface oiliness and to clinically and quantitatively, (via image analysis), evaluate varying levels of skin surface oiliness. Mineral oil was used to simulate skin surface oil. 40.5 microL of the mineral oil was applied within a two inch square area of interest on facial skin in twelve steps, from 1 to 40.5 microL, at 40% increments. The results indicate a strong

correlation between the quantitative skin surface oiliness measurements and the clinical assessments. This sensitive technique has the potential to be utilized in future studies to evaluate product efficacies in reducing skin oiliness.

Dermatology
Lim HW, Feldman SR, Van Voorhees AS, and Gelfand JM. Recommendations for phototherapy during the COVID-19 pandemic. *J Am Acad Dermatol* 2020; Epub ahead of print. PMID: 32339700. Full Text

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Dermatology
Lyons AB, **Kohli I**, Nahhas AF, **Braunberger TL**, **Mohammad TF**, Nicholson CL, Nartker NT, **Modi K**, Matsui MS, **Lim HW**, and **Hamzavi IH**. Trichloroacetic acid model to accurately capture the efficacy of treatments for postinflammatory hyperpigmentation. *Arch Dermatol Res* 2020; Epub ahead of print. PMID: 32253506. Full Text

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Postinflammatory hyperpigmentation (PIH) occurs following cutaneous injury and is common following resolution of acne especially in patients with skin of color. The objective of this study was to further validate a trichloroacetic acid (TCA)-induced PIH model and compare it to acne-induced PIH using topical bakuchiol, a botanical extract that has been shown to have antimicrobial, anti-inflammatory, antioxidant, and antiacne properties. A prospective, non-randomized clinical trial was conducted on subjects with skin phototypes IV-VI with a history of acne-induced PIH. Subjects applied bakuchiol or vehicle cream twice daily to 2 acne-induced and 2 TCA-induced PIH lesions for 28 days with a third lesion serving as a control in each group. Degree of improvement was defined as the change in the Investigator Global Assessment (IGA) score over 28 days of treatment. Twenty subjects (6 males, 14 females) completed the study. For TCA-induced PIH sites, there was a statistically significant ($p < 0.05$) degree of improvement with bakuchiol treatment (- 0.50 +/- 0.18) compared to vehicle (0.05 +/- 0.15) and control (- 0.06 +/- 0.17). For acne-induced PIH, there was a greater degree of improvement for bakuchiol (- 1.06 +/- 0.23) when compared to vehicle (- 0.56 +/- 0.16) and control (- 0.69 +/- 0.18); however, statistical significance was not reached ($p > 0.05$). TCA-induced PIH sites were uniform in size and pigment intensity thereby allowing better comparison among sites. This emphasizes the relevance of using this model for PIH which may help reduce the barriers in clinical trials and help improve access to treatments for patients who suffer from PIH. The results suggest that topical bakuchiol may decrease the severity of PIH.

Dermatology
Lyons AB, Peacock A, McKenzie SA, **Jacobsen G**, Naik HB, Shi VY, **Hamzavi IH**, and Hsiao JL. Retrospective Cohort Study of Pregnancy Outcomes in Hidradenitis Suppurativa. *Br J Dermatol* 2020; Epub ahead of print. PMID: 32333790. Full Text

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Hidradenitis suppurativa (HS) disproportionately affects women of childbearing age; however, there has been a paucity of literature in the field of HS and pregnancy.(1) The objective of this study was to examine pregnancy complications, pregnancy outcomes, and neonatal outcomes in patients with HS.

Dermatology
Lyons AB, Peacock A, McKenzie SA, **Jacobsen G**, Naik HB, Shi VY, **Hamzavi IH**, and Hsiao JL. Evaluation of Hidradenitis Suppurativa Disease Course During Pregnancy and Postpartum. *JAMA Dermatol* 2020; Epub ahead of print. PMID: 32347884. Full Text

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Importance: Hidradenitis suppurativa (HS) disproportionately affects women of childbearing potential. There is a paucity of data regarding the HS disease course during pregnancy and in the postpartum period. Objective: To explore the HS disease course during pregnancy and in the postpartum period. Design, Setting, and Participants: A retrospective cohort study was conducted on patients in the Henry Ford Health System, Detroit, Michigan-a large, academic, urban referral center. Women with a diagnosis of HS who became pregnant between January 1, 2008, and December 31, 2018, were included. International Classification of Diseases, Ninth Revision, and International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, were used for identification of the diagnosis. Exposures: Pregnancy in patients with HS. Main Outcomes and Measures: Hidradenitis suppurativa disease status during pregnancy and the postpartum period. Results: A total of 127 women with HS were included in this study and accounted for 202 pregnancies. Of the 202 pregnancies, 171 were in black women, 25 in white women, 3 in women of other race/ethnicity, and 3 had unreported data. Mean (SD) age at HS onset was 19.3 (5.6) years; at time of HS diagnosis, 24.4 (5.3) years; and at time of pregnancy, 25.9 (5.0) years. The disease worsened during pregnancy in 70 pregnancies (61.9%), did not change in 34 pregnancies (30.1%), and improved in 9 pregnancies (8.0%). Hidradenitis suppurativa exacerbated in the postpartum period after 82 of 124 pregnancies (66.1%). Dermatologists were involved in managing HS in 28 pregnancies (14.4%) and for a higher proportion of patients with more severe Hurley stage as compared with cases of mild disease (stage 3: 7 of 18 [38.9%] vs stage 1: 10 of 100 [10.0%] or stage 2: 11 of 67 [16.4%]; P = .004). In addition, HS medical treatment was administered during 77 pregnancies (38.1%), while HS procedural treatment was administered during 34 pregnancies (16.8%). A significantly higher proportion of patients whose care was managed by dermatologists vs those without dermatologist involvement received any HS medication (22 [78.6%] vs 53 [31.7%], P < .001) or any HS procedure (14 [50%] vs 19 [11.4%], P < .001) during pregnancy. Conclusions and Relevance: Despite a high rate of HS exacerbation during pregnancy and postpartum, this cohort study found that most of the patients did not receive HS-directed medical treatment or care from a dermatologist during pregnancy. Close monitoring and improved collaborative care between dermatology and obstetrics-gynecology services is warranted.

Dermatology

Lyons AB, Shabeeb N, Nicholson CL, **Braunberger TL**, Peacock A, and **Hamzavi IH**. Emerging medical treatments for hidradenitis suppurativa. *J Am Acad Dermatol* 2020; Epub ahead of print. PMID: 32289386. Full Text

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Hidradenitis suppurativa (HS) is a chronic inflammatory disease affecting intertriginous skin areas, and it is characterized by recurrent painful episodes of inflammatory drainage. While the pathophysiology of HS is not fully understood, recent research points to an imbalance of cytokines as a contributing factor to the associated symptoms of purulent drainage and sinus tract formation. HS lesions are often characterized by a superimposed pathogenic/commensal bacterial infection that can improve with targeted antibiotic therapy. New medical treatments have emerged in recent years, many of which specifically work against a variety of pro-inflammatory mediators associated with HS. These newer, specified treatment options, in conjunction with surgery and lasers, are thought to provide positive outcomes and an overall improvement in quality of life in patients with HS.

Dermatology

Lyons AB, Trullas C, **Kohli I**, **Hamzavi IH**, and **Lim HW**. Photoprotection Beyond Ultraviolet Radiation: A Review of Tinted Sunscreens. *J Am Acad Dermatol* 2020; Epub ahead of print. PMID: 32335182. Full Text

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Both ultraviolet radiation and visible light have biologic effects on the skin. Visible light can induce erythema in light skinned individuals and pigmentation in dark skinned individuals. Broad spectrum sunscreens protect against ultraviolet radiation and do not adequately protect against visible light. For a sunscreen to protect against visible light, it must be visible on the skin. Inorganic filters (also known as mineral filters), namely, zinc oxide and titanium dioxide, are used in the form of nanoparticles in sunscreens to minimize the chalky and white appearance on the skin; as such, they do not protect against visible light. Tinted sunscreens use different formulations and concentrations of iron oxides and pigmentary titanium dioxide to provide protection against visible light. Many shades of tinted sunscreens are available by combining different amounts of iron oxides and pigmentary titanium dioxide to cater to all skin phototypes. Therefore, tinted sunscreens are beneficial for patients with

visible light-induced photodermatoses and those with hyperpigmentation disorders such as melasma and post-inflammatory hyperpigmentation.

Dermatology
Narla S, **Lyons AB**, **Kohli I**, **Torres AE**, **Parks-Miller A**, **Ozog DM**, **Hamzavi IH**, and **Lim HW**. The Importance of the Minimum Dosage Necessary for UVC Decontamination of N95 Respirators during the COVID-19 Pandemic. *Photodermatol Photoimmunol Photomed* 2020; Epub ahead of print. PMID: 32291807. Full Text

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The World Health Organization (WHO) recently released a press report highlighting the severe shortage of personal protective equipment (PPE) that is endangering healthcare workers worldwide during the COVID-19 pandemic.(1) To meet this urgent need, healthcare institutions across the world have begun to utilize the germicidal properties of ultraviolet C (UVC) to decontaminate N95 respirators so that they can be reused.(2) It is clearly crucial that the dose of UVC delivered is sufficient to kill any viable SARS-CoV-2, the causative virus of the COVID-19 pandemic, that may be present on the respirators.

Dermatology
Patel N, **Konda S**, and **Lim HW**. Dupilumab for the Treatment of Chronic Actinic Dermatitis. *Photodermatol Photoimmunol Photomed* 2020; Epub ahead of print. PMID: 32320500. Full Text

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Chronic actinic dermatitis (CAD) is an immune-mediated photodermatosis characterized by chronic, pruritic, eczematous, and often lichenified plaques distributed primarily upon sun-exposed skin.(1) The pathophysiology is believed to involve a delayed-type hypersensitivity reaction to an endogenous, photoinduced, cutaneous antigen, which has been speculated to be DNA.(1) First-line management options include strict photoprotection, topical corticosteroids (TCS), and topical calcineurin inhibitors (TCI). However, these are rarely sufficient on their own. Thus, many systemic therapies are often utilized with varying degrees of success.

Dermatology
Robinson G, Townsend S, and **Jahnke MN**. Molluscum Contagiosum: Review and Update on Clinical Presentation, Diagnosis, Risk, Prevention, and Treatment. *Current Dermatology Reports* 2020; 9(1):83-92. PMID: Not assigned. Request Article

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Purpose of Review: Molluscum contagiosum (MC) is a self-limited cutaneous viral infection that most commonly affects children and immunocompromised populations. This review provides an update on the clinical manifestations, risk, diagnosis, treatment, and prevention of this frequently encountered infection. Recent Findings: A recent Cochrane review concluded that there is insufficient evidence to establish the superiority of any specific treatment modality or to confirm that active intervention is superior to benign neglect (van der Wouden JC et al., Cochrane Database Syst Rev 5:CD004767, 2017). Interim pilot study data suggests that cantharidin outperforms placebo (Guzman AK et al., Int J Dermatol 57:1001–1006, 2018). Imiquimod is no longer recommended for treatment of MC (van der Wouden JC et al., Cochrane Database Syst Rev 5:CD004767, 2017; Papadopoulos EJ, https://www.fda.gov/files/drugs/published/N20-723S020-Imiquimod-Clinical-BPCA.pdf, 2006; Katz KA et al., Pediatr Dermatol 35:282–283, 2018). Summary: Optimal management strategies for MC remain unclear due to the multitude of proposed therapies, lack of high-quality evidence, and uncertain benefit of intervention for uncomplicated disease. Aside from watchful waiting, destructive therapies such as cantharidin and curettage are among the best studied methods and remain the treatment of choice for most patients.

Dermatology
Torres AEE, **Lyons AB**, **Hamzavi IH**, and **Lim HW**. Role of phototherapy in the era of biologics. *J Am Acad Dermatol* 2020; Epub ahead of print. PMID: 32339702. Full Text

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Phototherapy is a safe and effective treatment for many dermatologic conditions. With the advent of novel biologics and small molecule inhibitors, it is important to critically evaluate the role of phototherapy in dermatology. Surveys have shown that many dermatology residency programs do not dedicate time to teach residents how to prescribe or administer phototherapy. Limitations of phototherapy include access to a center, time required for treatments, and insurance approval. Home phototherapy, a viable option, is also underutilized. However, it should be emphasized that modern phototherapy has been in use for over 40 years, has an excellent safety profile, and does not require laboratory monitoring. It can be safely combined with many other treatment modalities including biologics and small molecule inhibitors. In addition, phototherapy costs significantly less than these novel agents. Dermatologists are the only group of physicians who have the expertise and proper training to deliver this treatment modality to our patients. Therefore, in order to continue to deliver high quality, cost-effective care, it is imperative that phototherapy be maintained as an integral part of the dermatology treatment armamentarium.

Dermatology
Vellaichamy G, **Chadha A**, **Hamzavi IH**, and **Lim HW**. Polymorphic Light Eruption Sine Eruptione: A Variant of Polymorphous Light Eruption. *Photodermatol Photoimmunol Photomed* 2020; Epub ahead of print. PMID: 32323883. Full Text

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Polymorphous light eruption (PMLE) is the most common immunologically-mediated photodermatosis; it usually presents as a pruritic, papular eruption in sun-exposed regions of the skin hours to days after sun exposure. Several variants of PMLE have been described, manifesting with varying morphologies but with photosensitivity as a common etiology. Polymorphic light eruption sine eruptione (PLESE), a rare variant presenting as sun-induced pruritus without cutaneous eruption, has been reported in a single cohort of seven patients in 1988. We report a case of a 62-year-old white female who developed PLESE.

Dermatology
Worden A, **Yoho DJ**, **Houin H**, **Moquin K**, **Hamzavi I**, **Saab I**, and **Siddiqui A**. Factors Affecting Healing in the Treatment of Hidradenitis Suppurativa. *Ann Plast Surg* 2020; 84(4):436-440. PMID: 31688123. Full Text

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BACKGROUND: Hidradenitis suppurativa (HS) is a chronic debilitating condition. Treatment of HS depends on disease stage, goals of care, access to care, and frequency of symptoms. We present our experience with surgical treatment for patients with HS. METHODS: Patients were followed longitudinally for at least 2 years postsurgical intervention. Demographic data, participation in a multidisciplinary program, type of surgery, healing rates, and potential factors contributing to wound healing were retrospectively reviewed in all cases using multivariate analysis. RESULTS: Two hundred forty-eight patients met the inclusion criteria with a total of 810 involved sites. Overall, 59% of patients had Hurley stage 3 disease at the time of surgery. Healing rates of 80% were observed in stages 1 and 2, and 74% were observed in stage 3. Hurley stage was not a significant predictor of healing (P = 0.09). Surgical treatment consisted of 38% incision and drainage, 44% excision without closure, and 17% excision with primary closure. Incisional and excisional treatments healed 78% and 79%, respectively, at 2 years. Primarily repaired defects (grafts and flaps) were 68% healed at 2 years. Observed healing rates were uniform regardless of the number of sites involved (P = 0.959). Participation in the multidisciplinary program was the strongest predictor of healing (78% vs 45%, P = 0.004). Sex, age, body mass index, tobacco use, diabetes, presurgery hemoglobin, and family history of HS were statistically not significant. Continuation of immune modulating therapy within 2 weeks of surgery was a predictor of reduced healing (odds ratio, 0.23; P = 0.004), whereas holding biologics for at least 2 weeks was not significant (odds ratio, 1.99; P = 0.146). CONCLUSIONS: Participation in a multidisciplinary program is a strong predictor of long-term success when treating HS. Hurley score and number of involved sites did not correlate with successful healing after surgery. If taking biologics, we identified 2 weeks as an appropriate break from biologics before and after surgical intervention. Healing rates were highest with ablative procedures (incision and drainage, excision) alone.

Diagnostic Radiology
Griffith B, Rozenshtein A, Lewis M, Ali K, Thompson D, Makkar JS, Verma N, and Anderson JC. Shrinking IR Applicant Pool: Self-Selection at Work? *J Vasc Interv Radiol* 2020; Epub ahead of print. PMID: 32245719. Full Text

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Diagnostic Radiology

Jamali-Dinan SS, **Soltanian-Zadeh H**, **Bowyer SM**, Almohri H, Dehghani H, Elisevich K, and Nazem-Zadeh MR. A Combination of Particle Swarm Optimization and Minkowski Weighted K-Means Clustering: Application in Lateralization of Temporal Lobe Epilepsy. *Brain Topogr* 2020; Epub ahead of print. PMID: 32347472. Full Text

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K-Means is one of the most popular clustering algorithms that partitions observations into nonoverlapping subgroups based on a predefined similarity metric. Its drawbacks include a sensitivity to noisy features and a dependency of its resulting clusters upon the initial selection of cluster centroids resulting in the algorithm converging to local optima. Minkowski weighted K-Means (MWK-Means) addresses the issue of sensitivity to noisy features, but is sensitive to the initialization of clusters, and so the algorithm may similarly converge to local optima. Particle Swarm Optimization (PSO) uses a globalized search method to solve this issue. We present a hybrid Particle Swarm Optimization (PSO) + MWK-Means clustering algorithm to address all the above problems in a single framework, while maintaining benefits of PSO and MWK Means methods. This study investigated the utility of this approach in lateralizing the epileptogenic hemisphere for temporal lobe epilepsy (TLE) cases using magnetoencephalography (MEG) coherence source imaging (CSI) and diffusion tensor imaging (DTI). Using MEG-CSI, we analyzed preoperative resting state MEG data from 17 adults TLE patients with Engel class I outcomes to determine coherence at 54 anatomical sites and compared the results with 17 age- and gender-matched controls. Fiber-tracking was performed through the same anatomical sites using DTI data. Indices of both MEG coherence and DTI nodal degree were calculated. A PSO + MWK-Means clustering algorithm was applied to identify the side of temporal lobe epileptogenicity and distinguish between normal and TLE cases. The PSO module was aimed at identifying initial cluster centroids and assigning initial feature weights to cluster centroids and, hence, transferring to the MWK-Means module for the final optimal clustering solution. We demonstrated improvements with the use of the PSO + MWK-Means clustering algorithm compared to that of K-Means and MWK-Means independently. PSO + MWK-Means was able to successfully distinguish between normal and TLE in 97.2% and 82.3% of cases for DTI and MEG data, respectively. It also lateralized left and right TLE in 82.3% and 93.6% of cases for DTI and MEG data, respectively. The proposed optimization and clustering methodology for MEG and DTI features, as they relate to focal epileptogenicity, would enhance the identification of the TLE laterality in cases of unilateral epileptogenicity.

Diagnostic Radiology

Yaguchi G, **Tang HJ**, **Deebajah M**, **Keeley J**, **Pantelic M**, **Williamson S**, **Gupta N**, **Peabody JO**, **Menon M**, **Dabaja A**, and Alanee S. The effect of multiplicity of PI-RADS 3 lesions on cancer detection rate of confirmatory targeted biopsy in patients diagnosed with prostate cancer and managed with active surveillance. *Urol Oncol* 2020; Epub ahead of print. PMID: 32265090. Full Text

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BACKGROUND AND OBJECTIVE: To determine the effect of multiplicity of prostate imaging reporting and data system assessment category 3 (PI-RADS 3) lesions on cancer detection rate (CDR) of confirmatory targeted biopsy of such lesion in patients diagnosed with prostate cancer and managed with active surveillance. METHODS: This study was conducted at a single academic institution. There were 91 men with >/= 1 PI-RADS 3 lesion detected through magnetic resonance imaging (MRI) after systematic prostate biopsy in the course of management of patients diagnosed with prostate cancer with active surveillance. We compared the CDRs based on targeted biopsy of PI-RADS 3 lesions that occurred (1) as solitary lesions, (2) as 1 of multiple PI-RADS 3 only lesions, or (3) with >/= 1 higher grade lesion. RESULTS: Median age was 65.0 years (interquartile range 59.5-70.0), median prostate specific antigen was 5.95 ng/ml (interquartile range 4.30-8.83), and median prostate specific antigen density was 0.161 ng/ml(2) (0.071-0.194). Forty-three men had solitary PI-RADS 3 lesions, 22 had multiple PI-RADS 3 only lesions, and 26 had multiple lesions with >/= 1 higher grade lesion. The overall CDR (Gleason score >/= 3+3) based on confirmatory MRI targeted biopsy in a given PI-RADS 3 lesion in each group was 23%, 45%, and 54%,

respectively (P=0.0274). The CDRs for clinically significant disease (Gleason score >/= 3+4) were 16%, 32%, and 35%, respectively (P=0.1701). CONCLUSIONS: Coexisting lesions increase the CDR of confirmatory MRI targeted biopsy of PI-RADS 3 lesions in patients managed with active surveillance. Risk stratification algorithms for PI-RADS 3 lesion to guide biopsy and management decisions may consider including multiplicity of lesions.

Emergency Medicine

Miller J, McNaughton C, **Joyce K**, **Binz S**, and Levy P. Hypertension Management in Emergency Departments. *Am J Hypertens* 2020; Epub ahead of print. PMID: 32307541. Full Text

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Elevated blood pressure is pervasive among patients that visit emergency departments for their care. In this review article, we outline the current approach to the management of these individuals and highlight the crucial role emergency medicine clinicians play in reducing the morbidity associated with elevated blood pressure. We highlight the critical importance of immediate treatment when elevated blood pressure contributes to new or worsening end-organ injury but emphasize that such hypertensive emergencies are rare. For the vast majority of patients with elevated blood pressure in the emergency department who do not have new or worsening end-organ injury from elevated blood pressure, immediate blood pressure reduction within the emergency department is not recommended or safe. Nonetheless, within weeks after an emergency department visit, there is a pressing need to improve the care of patients with elevated or previously undiagnosed hypertension. For many, it may be their only regular point of engagement with the healthcare system. To address this, we present novel perspectives that envision a new role for emergency medicine in chronic hypertension management - one that acknowledges the significant population-level gaps in blood pressure control that contribute to disparities in cardiovascular disease and sets the stage for future changes in systems-based practice.

Endocrinology and Metabolism

Roshandel D, Chen Z, Canty AJ, Bull SB, Natarajan R, Paterson AD, **Bhan A**, **Jones JK**, **Kruger D**, **Edwards PA**, **Remtema H**, **Angus E**, **Galprin A**, **McLellan M**, **Thomas A**, **Carey JD**, and **Whitehouse F**. DNA methylation age calculators reveal association with diabetic neuropathy in type 1 diabetes. *Clin Epigenetics* 2020; 12(1):52. PMID: 32248841. Request Article

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BACKGROUND: Many CpGs become hyper or hypo-methylated with age. Multiple methods have been developed by Horvath et al. to estimate DNA methylation (DNAm) age including Pan-tissue, Skin & Blood, PhenoAge, and GrimAge. Pan-tissue and Skin & Blood try to estimate chronological age in the normal population whereas PhenoAge and GrimAge use surrogate markers associated with mortality to estimate biological age and its departure from chronological age. Here, we applied Horvath's four methods to calculate and compare DNAm age in 499 subjects with type 1 diabetes (T1D) from the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) study using DNAm data measured by Illumina EPIC array in the whole blood. Association of the four DNAm ages with development of diabetic complications including cardiovascular diseases (CVD), nephropathy, retinopathy, and neuropathy, and their risk factors were investigated. RESULTS: Pan-tissue and GrimAge were higher whereas Skin & Blood and PhenoAge were lower than chronological age ($p < 0.0001$). DNAm age was not associated with the risk of CVD or retinopathy over 18-20 years after DNAm measurement. However, higher PhenoAge (beta = 0.023, p = 0.007) and GrimAge (beta = 0.029, p = 0.002) were associated with higher albumin excretion rate (AER), an indicator of diabetic renal disease, measured over time. GrimAge was also associated with development of both diabetic peripheral neuropathy (OR = 1.07, p = 9.24E-3) and cardiovascular autonomic neuropathy (OR = 1.06, p = 0.011). Both HbA1c (beta = 0.38, p = 0.026) and T1D duration (beta = 0.01, p = 0.043) were associated with higher PhenoAge. Employment (beta = - 1.99, p = 0.045) and leisure time (beta = - 0.81, p = 0.022) physical activity were associated with lower Pan-tissue and Skin & Blood, respectively. BMI (beta = 0.09, p = 0.048) and current smoking (beta = 7.13, p = 9.03E-50) were positively associated with Skin & Blood and GrimAge, respectively. Blood pressure, lipid levels, pulse rate, and alcohol consumption were not associated with DNAm age regardless of the method used. CONCLUSIONS: Various methods of measuring DNAm age are sub-optimal in detecting people at higher risk of developing diabetic complications although some work better than the others.

Endocrinology and Metabolism

White RJ, Jerjes-Sanchez C, Bohns Meyer GM, Pulido T, Sepulveda P, Wang KY, Grunig E, Hiremath S, Yu Z, Gangcheng Z, Yip WLJ, Zhang S, Khan A, Deng CQ, Grover R, Tapson VF, **Awdish R**, and **Cajigas H**. Combination Therapy with Oral Treprostinil for Pulmonary Arterial Hypertension. A Double-Blind Placebo-controlled Clinical Trial. *Am J Respir Crit Care Med* 2020; 201(6):707-717. PMID: 31765604. Full Text

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Rationale: Oral treprostinil improves exercise capacity in patients with pulmonary arterial hypertension (PAH), but the effect on clinical outcomes was unknown.Objectives: To evaluate the effect of oral treprostinil compared with placebo on time to first adjudicated clinical worsening event in participants with PAH who recently began approved oral monotherapy.Methods: In this event-driven, double-blind study, we randomly allocated 690 participants (1:1 ratio) with PAH to receive placebo or oral treprostinil extended-release tablets three times daily. Eligible participants were using approved oral monotherapy for over 30 days before randomization and had a 6-minute-walk distance 150 m or greater. The primary endpoint was the time to first adjudicated clinical worsening event: death; hospitalization due to worsening PAH; initiation of inhaled or parenteral prostacyclin therapy; disease progression; or unsatisfactory long-term clinical response.Measurements and Main Results: Clinical worsening occurred in 26% of the oral treprostinil group compared with 36% of placebo participants (hazard ratio, 0.74; 95% confidence interval, 0.56-0.97; P = 0.028). Key measures of disease status, including functional class, Borg dyspnea score, and N-terminal pro-brain natriuretic peptide, all favored oral treprostinil treatment at Week 24 and beyond. A noninvasive risk stratification analysis demonstrated that oral treprostinil-assigned participants had a substantially higher mortality risk at baseline but achieved a lower risk profile from Study Weeks 12-60. The most common adverse events in the oral treprostinil group were headache, diarrhea, flushing, nausea, and vomiting.Conclusions: In participants with PAH, addition of oral treprostinil to approved oral monotherapy reduced the risk of clinical worsening.Clinical trial registered with www.clinicaltrials.gov (NCT01560624).

Gastroenterology

Agbim U, Sharma A, Maliakkal B, Karri S, Yazawa M, Goldkamp W, Podila PSB, Vanatta JM, **Gonzalez H**, Molnar MZ, Nair SP, Eason JD, and Satapathy SK. Outcomes of Liver Transplant Recipients With Acute-on-Chronic Liver Failure Based on EASL-CLIF Consortium Definition: A Single-center Study. *Transplant Direct* 2020; 6(4):e544. PMID: 32309630. Full Text

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The impact of acute-on-chronic liver failure (ACLF) defined by European Association for the Study of the Liver-Chronic Liver Failure in liver transplant (LT) recipients has not been well characterized. The aim of the study was to assess early posttransplant morbidity and survival of ACLF patients. Methods: Eight hundred twenty-five consecutive LT patients (04/2006-03/2013) were included in a retrospective analysis. Of the 690 evaluable patients, 589 had no ACLF, and the remaining 101 were grouped into ACLF Grades 1-3 (ACLF Grade 1: 50 [49.5%], ACLF Grade 2: 32 [31.7%], and ACLF Grade 3: 19 [18.8%]). Results: LT recipients transplanted in the context of ACLF had significantly increased serum creatinine (2.27 +/- 1.16 versus 0.98 +/- 0.32; P < 0.0001), and inferior 1-year graft (90% versus 78%; P < 0.0001) and patient survival (92% versus 82%; P = 0.0004) by Kaplan-Meier survival analysis; graft and patient survival correlated negatively with increasing severity of ACLF.

One-year graft and patient survival were lower in those with high ACLF (Grade 2 and 3) irrespective of Model for End-Stage Liver Disease compared with other groups. The ACLF group had longer intensive care unit stays (10.6 +/- 19.5 versus 4.2 +/- 9; P < 0.0001), hospital stays (20.9 +/- 25.9 versus 11.7 +/- 11.4; P < 0.0001), and increased surgical re-exploration (26.7 % versus 14.6%, P = 0.002). Conclusions: Patients with ACLF undergoing LT have significantly higher resource utilization, inferior graft survival and patient survival, and renal dysfunction at 1 year. The combination of ACLF and Model for End-Stage Liver Disease can be considered when determining the suitability for potential transplantation.

Gastroenterology
Gonzalez HC, and **Gordon SC**. Hepatitis C: Does Successful Treatment Alter the Natural History and Quality of Life? *Gastroenterology Clinics of North America* 2020; Epub ahead of print. PMID: Not assigned. Full Text

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The cure of chronic hepatitis C infection has a major impact on the morbidity and mortality of infected patients. It is now clear that sustained virologic response improves overall survival and significantly reduces the risk of liver failure, fibrosis progression, need of liver transplantation, and incidence of hepatocellular carcinoma. Moreover, hepatitis C eradication improves a broad range of extrahepatic manifestations, such as dermatologic, neoplastic, cardiovascular, and endocrine, and improves quality of life.

Gastroenterology
Spradling PR, Xing J, **Rupp LB**, Moorman AC, **Gordon SC**, **Lu M**, Teshale EH, Boscarino JA, Schmidt MA, Daida YG, and Holmberg SD. Low Uptake of Direct-acting Antiviral Therapy Among Hepatitis C Patients With Advanced Liver Disease and Access to Care, 2014-2017. *J Clin Gastroenterol* 2020; Epub ahead of print. PMID: 32250999. Full Text

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GOALS: To determine the proportion and characteristics of adults with hepatitis C at health care organizations in 4 US states who initiated direct-acting antivirals (DAAs). BACKGROUND: There are almost no data to assess the penetrance of treatment of the hepatitis C population in general US health care settings. STUDY: We conducted a prospective observational study using electronic clinical, pharmacy, and mortality data to determine the fraction of patients who initiated DAAs between January 2014 and December 2017, by start date and regimen. We used stepwise multivariate logistic regression analysis to identify sociodemographic and clinical characteristics associated with receipt of DAAs. RESULTS: Of 8823 patients, 2887 (32.7%) received DAAs. Quarterly (Q) uptake ranged from 1.1% in Q3 2014 to a high of 5.6% in Q2 2015. Characteristics associated with receipt of DAAs included age 51 to 70 years, higher income, pre-2014 treatment failure, and higher noninvasive fibrosis score (FIB4); however, over one half of patients with FIB4 scores >3.25, consistent with severe liver disease, were not treated. A lower likelihood of initiation was associated with Medicaid coverage. Of 5936 patients who did not initiate treatment, 911 (15.3%) had died and 2774 (46.7%) had not had a clinical encounter in >/=12 months by the end of the study. Fewer than 1% of DAA prescriptions originated from nonspecialty providers. CONCLUSIONS: During 4 calendar years of follow-up, one third of patients initiated DAAs. Large fractions of untreated patients had advanced liver disease, died, or were lost to follow-up. Even among patients in integrated health care systems, receipt of DAAs was limited.

Global Health Initiative
Lepard JR, Corley J, Sankey EW, **Prentiss T**, Rocque B, Park KB, **Rock J**, Hlaing K, and Myaing W. Training Neurosurgeons in Myanmar and Surrounding Countries: The Resident Perspective. *World Neurosurg* 2020; Epub ahead of print. PMID: 32251819. Full Text

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INTRODUCTION: In recent decades there has been a significant expansion of neurosurgical capabilities in low-and-middle income countries and particularly in Southeast Asia. Despite these developments, little is known about the structure and quality of local neurosurgical training paradigms. METHODS: A 36-question survey was administered to neurosurgical trainees in-person at the Southeast Asian Neurosurgical Bootcamp to assess demographics, structure, and exposure of neurosurgical training in Southeast Asia. RESULTS: 45 out of 47 possible respondents participated in the survey. 78% were male with an age range of 26-40 years. Neurosurgical training most commonly consisted of three (n=22, 49%) or six years (n=14, 31%). The majority of respondents (70.5%) were from Myanmar with the remainder coming from Indonesia, Cambodia, Thailand, and Nepal. Most residents (n=38, 84%) used textbooks as their primary study resource. Only 24 (53%) residents indicated that they had free access to online neurosurgical journals via their training institution. The majority (n=27, 60%) reported that less than 750 cases were performed at their institution per year; with a median of 70% (interquartile range: 50-80%) being emergent. The most commonly reported procedures were trauma craniotomies and ventriculoperitoneal shunting. The least commonly reported procedures were endovascular techniques and spinal instrumentation. CONCLUSIONS: While the unmet burden of neurosurgical disease remains high, local training programs are devoting significant efforts to provide a sustainable solution to the problem of neurosurgical workforce. High income country institutions should partner with global colleagues to ensure high-quality neurosurgical care for all people regardless of location and income.

Hematology/Oncology
Aw Yong KM, Ulintz PJ, Caceres S, Cheng X, Bao L, Wu Z, **Jiagge EM**, and Merajver SD. Heterogeneity at the invasion front of triple negative breast cancer cells. *Sci Rep* 2020; 10(1):5781. PMID: 32238832. Full Text

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Identifying better predictive and prognostic biomarkers for the diagnosis and treatment of triple negative breast cancer (TNBC) is complicated by tumor heterogeneity ranging from responses to therapy, mutational burden, and clonal evolution. To overcome the gap in our understanding of tumor heterogeneity, we hypothesized that isolating and studying the gene expression profile of invasive tumor cell subpopulations would be a crucial step towards achieving this goal. In this report, we utilized a fluidic device previously reported to be capable of supporting long-term three-dimensional growth and invasion dynamics of cancer cells. Live invading and matched non-invading SUM149 inflammatory breast cancer cells were enriched using this device and these two functionally distinct subpopulations were tested for differences in gene expression using a gene expression microarray. 305 target genes were identified to have altered expression in the invading cells compared to the non-invading tumoroid cells. Gene ontology analysis of the gene panel identified multiple biological roles ranging from extracellular matrix reorganization to modulation of the immune response and Rho signaling. Interestingly, the genes associated with the invasion front differ between different samples, consistent with inter- and intra-tumor heterogeneity. This work suggests the impact of heterogeneity in biomarker discovery should be considered as cancer therapy increasingly heads towards a personalized approach.

Hematology/Oncology
Fisher BJ, Pugh SL, Macdonald DR, Chakravatri A, Lesser GJ, Fox S, Rogers CL, Werner-Wasik M, **Doyle T**, Bahary JP, Fiveash JB, Bovi JA, Howard SP, Michael Yu HH, D'Souza D, Laack NN, Barani IJ, Kwok Y, Wahl DR, Strasser JF, Won M, and Mehta MP. Phase II Study of a Temozolomide-Based Chemo-radiotherapy Regimen for High Risk Low-Grade Gliomas: Long-term Results of Radiation Therapy Oncology Group (RTOG) 0424. *Int J Radiat Oncol Biol Phys* 2020; Epub ahead of print. PMID: 32251755. Full Text

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University of Alabama at Birmingham Medical Center.
Froedtert and the Medical College of Wisconsin.
University of Wisconsin Hospital.
H. Lee Moffitt Cancer Center & Research Institute.
Mayo Clinic.
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University of Maryland/Greenebaum Cancer Center.
University of Michigan Medical Center.
Christiana Care Health Services, Inc.
Miami Cancer Institute.

PURPOSE: To report the long-term outcomes of the YYY1 study of a high-risk low-grade gliomas (LGG) population treated with concurrent and adjuvant temozolomide (TMZ) and radiotherapy (RT). PATIENTS/METHODS: For this single-arm phase II study, LGG patients with >3 risk factors (age >40, astrocytoma, bi-hemispheric tumor, size >6 cm or preoperative neurologic function status >1) received RT (54 Gy/30 fractions) with TMZ and up to 12 cycles of post-RT TMZ. The initial primary endpoint p was overall survival (OS) at 3 years after registration. Secondary endpoints included: progression-free survival (PFS), and the association of survival outcomes with methylation status. The initial 3 year report of this study was published in 2015. RESULTS: The study accrued 136 patients, of whom 129 were analyzable. The median follow-up for surviving patients is 9.0 years. The 3-year OS is 73.5% (95% CI: 65.8-81.1%), numerically superior to the 3 year OS historical control(1) OS of 54% (p<0.001). The median survival time is 8.2 years (95% CI: 5.6-9.1). Five- and 10-year OS rates are 60.9% and 34.6% respectively and 5- and 10-year PFS rates are 46.8% and 25.5% respectively. CONCLUSIONS: The long-term results confirmed the findings from the initial reportfor efficacy suggesting OS and PFS outcomes with the RT-TMZ regimen exceeding historical control control groups treated with radiation alone. Toxicity was acceptable.

Hematology/Oncology
Liaqat H, Ammad Ud Din M, and **Malik D**. Poroid Hidradenoma; a Benign Lesion Masking as Malignant Breast Tumor. *Qjm* 2020; Epub ahead of print. PMID: 32240315. Full Text

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Hematology/Oncology
Thanikachalam K, **Damarla V**, **Seixas T**, **Dobrosotskaya I**, **Wollner I**, **Kwon D**, **Winters K**, **Raoufi M**, **Li J**, **Siddiqui F**, and **Khan G**. Neoadjuvant Phase II Trial of Chemoradiotherapy in Patients With Resectable and Borderline Resectable Pancreatic Cancer. *Am J Clin Oncol* 2020; Epub ahead of print. PMID: 32251119. Full Text

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BACKGROUND: Pancreatic ductal adenocarcinoma is a largely incurable cancer. Surgical resection remains the only potential option for cure. Even in surgically resectable patients, only about 10% to 20% are long-term survivors. Emerging data suggest a role for neoadjuvant therapy to target occult micrometastatic disease. AIM: To report our institutional experience with a novel neoadjuvant chemoradiation (CRT) regimen in resectable and borderline resectable pancreatic cancer. MATERIALS AND METHODS: Patients were treated with 2 cycles of induction chemotherapy with FOLFOX and then received CRT with gemcitabine and intensity-modulated radiotherapy (IMRT). RESULTS: From April 2014 to June 2017, 24 patients were enrolled. Eighteen patients were borderline resectable and 6 patients were resectable. All patients received induction chemotherapy with FOLFOX. Thirteen patients underwent pancreatectomy after CRT with a resection rate of 62%. R0 resection achieved in 11 patients (84.6%) and 2 patients had R1 resection (15.4%). For patients who underwent resection, the median progression-free survival (PFS) was 31 months, 1-year PFS rate was 69.2% (95% confidence interval [CI], 0.48-0.99), and 2-year PFS rate was 51.9% (95% CI, 0.3-0.89). Median overall survival (OS) was 34.8 months (95% CI, 1.045 to infinity), 1-year OS rate was 91.7% (95% CI, 0.77-1.0), and 2-year OS rate was 75% (95% CI, 0.54-1.0). Median CA 19-9 at screening for patients who underwent surgery was 659 (range, 18 to 2154), which decreased to 146.9 (range, 18 to 462) after CRT before resection. CONCLUSION: Neoadjuvant therapy for borderline resectable and resectable pancreatic ductal adenocarcinoma with CRT facilitated R0 resection in 84% patients who underwent surgery.

Infectious Diseases
Dabbagh MF, **Aurora L**, **D'Souza P**, **Weinmann AJ**, **Bhargava P**, and **Basir MB**. Cardiac Tamponade Secondary to COVID-19. *JACC Case Rep* 2020; Epub ahead of print. PMID: 32328588. Request Article

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A 67-year-old female presented with upper respiratory symptoms and was diagnosed with COVID-19. She was found to have a large hemorrhagic pericardial effusion with echocardiographic signs of tamponade and mild left ventricular impairment. Clinical course was complicated by development of Takotsubo cardiomyopathy. She was treated with pericardiocentesis, colchicine, corticosteroids and hydroxychloroquine with improvement in symptoms.

Infectious Diseases
Fowler VG, Jr., Das AF, Lipka-Diamond J, Schuch R, Pomerantz R, Jauregui-Peredo L, Bressler A, Evans DC, Moran GJ, Rupp ME, Wise RA, Corey GR, **Zervos M**, Douglas PS, and Cassino C. Exebacase for Staphylococcus aureus bloodstream infection and endocarditis. *J Clin Invest* 2020; Epub ahead of print. PMID: 32271718. Request Article

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BACKGROUNDNovel therapeutic approaches are critically needed for Staphylococcus aureus bloodstream infections (BSI), particularly for methicillin-resistant S. aureus (MRSA). Exebacase, a first-in-class antistaphylococcal lysin, is a direct lytic agent that is rapidly bacteriolytic, eradicates biofilms, and synergizes with antibiotics.METHODSIn this superiority-design study, we randomly assigned 121 patients with S. aureus BSI/endocarditis to receive a single dose of exebacase or placebo. All patients received standard-of-care antibiotics. The primary efficacy endpoint was clinical outcome (responder rate) at Day 14.RESULTSClinical responder rates at Day 14 were 70.4% and 60.0% in the exebacase + antibiotics and antibiotics alone groups, respectively (difference=10.4, 90% CI [-6.3, 27.2], p-value=0.31), and were 42.8 percentage points higher in the pre-specified exploratory MRSA subgroup (74.1% vs. 31.3%, difference=42.8, 90% CI [14.3, 71.4], ad hoc p value=0.01). Rates of adverse events (AEs) were similar in both groups. No AEs of hypersensitivity to exebacase were reported. Thirty-day all-cause mortality rates were 9.7% and 12.8% in the exebacase + antibiotics and antibiotics alone groups, respectively, with a notable difference in MRSA (3.7% vs. 25.0%, difference= -21.3, 90% CI [-45.1, 2.5], ad hoc p-value=0.06). Among MRSA patients in the United States, median length-of-stay was 4-days shorter and 30-day hospital readmission rates were 48 percentage points lower in the exebacase-treated group compared with antibiotics alone.CONCLUSIONSThis study establishes proof-of-concept for exebacase and direct lytic agents as potential therapeutics and supports conduct of a confirmatory study focused on exebacase to treat MRSA BSI.

Infectious Diseases
Morrison AR, **Johnson JM**, **Ramesh M**, **Bradley P**, **Jennings J**, and **Smith ZR**. Letter to the Editor: Acute hypertriglyceridemia in patients with COVID-19 receiving tocilizumab. *J Med Virol* 2020; Epub ahead of print. PMID: 32314799. Full Text

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Tocilizumab is an interleukin-6 (IL-6) receptor antibody and is progressing as a viable and promising treatment option in patients with severe coronavirus disease 2019 (COVID-19). IL-6 is known to have both immunomodulatory and metabolic actions. In this letter we outline two cases of acute hypertriglyceridemia in patients with COVID-19 treated with tocilizumab: one with elevated biomarkers consistent with acute pancreatitis the other without. Given the paucity of robust clinical trial data for most COVID-19 pharmacotherapies at this time, clinicians should continue to remain steadfast in recognition of

interventions that improve clinical outcomes and vigilant in monitoring for acute adverse effects that are difficult to detect in clinical trials with small sample sizes. The observations from our two cases highlight the complex, not fully elucidated interrelationship between elevated IL-6 and pharmacologic interventions impacting this pathway. Clinicians should consider monitoring for hypertriglyceridemia and acute pancreatitis as described with chronic tocilizumab use for rheumatoid arthritis in those receiving it for COVID-19. This article is protected by copyright. All rights reserved.

Internal Medicine
Gupta A, **Fouad L**, **Basir M**, **Neupane S**, **Zaidan M**, **Koenig G**, **Alqarqaz M**, **Villablanca PA**, **O'Neill WW**, and **Alaswad K**. Safety and effectiveness of MANTA vascular closure device after large-bore mechanical circulatory support: Real-world experience. *Cardiovascular Revascularization Medicine* 2020; Epub ahead of print. PMID: Not assigned. Full Text

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Background: Real world safety and effectiveness of MANTA vascular closure device (VCD) for large bore arteriotomy closure after decannulation of mechanical circulatory support (MCS) devices is not known. Methods: All consecutive patients who underwent large bore arteriotomy closure with MANTA VCD following decannulation of MCS between February to October 2019 at a large tertiary care academic medical center were included. Safety and effectiveness of MANTA VCD was assessed on immediate post-closure angiogram for 23 access sites, and immediate post-closure duplex arterial ultrasound or manual vascular examination for 1 access site each. Technical success was defined as achievement of arteriotomy closure in absence of major bleeding or access site endovascular or surgical intervention. Results: A total of 25 MANTA VCD were placed in 22 unique patients by 7 different operators. A 14 Fr or 18 Fr MANTA VCD was used in 15 (60%) and 10 (40%) of deployments, respectively via transfemoral (n = 23, 92%) or transaxillary (n = 2, 8%) access. Technical success was achieved in 24 of 25 (96%) cases. Minor access site bleeding occurred in 3 patients (12%) and failure of MANTA VCD with major access site bleeding occurred in 1 patient (4%) requiring endovascular balloon tamponade. No cases of retroperitoneal bleeding, collagen plug embolization, covered stent placement, or surgical vascular repair were observed. Conclusion: In this single center experience, the use of MANTA VCD for large bore arteriotomy closure following percutaneous decannulation of MCS devices appears to be safe and effective. Larger multicenter studies of efficacy, safety, and cost-effectiveness are needed.

Internal Medicine
Liaqat H, Ammad Ud Din M, and **Malik D**. Poroid Hidradenoma; a Benign Lesion Masking as Malignant Breast Tumor. *Qjm* 2020; Epub ahead of print. PMID: 32240315. Full Text

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Internal Medicine
Lyons AB, **Kohli I**, Nahhas AF, **Braunberger TL**, **Mohammad TF**, Nicholson CL, Nartker NT, **Modi K**, Matsui MS, **Lim HW**, and **Hamzavi IH**. Trichloroacetic acid model to accurately capture the efficacy of treatments for postinflammatory hyperpigmentation. *Arch Dermatol Res* 2020; Epub ahead of print. PMID: 32253506. Full Text

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Postinflammatory hyperpigmentation (PIH) occurs following cutaneous injury and is common following resolution of acne especially in patients with skin of color. The objective of this study was to further validate a trichloroacetic acid (TCA)-induced PIH model and compare it to acne-induced PIH using topical bakuchiol, a botanical extract that has been shown to have antimicrobial, anti-inflammatory, antioxidant, and antiacne properties. A prospective, non-randomized clinical trial was conducted on subjects with skin phototypes IV-VI with a history of acne-induced PIH. Subjects applied bakuchiol or vehicle cream twice daily to 2 acne-induced and 2 TCA-induced PIH lesions for 28 days with a third lesion serving as a control in each group. Degree of improvement was defined as the change in the Investigator Global Assessment (IGA) score over 28 days of treatment. Twenty subjects (6 males, 14 females) completed the study. For TCA-induced PIH sites, there was a statistically significant ($p < 0.05$) degree of improvement with bakuchiol treatment (- 0.50 +/- 0.18) compared to vehicle (0.05 +/- 0.15) and control (- 0.06 +/- 0.17). For acne-induced PIH, there was a greater degree of improvement for bakuchiol (- 1.06 +/- 0.23) when compared to vehicle (- 0.56 +/- 0.16) and control (- 0.69 +/- 0.18); however, statistical significance was not reached ($p > 0.05$). TCA-induced PIH sites were uniform in size and pigment intensity thereby allowing better comparison among sites. This

emphasizes the relevance of using this model for PIH which may help reduce the barriers in clinical trials and help improve access to treatments for patients who suffer from PIH. The results suggest that topical bakuchiol may decrease the severity of PIH.

Internal Medicine
Refaai MA, **Shah V**, and Fernando R. Performance of the microINR Point-of-Care System: A Multicenter Clinical Trial. *Thromb Haemost* 2020; 120(4):687-691. PMID: 32299116. Full Text

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INTRODUCTION: There are limited publications about the microINR point-of-care (POC) system (iLine Microsystems). The current microINR POC system was compared with the ACL TOP 500 laboratory analyzer (Instrumentation Laboratory) and with the CoaguChek XS POC system (Roche Diagnostics). METHODS: This study was performed at three United States medical centers. Sixty-eight nonanticoagulated normal donors and 245 warfarin anticoagulated patients were included. Testing was performed in duplicate using capillary blood samples for the POC systems and venous blood samples for the laboratory testing. Accuracy and imprecision were assessed. RESULTS: Comparing microINR to ACL revealed a correlation coefficient (r) of 0.973, a slope of 1.00 (95% confidence interval [CI], 0.97-1.03), and an intercept of 0.08 (95% CI, 0.04-0.15). When compared with the CoaguChek XS, r was 0.977 with a slope of 0.92 (95% CI, 0.89-0.94) and an intercept of 0.15 (95% CI, 0.08-0.19). Predicted bias values at international normalized ratio (INR) 2.0, 3.5, and 4.5 were </= 5% against both references. Agreement with ACL was 97, 95, and 100% for the INR ranges of < 2.0 +/- 0.40, 2.0 to 4.5 +/- 20%, and >/= 4.5 +/- 25%, respectively. Agreement for the combined INR ranges was 96% against ACL and > 96% against the CoaguChek XS. The coefficient of variation of the microINR was 5.03% for INR < 2.0 and 4.68% for the therapeutic INR range 2.0 to 3.5. CONCLUSION: The microINR results demonstrate adequate imprecision and accuracy to both ACL and CoaguChek XS. This indicates that monitoring INR by this microINR POC system is reliable and acceptable for the management of warfarin therapy.

Nephrology
McCullough PA, Eidt J, Rangaswami J, Lerma E, Tumlin J, Wheelan K, Katz N, Lepor NE, Vijay K, **Soman S**, Singh B, McCullough SP, McCullough HB, Palazzuoli A, Ruocco GM, and Ronco C. Urgent need for individual mobile phone and institutional reporting of at home, hospitalized, and intensive care unit cases of SARS-CoV-2 (COVID-19) infection. *Rev Cardiovasc Med* 2020; 21(1):1-7. PMID: 32259899. Request Article

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Approximately 90 days of the SARS-CoV-2 (COVID-19) spreading originally from Wuhan, China, and across the globe has led to a widespread chain of events with imminent threats to the fragile relationship between community health and economic health. Despite near hourly reporting on this crisis, there has been no regular, updated, or accurate reporting of hospitalizations for COVID-19. It is known that many test-positive individuals may not develop symptoms or have a mild self-limited viral syndrome consisting of fever, malaise, dry cough, and constitutional symptoms. However some individuals develop a more fulminant syndrome including viral pneumonia, respiratory failure requiring oxygen, acute respiratory distress syndrome requiring mechanical ventilation, and in substantial fractions leading to death attributable to COVID-19. The pandemic is evolving in a clustered, non-inform fashion resulting in many hospitals with preparedness but few or no cases, and others that are completely overwhelmed. Thus, a considerable risk of spread when personal protection equipment becomes exhausted and a large fraction of mortality in those not offered mechanical ventilation are both attributable to a crisis due to maldistribution of resources. The pandemic is amenable to self-reporting through a mobile phone application that could

obtain critical information on suspected cases and report on the results of self testing and actions taken. The only method to understand the clustering and the immediate hospital resource needs is mandatory, uniform, daily reporting of hospital censuses of COVID-19 cases admitted to hospital wards and intensive care units. Current reports of hospitalizations are delayed, uncertain, and wholly inadequate. This paper urges all the relevant stakeholders to take up self-reporting and reporting of hospitalizations of COVID-19 as an urgent task in combating this devastating pandemic.

Neurology
Bowyer SM, Pang EW, Huang M, Papanicolaou AC, and Lee RR. Presurgical Functional Mapping with Magnetoencephalography. *Neuroimaging Clin N Am* 2020; 30(2):159-174. PMID: 32336404. Full Text

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Noninvasive functional brain imaging with magnetoencephalography (MEG) is regularly used to map the eloquent cortex associated with somatosensory, motor, auditory, visual, and language processing before a surgical resection to determine if the functional areas have been reorganized. Most tasks can also be performed in the pediatric population. To acquire an optimal MEG study for any of these modalities, the patient needs to be well rested and attending to the stimulation.

Neurology
Fan B, **Pan W**, **Wang X**, **Wei M**, **He A**, **Zhao A**, **Chopp M**, **Zhang ZG**, and **Liu XS**. Long non-coding RNA mediates stroke-induced neurogenesis. *Stem Cells* 2020; Epub ahead of print. PMID: 32346940. Full Text

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Neurogenesis contributes to post-stroke recovery. Long non-coding RNAs (lncRNAs) participate in the regulation of stem cell self-renewal and differentiation. However, the role of lncRNAs in stroke-induced neurogenesis remains unknown. In this study, we found that H19 was the most highly upregulated lncRNA in neural stem cells (NSCs) of the subventricular zone (SVZ) of rats subjected to focal cerebral ischemia. Deletion of H19 suppressed cell proliferation, promoted cell death and blocked NSC differentiation. RNA sequencing analysis revealed that genes deregulated by H19 knockdown were those that are involved in transcription, apoptosis, proliferation, cell cycle and response to hypoxia. H19 knockdown significantly increased the transcription of cell cycle-related genes including p27, whereas overexpression of H19 substantially reduced expression of these genes through the interaction with chromatin remodeling proteins EZH2 and SUZ12. Moreover, H19 regulated neurogenesis-related miRNAs. Inactivation of H19 in NSCs of ischemic rats attenuated spontaneous functional recovery after stroke. Collectively, our data provide novel insights into the epigenetic regulation of lncRNAs in stroke-induced neurogenesis. (c) AlphaMed Press 2020 SIGNIFICANCE STATEMENT: Adult neurogenesis contributes to neurological function. Elucidating the underlying molecular mechanisms in post-stroke neurogenesis could provide new therapies to amplify endogenous neurogenesis and to improve neurological function during stroke recovery. The present study for the first time reveals that stroke substantially changes lncRNA profiles and lncRNA-mRNA co-expression networks in the neural stem cells. Furthermore, we demonstrate that lncRNA H19 mediates stroke-augmented neurogenesis by recruiting chromatin remodeling proteins and regulating microRNA expression to modulate neurogenesis-related transcription. Our results provide new insights into the epigenetic control of adult neurogenesis after cerebral ischemia.

Neurology
Hamalainen M, Huang M, and **Bowyer SM**. Magnetoencephalography Signal Processing, Forward Modeling, Magnetoencephalography Inverse Source Imaging, and Coherence Analysis. *Neuroimaging Clin N Am* 2020; 30(2):125-143. PMID: 32336402. Full Text

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Magnetoencephalography (MEG) is a noninvasive functional imaging technique for the brain. MEG directly measures the magnetic signal due to neuronal activation in gray matter with high spatial localization accuracy. The first part of this article covers the overall concepts of MEG and the forward and inverse modeling techniques. It is followed by examples of analyzing evoked and resting-state MEG signals using a high-resolution MEG source imaging technique. Next, different techniques for connectivity and network analysis are reviewed with examples showing connectivity estimates from resting-state and epileptic activity.

Neurology
Jamali-Dinan SS, **Soltanian-Zadeh H**, **Bowyer SM**, Almohri H, Dehghani H, Elisevich K, and Nazem-Zadeh MR. A Combination of Particle Swarm Optimization and Minkowski Weighted K-Means Clustering: Application in Lateralization of Temporal Lobe Epilepsy. *Brain Topogr* 2020; Epub ahead of print. PMID: 32347472. Full Text

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K-Means is one of the most popular clustering algorithms that partitions observations into nonoverlapping subgroups based on a predefined similarity metric. Its drawbacks include a sensitivity to noisy features and a dependency of its resulting clusters upon the initial selection of cluster centroids resulting in the algorithm converging to local optima. Minkowski weighted K-Means (MWK-Means) addresses the issue of sensitivity to noisy features, but is sensitive to the initialization of clusters, and so the algorithm may similarly converge to local optima. Particle Swarm Optimization (PSO) uses a globalized search method to solve this issue. We present a hybrid Particle Swarm Optimization (PSO) + MWK-Means clustering algorithm to address all the above problems in a single framework, while maintaining benefits of PSO and MWK Means methods. This study investigated the utility of this approach in lateralizing the epileptogenic hemisphere for temporal lobe epilepsy (TLE) cases using magnetoencephalography (MEG) coherence source imaging (CSI) and diffusion tensor imaging (DTI). Using MEG-CSI, we analyzed preoperative resting state MEG data from 17 adults TLE patients with Engel class I outcomes to determine coherence at 54 anatomical sites and compared the results with 17 age- and gender-matched controls. Fiber-tracking was performed through the same anatomical sites using DTI data. Indices of both MEG coherence and DTI nodal degree were calculated. A PSO + MWK-Means clustering algorithm was applied to identify the side of temporal lobe epileptogenicity and distinguish between normal and TLE cases. The PSO module was aimed at identifying initial cluster centroids and assigning initial feature weights to cluster centroids and, hence, transferring to the MWK-Means module for the final optimal clustering solution. We demonstrated improvements with the use of the PSO + MWK-Means clustering algorithm compared to that of K-Means and MWK-Means independently. PSO + MWK-Means was able to successfully distinguish between normal and TLE in 97.2% and 82.3% of cases for DTI and MEG data, respectively. It also lateralized left and right TLE in 82.3% and 93.6% of cases for DTI and MEG data, respectively. The proposed optimization and clustering methodology for MEG and DTI features, as they relate to focal epileptogenicity, would enhance the identification of the TLE laterality in cases of unilateral epileptogenicity.

Neurology
Medalla M, Chang W, Calderazzo SM, Go V, Tsolias A, Goodliffe JW, Pathak D, De Alba D, Pessina M, Rosene DL, **Buller B**, and Moore TL. Treatment with Mesenchymal-Derived Extracellular Vesicles Reduces Injury-Related Pathology in Pyramidal Neurons of Monkey Perilesional Ventral Premotor Cortex. *J Neurosci* 2020; 40(17):3385-3407. PMID: 32241837. Full Text

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Functional recovery after cortical injury, such as stroke, is associated with neural circuit reorganization, but the underlying mechanisms and efficacy of therapeutic interventions promoting neural plasticity in primates are not well understood. Bone

marrow mesenchymal stem cell-derived extracellular vesicles (MSC-EVs), which mediate cell-to-cell inflammatory and trophic signaling, are thought be viable therapeutic targets. We recently showed, in aged female rhesus monkeys, that systemic administration of MSC-EVs enhances recovery of function after injury of the primary motor cortex, likely through enhancing plasticity in perilesional motor and premotor cortices. Here, using in vitro whole-cell patch-clamp recording and intracellular filling in acute slices of ventral premotor cortex (vPMC) from rhesus monkeys (Macaca mulatta) of either sex, we demonstrate that MSC-EVs reduce injury-related physiological and morphologic changes in perilesional layer 3 pyramidal neurons. At 14-16 weeks after injury, vPMC neurons from both vehicle- and EV-treated lesioned monkeys exhibited significant hyperexcitability and predominance of inhibitory synaptic currents, compared with neurons from nonlesioned control brains. However, compared with vehicle-treated monkeys, neurons from EV-treated monkeys showed lower firing rates, greater spike frequency adaptation, and excitatory:inhibitory ratio. Further, EV treatment was associated with greater apical dendritic branching complexity, spine density, and inhibition, indicative of enhanced dendritic plasticity and filtering of signals integrated at the soma. Importantly, the degree of EV-mediated reduction of injury-related pathology in vPMC was significantly correlated with measures of behavioral recovery. These data show that EV treatment dampens injury-related hyperexcitability and restores excitatory:inhibitory balance in vPMC, thereby normalizing activity within cortical networks for motor function.SIGNIFICANCE STATEMENT Neuronal plasticity can facilitate recovery of function after cortical injury, but the underlying mechanisms and efficacy of therapeutic interventions promoting this plasticity in primates are not well understood. Our recent work has shown that intravenous infusions of mesenchymal-derived extracellular vesicles (EVs) that are involved in cell-to-cell inflammatory and trophic signaling can enhance recovery of motor function after injury in monkey primary motor cortex. This study shows that this EV-mediated enhancement of recovery is associated with amelioration of injury-related hyperexcitability and restoration of excitatory-inhibitory balance in perilesional ventral premotor cortex. These findings demonstrate the efficacy of mesenchymal EVs as a therapeutic to reduce injury-related pathologic changes in the physiology and structure of premotor pyramidal neurons and support recovery of function.

Neurology
Noh T, **Osman G**, **Chedid M**, and **Hefzy H**. Nitrous oxide-induced demyelination: Clinical presentation, diagnosis and treatment recommendations. *J Neurol Sci* 2020; 414:116817. PMID: 32302804. Full Text

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BACKGROUND: Recreational use of nitrous oxide (NO) in the general public has led to increasing reports of NO-induced demyelination (NOID). We describe the varying clinical presentations and pathophysiology, and offer a treatment paradigm. METHODS: A literature search of MEDLINE and EMBASE resulted in 42 publications with 37 studies meeting the inclusion criteria, for a total of 51 patients. Our case series included 5 patients seen from 2014 to 2018 followed over 3-60 months. RESULTS: Those with sensory symptoms and subjective weakness were categorized as having "mild" symptoms (25%). Symptoms indicating involvement outside the dorsal columns such as observer-graded weakness were categorized as "moderate" (61%). Patients with the aforementioned plus cognitive effects were categorized as "severe" (12%). There was no dose-dependent relationship between the amount of NO used and clinical impairment. There was a trend between the severity of neurologic impairment and serum levels of B12. Two patients were noncompliant. One initiated only oral therapy and did not improve. One received injections a month apart and worsened. CONCLUSIONS: Patients with NOID tend to have worse symptoms when presenting with lower serum vitamin B12 levels and have good recovery rates when treated with intramuscular B12 and oral supplementation.

Neurology
Parikh NS, Kamel H, Navi BB, Iadecola C, Merkler AE, Jesudian A, Dawson J, Falcone GJ, Sheth KN, Roh DJ, Elkind MSV, Hanley DF, Ziai WC, Murthy SB, and **Mayer SA**. Liver Fibrosis Indices and Outcomes After Primary Intracerebral Hemorrhage. *Stroke* 2020; 51(3):830-837. PMID: 31906832. Full Text

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Brain Injury Outcomes Division (D.F.H.), Johns Hopkins University School of Medicine, Baltimore, MD.
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Background and Purpose- Cirrhosis-clinically overt, advanced liver disease-is associated with an increased risk of hemorrhagic stroke and poor stroke outcomes. We sought to investigate whether subclinical liver disease, specifically liver fibrosis, is associated with clinical and radiological outcomes in patients with primary intracerebral hemorrhage. Methods- We performed a retrospective cohort study using data from the Virtual International Stroke Trials Archive-Intracerebral Hemorrhage. We included adult patients with primary intracerebral hemorrhage presenting within 6 hours of symptom onset. We calculated 3 validated fibrosis indices-Aspartate Aminotransferase-Platelet Ratio Index, Fibrosis-4 score, and Nonalcoholic Fatty Liver Disease Fibrosis Score-and modeled them as continuous exposure variables. Primary outcomes were admission hematoma volume and hematoma expansion. Secondary outcomes were mortality, and the composite of major disability or death, at 90 days. We used linear and logistic regression models adjusted for previously established risk factors. Results- Among 432 patients with intracerebral hemorrhage, the mean Aspartate Aminotransferase-Platelet Ratio Index, Fibrosis-4, and Nonalcoholic Fatty Liver Disease Fibrosis Score values on admission reflected intermediate probabilities of fibrosis, whereas standard hepatic assays and coagulation parameters were largely normal. After adjusting for potential confounders, Aspartate Aminotransferase-Platelet Ratio Index was associated with hematoma volume (beta, 0.20 [95% CI, 0.04-0.36]), hematoma expansion (odds ratio, 1.6 [95% CI, 1.1-2.3]), and mortality (odds ratio, 1.8 [95% CI, 1.1-2.7]). Fibrosis-4 was also associated with hematoma volume (beta, 0.27 [95% CI, 0.07-0.47]), hematoma expansion (odds ratio, 1.9 [95% CI, 1.2-3.0]), and mortality (odds ratio, 2.0 [95% CI, 1.1-3.6]). Nonalcoholic Fatty Liver Disease Fibrosis Score was not associated with any outcome. Indices were not associated with the composite of major disability or death. Conclusions- In patients with largely normal liver chemistries, 2 liver fibrosis indices were associated with admission hematoma volume, hematoma expansion, and mortality after intracerebral hemorrhage.

Neurology
Viarasilpa T, Ghosh P, Gidwani S, Lantigua H, De Marchis GM, Panyavachiraporn N, Schmidt JM, Lee K, Badjatia N, Agarwal S, Claassen J, and **Mayer SA**. Prognostic Significance of Sentinel Headache Preceding Aneurysmal Subarachnoid Hemorrhage. *World Neurosurg* 2020; Epub ahead of print. PMID: 32339738. Full Text

Department of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand.
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Neurosurgery
Asmaro K, **Rock J**, and **Craig J**. Expanded Endonasal Approach for Resection of Extradural Infratemporal Fossa Trigeminal Schwannoma: 2-Dimensional Operative Video. *Oper Neurosurg (Hagerstown)* 2020; Epub ahead of print. PMID: 32348506. Request Article

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The infratemporal fossa (ITF) is bounded superiorly by the skull base, specifically the greater wing of the sphenoid, which contains foramen ovale. It is bordered posteriorly by the temporal bone, including the petrous portion of the carotid canal, anteriorly by the posterior wall of the maxillary sinus, laterally by the mandible, and medially by the pterygoid body and lateral pterygoid plate.1-3 In this video, we report a case of a rare, exclusively extradural, schwannoma originating from the third division of the trigeminal nerve with a widened foramen ovale at the skull base. The tumor filled the ITF and extended laterally just through the sigmoid notch of the mandible. The patient complained of left cheek and lower jaw numbness and intermittent left jaw spasms. The tumor was deemed appropriate for endoscopic resection. To access the ITF, left-sided endoscopic sinus surgery, a modified endoscopic Denker's approach,4 and posterior nasal septectomy were first performed. A nasoseptal flap was also harvested in case an intraoperative cerebrospinal fluid (CSF) leak required repair. Dissection was carried out through the posterior wall of the maxillary sinus and pterygopalatine fossa to reach the ITF. Tumor resection was achieved through a 2-surgeon, 4-handed approach in which appropriate traction and countertraction were carefully applied to tease the tumor away from the skull base and dehiscent carotid canal. No CSF leak or carotid injury occurred, and the posterior maxillary sinus

wall defect was repaired with the nasoseptal flap. The patient did well postoperatively. The patient consented to the procedure in a standard fashion.

Neurosurgery
Haider SA, Shank CD, and **Walters BC**. Commentary: The Role of Stereotactic Radiosurgery in the Management of Brain Metastases From a Health-Economic Perspective: A Systematic Review. *Neurosurgery* 2020; Epub ahead of print. PMID: 32320033. Full Text

Department of Neurosurgery, Henry Ford Health System, Detroit, Michigan.
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Neurosurgery
Lepard JR, Corley J, Sankey EW, **Prentiss T**, Rocque B, Park KB, **Rock J**, Hlaing K, and Myaing W. Training Neurosurgeons in Myanmar and Surrounding Countries: The Resident Perspective. *World Neurosurg* 2020; Epub ahead of print. PMID: 32251819. Full Text

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INTRODUCTION: In recent decades there has been a significant expansion of neurosurgical capabilities in low-and-middle income countries and particularly in Southeast Asia. Despite these developments, little is known about the structure and quality of local neurosurgical training paradigms. METHODS: A 36-question survey was administered to neurosurgical trainees in-person at the Southeast Asian Neurosurgical Bootcamp to assess demographics, structure, and exposure of neurosurgical training in Southeast Asia. RESULTS: 45 out of 47 possible respondents participated in the survey. 78% were male with an age range of 26-40 years. Neurosurgical training most commonly consisted of three (n=22, 49%) or six years (n=14, 31%). The majority of respondents (70.5%) were from Myanmar with the remainder coming from Indonesia, Cambodia, Thailand, and Nepal. Most residents (n=38, 84%) used textbooks as their primary study resource. Only 24 (53%) residents indicated that they had free access to online neurosurgical journals via their training institution. The majority (n=27, 60%) reported that less than 750 cases were performed at their institution per year; with a median of 70% (interquartile range: 50-80%) being emergent. The most commonly reported procedures were trauma craniotomies and ventriculoperitoneal shunting. The least commonly reported procedures were endovascular techniques and spinal instrumentation. CONCLUSIONS: While the unmet burden of neurosurgical disease remains high, local training programs are devoting significant efforts to provide a sustainable solution to the problem of neurosurgical workforce. High income country institutions should partner with global colleagues to ensure high-quality neurosurgical care for all people regardless of location and income.

Neurosurgery
Noh T, **Osman G**, **Chedid M**, and **Hefzy H**. Nitrous oxide-induced demyelination: Clinical presentation, diagnosis and treatment recommendations. *J Neurol Sci* 2020; 414:116817. PMID: 32302804. Full Text

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Department of Neurology, Henry Ford West Bloomfield Hospital, 6777 West Maple Road, West Bloomfield, MI 48322, USA. Electronic address: hhefzy1@hfhs.org.

BACKGROUND: Recreational use of nitrous oxide (NO) in the general public has led to increasing reports of NO-induced demyelination (NOID). We describe the varying clinical presentations and pathophysiology, and offer a treatment paradigm. METHODS: A literature search of MEDLINE and EMBASE resulted in 42 publications with 37 studies meeting the inclusion criteria, for a total of 51 patients. Our case series included 5 patients seen from 2014 to 2018 followed over 3-60 months.

RESULTS: Those with sensory symptoms and subjective weakness were categorized as having "mild" symptoms (25%). Symptoms indicating involvement outside the dorsal columns such as observer-graded weakness were categorized as "moderate" (61%). Patients with the aforementioned plus cognitive effects were categorized as "severe" (12%). There was no dose-dependent relationship between the amount of NO used and clinical impairment. There was a trend between the severity of neurologic impairment and serum levels of B12. Two patients were noncompliant. One initiated only oral therapy and did not improve. One received injections a month apart and worsened. CONCLUSIONS: Patients with NOID tend to have worse symptoms when presenting with lower serum vitamin B12 levels and have good recovery rates when treated with intramuscular B12 and oral supplementation.

Neurosurgery
Schwalb JM. Commentary: Percutaneous Trigeminal Stimulation for Intractable Facial Pain: A Case Series. *Neurosurgery* 2020; Epub ahead of print. PMID: 32348492. Full Text

Department of Neurosurgery, Henry Ford West Bloomfield, West Bloomfield Township, Michigan.

Neurosurgery
Snyder JM, **Pawloski JA**, and **Poisson LM**. Developing Real-world Evidence-Ready Datasets: Time for Clinician Engagement. *Curr Oncol Rep* 2020; 22(5):45. PMID: 32297007. Full Text

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PURPOSE OF REVIEW: Real-world data (RWD) applications in healthcare that support learning health systems and pragmatic clinical trials are gaining momentum, largely due to legislation supporting real-world evidence (RWE) for drug approvals. Clinical notes are thought to be the cornerstone of RWD applications, particularly for conditions with limited effective treatments, extrapolation of treatments from other conditions, or heterogenous disease biology and clinical phenotypes. RECENT FINDINGS: Here, we discuss current issues in applying RWD captured at the point-of-care and provide a framework for clinicians to engage in RWD collection. To achieve clinically meaningful results, RWD must be reliably captured using consistent terminology in the description of our patients. RWD complements traditional clinical trials and research by informing the generalizability of results, generating new hypotheses, and creating a large data network for scientific discovery. Effective clinician engagement in the development of RWD applications is necessary for continued progress in the field.

Neurosurgery
Zervos TM, **Scarpace L**, **Robin AM**, **Schwalb JM**, and **Air EL**. Adapting to Space Limitations During Prone Real-Time Magnetic Resonance Imaging-Guided Stereotaxic Laser Ablation: Technical Pearls. *Oper Neurosurg (Hagerstown)* 2020; 18(4):398-402. PMID: 31245819. Request Article

Department of Neurosurgery, Henry Ford Hospital, Detroit, Michigan.

BACKGROUND: New techniques of intraoperative magnetic resonance imaging (MRI)-guided stereotaxy enable minimally invasive approaches to intracranial pathology. Laser interstitial thermal therapy (LITT), convection-enhanced drug delivery, and stereotactic biopsy can be performed with a real-time confirmation of location and the ability to adjust for intracranial shift during the procedure. However, these procedures are constrained by patient positioning and the need for trajectories that avoid collision between stereotactic elements and the small MRI bore. To our knowledge, this is the first report to outline the technical details of safe intraoperative MRI (iMRI)-guided stereotaxy, performed with prone positioning. OBJECTIVE: To present technical pearls to guide the safe conduction of iMRI-guided stereotaxy and LITT while in the prone position. METHODS: The details of the positioning and trajectories for a series of patients who underwent Clearpoint(R) (MRI Interventions Inc) frameless real-time MRI-guided stereotaxis using a posterior approach were reviewed. RESULTS: In this series, 5 patients underwent selective amygdalohippocampectomy, and 2 underwent tumor biopsy/ablation while in the prone position without any complications. CONCLUSION: Prone iMRI procedures can be performed safely even in a 60-cm MRI bore.

Nursing
Doe S, **Petersen S**, **Buekers T**, and **Swain M**. Does a Multidisciplinary Approach to Invasive Breast Cancer Care Improve Time to Treatment and Patient Compliance? *J Natl Med Assoc* 2020; Epub ahead of print. PMID: 32291070. Request Article

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PURPOSE: This study aimed to evaluate whether comprehensive multidisciplinary care (cMDC) for breast cancer patients affected time from diagnosis to treatment, compliance with appointments and to assess for racial disparities. METHODS: This institutional review board approved retrospective study included adult patients diagnosed with invasive breast cancer between February 2015 and February 2017 and treated at an academic health system where the cMDC program was implemented in February 2016. The cMDC and non-cMDC groups as well as black and white patients were compared to assess time from diagnosis (date of pathology result indicating invasive breast cancer) to treatment (date of surgery or chemotherapy). Compliance was measured by appointments characterized as "no shows" or "canceled due to personal reasons" in the electronic medical record. RESULTS: Of 541 patients (419 cMDC and 122 non-cMDC), mean time from diagnosis to treatment was significantly longer for blacks than whites in the non-cMDC group (46.9 +/- 64.6 days vs 28.2 +/- 14.8 days, p = 0.024) and the cMDC group (39.9 +/- 34.1 days vs 31.4 +/- 16.3 days, p = 0.001). Of 38 (7.2%) patients who started treatment > 60 days after diagnosis, 25 (65.8%) were black. Implementation of cMDC significantly improved patient compliance (missed appointments 4.9 +/- 7.6 non-cMDC vs 3.2 +/- 4.6 cMDC, p = 0.029). CONCLUSION: Use of cMDC for invasive breast cancer at our institution highlighted an area for improvement for care administered to blacks and improved patient compliance with appointments.

Nursing

Roshandel D, Chen Z, Canty AJ, Bull SB, Natarajan R, Paterson AD, **Bhan A**, **Jones JK**, **Kruger D**, **Edwards PA**, **Remtema H**, **Angus E**, **Galprin A**, **McLellan M**, **Thomas A**, **Carey JD**, and **Whitehouse F**. DNA methylation age calculators reveal association with diabetic neuropathy in type 1 diabetes. *Clin Epigenetics* 2020; 12(1):52. PMID: 32248841. Request Article

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BACKGROUND: Many CpGs become hyper or hypo-methylated with age. Multiple methods have been developed by Horvath et al. to estimate DNA methylation (DNAm) age including Pan-tissue, Skin & Blood, PhenoAge, and GrimAge. Pan-tissue and Skin & Blood try to estimate chronological age in the normal population whereas PhenoAge and GrimAge use surrogate markers associated with mortality to estimate biological age and its departure from chronological age. Here, we applied Horvath's four methods to calculate and compare DNAm age in 499 subjects with type 1 diabetes (T1D) from the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) study using DNAm data measured by Illumina EPIC array in the whole blood. Association of the four DNAm ages with development of diabetic complications including cardiovascular diseases (CVD), nephropathy, retinopathy, and neuropathy, and their risk factors were investigated. RESULTS: Pan-tissue and GrimAge were higher whereas Skin & Blood and PhenoAge were lower than chronological age (p < 0.0001). DNAm age was not associated with the risk of CVD or retinopathy over 18-20 years after DNAm measurement. However, higher PhenoAge (beta = 0.023, p = 0.007) and GrimAge (beta = 0.029, p = 0.002) were associated with higher albumin excretion rate (AER), an indicator of diabetic renal disease, measured over time. GrimAge was also associated with development of both diabetic peripheral neuropathy (OR = 1.07, p = 9.24E-3) and cardiovascular autonomic neuropathy (OR = 1.06, p = 0.011). Both HbA1c (beta = 0.38, p = 0.026) and T1D duration (beta = 0.01, p = 0.043) were associated with higher PhenoAge. Employment (beta = - 1.99, p = 0.045) and leisure time (beta = - 0.81, p = 0.022) physical activity were associated with lower Pan-tissue and Skin & Blood, respectively. BMI (beta = 0.09, p = 0.048) and current smoking (beta = 7.13, p = 9.03E-50) were positively associated with Skin & Blood and GrimAge, respectively. Blood pressure, lipid levels, pulse rate, and alcohol consumption were not associated with DNAm age regardless of the method used. CONCLUSIONS: Various methods of measuring DNAm age are sub-optimal in detecting people at higher risk of developing diabetic complications although some work better than the others.

Nursing

White RJ, Jerjes-Sanchez C, Bohns Meyer GM, Pulido T, Sepulveda P, Wang KY, Grunig E, Hiremath S, Yu Z, Gangcheng Z, Yip WLJ, Zhang S, Khan A, Deng CQ, Grover R, Tapson VF, **Awdish R**, and **Cajigas H**. Combination Therapy with Oral Treprostinil for Pulmonary Arterial Hypertension. A Double-Blind Placebo-controlled Clinical Trial. *Am J Respir Crit Care Med* 2020; 201(6):707-717. PMID: 31765604. Full Text

Division of Pulmonary and Critical Care Medicine and the Mary M. Parkes Center, University of Rochester Medical Center, Rochester, New York.
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Rationale: Oral treprostinil improves exercise capacity in patients with pulmonary arterial hypertension (PAH), but the effect on clinical outcomes was unknown.Objectives: To evaluate the effect of oral treprostinil compared with placebo on time to first adjudicated clinical worsening event in participants with PAH who recently began approved oral monotherapy.Methods: In this event-driven, double-blind study, we randomly allocated 690 participants (1:1 ratio) with PAH to receive placebo or oral treprostinil extended-release tablets three times daily. Eligible participants were using approved oral monotherapy for over 30 days before randomization and had a 6-minute-walk distance 150 m or greater. The primary endpoint was the time to first adjudicated clinical worsening event: death; hospitalization due to worsening PAH; initiation of inhaled or parenteral prostacyclin therapy; disease progression; or unsatisfactory long-term clinical response.Measurements and Main Results: Clinical worsening occurred in 26% of the oral treprostinil group compared with 36% of placebo participants (hazard ratio, 0.74; 95% confidence interval, 0.56-0.97; P = 0.028). Key measures of disease status, including functional class, Borg dyspnea score, and N-terminal pro-brain natriuretic peptide, all favored oral treprostinil treatment at Week 24 and beyond. A noninvasive risk stratification analysis demonstrated that oral treprostinil-assigned participants had a substantially higher mortality risk at baseline but achieved a lower risk profile from Study Weeks 12-60. The most common adverse events in the oral treprostinil group were headache, diarrhea, flushing, nausea, and vomiting.Conclusions: In participants with PAH, addition of oral treprostinil to approved oral monotherapy reduced the risk of clinical worsening.Clinical trial registered with www.clinicaltrials.gov (NCT01560624).

Obstetrics, Gynecology, and Women's Health

Doe S, **Petersen S**, **Buekers T**, and **Swain M**. Does a Multidisciplinary Approach to Invasive Breast Cancer Care Improve Time to Treatment and Patient Compliance? *J Natl Med Assoc* 2020; Epub ahead of print. PMID: 32291070. Request Article

Department of Women's Health Services, Breast Surgical Oncology, Henry Ford Hospital, 2799 W. Grand Blvd, Detroit, MI, 48202, USA.
Department of Women's Health Services, Breast Surgical Oncology, Henry Ford Hospital, 2799 W. Grand Blvd, Detroit, MI, 48202, USA; Department of General Surgery, Breast Surgical Oncology, Henry Ford Hospital, 2799 W. Grand Blvd, Detroit, MI, 48202, USA. Electronic address: MSwain1@hfhs.org.

PURPOSE: This study aimed to evaluate whether comprehensive multidisciplinary care (cMDC) for breast cancer patients affected time from diagnosis to treatment, compliance with appointments and to assess for racial disparities. METHODS: This institutional review board approved retrospective study included adult patients diagnosed with invasive breast cancer between February 2015 and February 2017 and treated at an academic health system where the cMDC program was implemented in February 2016. The cMDC and non-cMDC groups as well as black and white patients were compared to assess time from diagnosis (date of pathology result indicating invasive breast cancer) to treatment (date of surgery or chemotherapy). Compliance was measured by appointments characterized as "no shows" or "canceled due to personal reasons" in the electronic medical record. RESULTS: Of 541 patients (419 cMDC and 122 non-cMDC), mean time from diagnosis to treatment was significantly longer for blacks than whites in the non-cMDC group (46.9 +/- 64.6 days vs 28.2 +/- 14.8 days, p = 0.024) and the cMDC group (39.9 +/- 34.1 days vs 31.4 +/- 16.3 days, p = 0.001). Of 38 (7.2%) patients who started treatment > 60 days after diagnosis, 25 (65.8%) were black. Implementation of cMDC significantly improved patient compliance (missed appointments 4.9 +/- 7.6 non-cMDC vs 3.2 +/- 4.6 cMDC, p = 0.029). CONCLUSION: Use of cMDC for invasive breast cancer at our institution highlighted an area for improvement for care administered to blacks and improved patient compliance with appointments.

Ophthalmology and Eye Care Services

Barbosa J, Malbin B, **Le K**, and Lin X. Quantifying Areas of Vascular Leakage in Sickle Cell Retinopathy Using Standard and Widefield Fluorescein Angiography. *Ophthalmic Surg Lasers Imaging Retina* 2020; 51(3):153-158. PMID: 32211905. Request Article

BACKGROUND AND OBJECTIVE: To evaluate neovascular surface area change in sickle cell retinopathy following scatter photocoagulation treatment in wide- and standard-field fluorescein angiography (FA) scans using ImageJ software. PATIENTS AND METHODS: Images of 11 patients with wide- or standard-field FA scans pre- and post-treatment for sickle cell retinopathy were evaluated retrospectively by two graders using ImageJ. Graders traced lesions in the late arteriovenous phase and calculated the lesion area and intensity relative to the optic disc. Changes in area and intensity pre- to post-treatment were assessed using dependent t-tests. RESULTS: Pre- to post-treatment, lesion area decreased by 3.34 +/- 2.43 to 3.66 +/- 3.72 disc areas (P < .001), whereas intensity decreased by 11.36 +/- 25.87 to 22.97 +/- 69.25 units (P = .104). Neovascular area declined status post-aphotocoagulation by 3.83 +/- 3.65 disc areas (P = .003) for widefield images and by 2.81 +/- 3.55 discs areas (P = .034) for standard fluorescein images. No statistical difference in area reduction was appreciated between imaging modalities (P = .652) CONCLUSION: Neovascular area decreased significantly following scatter photocoagulation in both standard-field and widefield FA scans without an appreciable difference between imaging modalities. [Ophthalmic Surg Lasers Imaging Retina. 2020;51:153-158.].

Ophthalmology and Eye Care Services

Roshandel D, Chen Z, Canty AJ, Bull SB, Natarajan R, Paterson AD, **Bhan A**, **Jones JK**, **Kruger D**, **Edwards PA**, **Remtema H**, **Angus E**, **Galprin A**, **McLellan M**, **Thomas A**, **Carey JD**, and **Whitehouse F**. DNA methylation age calculators reveal association with diabetic neuropathy in type 1 diabetes. *Clin Epigenetics* 2020; 12(1):52. PMID: 32248841. Request Article

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BACKGROUND: Many CpGs become hyper or hypo-methylated with age. Multiple methods have been developed by Horvath et al. to estimate DNA methylation (DNAm) age including Pan-tissue, Skin & Blood, PhenoAge, and GrimAge. Pan-tissue and Skin & Blood try to estimate chronological age in the normal population whereas PhenoAge and GrimAge use surrogate markers associated with mortality to estimate biological age and its departure from chronological age. Here, we applied Horvath's four methods to calculate and compare DNAm age in 499 subjects with type 1 diabetes (T1D) from the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) study using DNAm data measured by Illumina EPIC array in the whole blood. Association of the four DNAm ages with development of diabetic complications including cardiovascular diseases (CVD), nephropathy, retinopathy, and neuropathy, and their risk factors were investigated. RESULTS: Pan-tissue and GrimAge were higher whereas Skin & Blood and PhenoAge were lower than chronological age ($p < 0.0001$). DNAm age was not associated with the risk of CVD or retinopathy over 18-20 years after DNAm measurement. However, higher PhenoAge (beta = 0.023, p = 0.007) and GrimAge (beta = 0.029, p = 0.002) were associated with higher albumin excretion rate (AER), an indicator of diabetic renal disease, measured over time. GrimAge was also associated with development of both diabetic peripheral neuropathy (OR = 1.07, p = 9.24E-3) and cardiovascular autonomic neuropathy (OR = 1.06, p = 0.011). Both HbA1c (beta = 0.38, p = 0.026) and T1D duration (beta = 0.01, p = 0.043) were associated with higher PhenoAge. Employment (beta = - 1.99, p = 0.045) and leisure time (beta = - 0.81, p = 0.022) physical activity were associated with lower Pan-tissue and Skin & Blood, respectively. BMI (beta = 0.09, p = 0.048) and current smoking (beta = 7.13, p = 9.03E-50) were positively associated with Skin & Blood and GrimAge, respectively. Blood pressure, lipid levels, pulse rate, and alcohol consumption were not associated with DNAm age regardless of the method used. CONCLUSIONS: Various methods of measuring DNAm age are sub-optimal in detecting people at higher risk of developing diabetic complications although some work better than the others.

Ophthalmology and Eye Care Services

White RJ, Jerjes-Sanchez C, Bohns Meyer GM, Pulido T, Sepulveda P, Wang KY, Grunig E, Hiremath S, Yu Z, Gangcheng Z, Yip WLJ, Zhang S, Khan A, Deng CQ, Grover R, Tapson VF, **Awdish R**, and **Cajigas H**. Combination Therapy with Oral Treprostinil for Pulmonary Arterial Hypertension. A Double-Blind Placebo-controlled Clinical Trial. *Am J Respir Crit Care Med* 2020; 201(6):707-717. PMID: 31765604. Full Text

Division of Pulmonary and Critical Care Medicine and the Mary M. Parkes Center, University of Rochester Medical Center, Rochester, New York.
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Wuhan Asia Heart Hospital, Wuhan Shi, China.
Department of Cardiology, National University Heart Centre, Singapore, Singapore.
Peking Union Medical College Hospital, Beijing, China.
Oregon Health and Science University, Portland, Oregon.
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Orthopedics/Bone and Joint
Bober K, **Kadado A**, **Charters M**, **Ayoola A**, and **North T**. Pain Control After Total Hip Arthroplasty: A Randomized Controlled Trial Determining Efficacy of Fascia Iliaca Compartment Blocks in the Immediate Postoperative Period. *J Arthroplasty* 2020; Epub ahead of print. PMID: 32222267. Full Text

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BACKGROUND: The purpose of this randomized controlled trial is to identify if a fascia iliaca block reduces postoperative pain and narcotic consumption and improves early functional outcomes in primary total hip arthroplasty (THA) performed through the mini-posterior approach. METHODS: Patients were recruited from September 2017 to September 2019. Eligible patients received a primary THA using a mini-posterior approach with epidural anesthesia. Postoperatively, patients were randomized to receive a fascia iliaca compartment block or a placebo block. Numeric Rating Scale pain scores, narcotic consumption, and functional outcomes were recorded at regular intervals postoperatively. RESULTS: Upon study completion, 122 patients were available for final analysis. There was no difference in the average pain scores at any time interval between the placebo and block groups during the first 24 hours (P = .21-.99). There was no difference in the morphine equivalents consumed between the groups during any time interval postoperatively (P = .06-.95). Functional testing showed no difference in regards to distance walked during the first therapy session (67.1 vs 68.3 ft., P = .92) and timed-up-and-go testing (63.7 vs 66.3 seconds, P = .86). There was an increased incidence of quadriceps weakness in the block group (22% vs 0%, P = .004) requiring alterations in therapy protocols. CONCLUSION: This randomized trial shows that a fascia iliaca compartment block does not improve functional performance and does not decrease pain levels or narcotic usage after mini-posterior THA, but does increase the risk of quadriceps weakness postoperatively. Based on these results we do not recommend routine fascia iliaca compartment blocks after THA performed with the mini-posterior approach.

Orthopedics/Bone and Joint
Day CS. CORR Insights(R): Operative Treatment Is Not Associated With More Relief of Depression Symptoms Than Nonoperative Treatment in Patients with Common Hand Illness. *Clin Orthop Relat Res* 2020; Epub ahead of print. PMID: 32271172. Full Text

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Orthopedics/Bone and Joint
Jebastin JAS, **Perry KD**, **Chitale DA**, **Mott MP**, **Sanchez J**, Fritchie KJ, **Palanisamy N**, and **Williamson SR**. Atypical Lipomatous Tumor/Well-Differentiated Liposarcoma With Features Mimicking Spindle Cell Lipoma. *Int J Surg Pathol* 2020; 28(3):336-340. PMID: 31672072. Full Text

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Atypical lipomatous tumor/well-differentiated liposarcoma (ALT/WDL) and spindle cell lipoma are lipomatous tumors with distinct clinical, molecular, and prognostic features. Although histological and immunophenotypic features can overlap between ALT/WDL and spindle cell lipoma, the oncogenesis and clinical behavior are markedly different. In borderline cases, molecular analysis for MDM2 or CDK4 amplification can aid in distinguishing ALT/WDL from spindle cell lipoma. Although dedifferentiated liposarcoma has been reported to harbor both MDM2 amplification and loss of the RB1 region, we are not aware of a reported RB1 loss in well-differentiated ALT/WDL. In this article, we present a 69-year-old woman with a lipomatous tumor in the gluteal region that histologically, immunohistochemically, and molecularly mimicked spindle cell lipoma (with positive immunohistochemical staining for CD34 and loss of the RB1 gene region), yet harbored amplification of MDM2 and CDK4 confirmed by fluorescence in situ hybridization, supporting classification as ALT/WDL. This case strengthens the argument that in atypical clinical contexts, molecular studies for MDM2/CDK4 should be considered in tumors resembling spindle cell lipoma.

Orthopedics/Bone and Joint
Moutzouros V, **Jildeh TR**, **Khalil LS**, **Schwartz K**, Hasan L, Matar RN, and **Okoroha KR**. A Multimodal Protocol to Diminish Pain Following Common Orthopedic Sports Procedures: Can We Eliminate Postoperative Opioids? *Arthroscopy* 2020; Epub ahead of print. PMID: 32353620. Full Text

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PURPOSE: To determine if postsurgical pain, measured by visual analogue scale (VAS), following common orthopedic sports procedures could be managed effectively with a nonopioid multimodal analgesic protocol. METHODS: This prospective study evaluated a custom multimodal non-opioid pain protocol in patients undergoing common orthopedic sports procedures by a single fellowship trained Orthopaedic Sports surgeon from May 2018 to December 2018. Procedures included anterior cruciate ligament reconstruction, rotator cuff repair, arthroscopic partial meniscectomy, and labrum repair. The non-opioid pain protocol consisted of preoperative analgesics, intraoperative local infiltration analgesia, and a postoperative pain regimen. Patient pain was immediately reported after surgery and 1 week postoperatively using the VAS, while rescue opioids (oxycodone 5 mg) used were recorded using a prescription opioid journal. Statistical analysis of patient VAS scores, demographic correlations, and comparison between opioid rescue users vs. nonusers was performed. RESULTS: A total of 141 patients were included. One week following surgery patients reported a mean VAS level of 3.2+/-2.3 and required on average 2.6+/-3.6 breakthrough oxycodone pills (8.6+/-12.0 morphine equivalents). Forty-five percent of patients did not require any breakthrough prescription opioids and reported satisfaction with pain management. Patients who required opioids were more likely to have a history of anxiety/depression (44.2% vs. 23.8%,P=.012) and reported higher pain scores as compared to non-users (3.94+/-2.5 vs. 2.41+/-1.75,P=.016). The most common side effect of the pain protocol was feeling drowsy (23.5%). All patients were satisfied with their pain management postoperatively. CONCLUSIONS: A multimodal, non-opioid pain protocol was found to be effective in managing postoperative pain following common orthopedic sports procedures. Patients were found to have low levels of pain, require minimal rescue opioids and had no severe side effects related to the protocol. These results suggest a non-opioid alternative to pain management following common orthopedic sports procedures.

Orthopedics/Bone and Joint
Roberts KC, Moser SE, Collins AC, McCardel BR, Schultz KA, Schaffer NE, **Tramer JS**, Carpenter CA, Pierce JM, Edwards A, Dubois KM, and Brummett CM. Prescribing and Consumption of Opioids After Primary, Unilateral Total Hip and Knee Arthroplasty in Opioid-Naive Patients. *J Arthroplasty* 2020; 35(4):960-965.e961. PMID: 31924487. Full Text

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BACKGROUND: This cohort study was designed to determine the discrepancy between the quantity of opioid prescribed vs that which was consumed after total knee arthroplasty (TKA) and total hip arthroplasty (THA) in opioid-naive patients. METHODS: Seven hundred twenty-three opioid-naive patients (426 TKAs and 297 THAs) from 7 hospitals in Michigan were contacted within 3 months of their surgery. Opioid prescribing and self-reported consumption was calculated in oral morphine equivalents (OMEs). Secondary outcomes included opioid refill in the first 90 days, pain in the first 7 days post-operatively, and satisfaction with pain care. RESULTS: For TKA, the mean prescribing was 632 mg OME (+/-229), and the mean consumption was 416 mg (+/-279). For THA, the mean prescribing was 584 mg OME (+/-335), and the mean consumption was 285 mg (+/-301). There were no associations between the amount of opioid prescribed and the likelihood of refill, post-operative pain, or satisfaction with pain control. The amount of opioid prescribed was associated with increased consumption, such that each increase of 1 pill was associated with approximately an additional half pill consumed after adjusting for other covariates. Moreover, 48.2% felt that they received "More" or "Much more" opioid than they needed. CONCLUSION: We recommend no more than 50 tablets of 5 mg oxycodone or its equivalent after TKA and 30 tablets after THA. Although dose reductions in other surgeries have not resulted in harm, continued assessment is needed to ensure that there are no unintended effects of opioid reduction, including worsened pain, decreased satisfaction, emergency department visits, or hospital readmissions. LEVEL OF EVIDENCE: Level III; Retrospective, cohort study.

Otolaryngology
Asmaro K, **Rock J**, and **Craig J**. Expanded Endonasal Approach for Resection of Extradural Infratemporal Fossa Trigeminal Schwannoma: 2-Dimensional Operative Video. *Oper Neurosurg (Hagerstown)* 2020; Epub ahead of print. PMID: 32348506. Request Article

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The infratemporal fossa (ITF) is bounded superiorly by the skull base, specifically the greater wing of the sphenoid, which contains foramen ovale. It is bordered posteriorly by the temporal bone, including the petrous portion of the carotid canal, anteriorly by the posterior wall of the maxillary sinus, laterally by the mandible, and medially by the pterygoid body and lateral pterygoid plate.1-3 In this video, we report a case of a rare, exclusively extradural, schwannoma originating from the third division of the trigeminal nerve with a widened foramen ovale at the skull base. The tumor filled the ITF and extended laterally just through the sigmoid notch of the mandible. The patient complained of left cheek and lower jaw numbness and intermittent left jaw spasms. The tumor was deemed appropriate for endoscopic resection. To access the ITF, left-sided endoscopic sinus surgery, a modified endoscopic Denker's approach,4 and posterior nasal septectomy were first performed. A nasoseptal flap was also harvested in case an intraoperative cerebrospinal fluid (CSF) leak required repair. Dissection was carried out through the posterior wall of the maxillary sinus and pterygopalatine fossa to reach the ITF. Tumor resection was achieved through a 2-surgeon, 4-handed approach in which appropriate traction and countertraction were carefully applied to tease the tumor away from the skull base and dehiscent carotid canal. No CSF leak or carotid injury occurred, and the posterior maxillary sinus wall defect was repaired with the nasoseptal flap. The patient did well postoperatively. The patient consented to the procedure in a standard fashion.

Otolaryngology
Chang SS. The Patient Perspective-A Valuable But Untapped Resource in Otolaryngology-Head and Neck Surgery. *JAMA Otolaryngol Head Neck Surg* 2020; Epub aheada of print. PMID: 32271365. Full Text

Henry Ford Cancer Institute, Henry Ford Health System, Detroit, Michigan.

Otolaryngology
Ellis MM, **Jones LR**, **Siddiqui F**, **Sunkara PR**, and **Ozog DM**. The Efficacy of Surgical Excision Plus Adjuvant Multimodal Therapies in the Treatment of Keloids: A Systematic Review and Meta-Analysis. *Dermatol Surg* 2020; Epub ahead of print. PMID: 32224709. Full Text

Department of Dermatology, Henry Ford Hospital, Detroit, Michigan.
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BACKGROUND: Research evaluating the efficacy of multimodal therapy for the treatment of keloids has reported combination regimens are most effective. OBJECTIVE: To compare recurrence rates for keloids treated with surgery plus one adjuvant

intervention (dual therapy) versus surgery plus 2 or more adjuvant interventions (triple therapy). MATERIALS AND METHODS: Systematic literature review and meta-analysis of combination treatment for keloids. RESULTS: After full-text review, we included 60 articles representing 5,547 keloids: 5,243 received dual therapy, 259 received triple therapy, and 45 received quadruple therapy (the latter 2 groups were combined for analysis). The difference in recurrence rates between dual (19%) and triple therapy (11.2%) was not significant (p = .343). However, the difference in recurrence rates between dual therapy using surgery and radiation (18.7%) and triple therapy using surgery, radiation, and a third intervention (7.7%) was significant (p = .002). The differences for surgery and intralesional triamcinolone (TAC) showed trends toward significance, because keloids treated with dual therapy (21.7%) had a higher recurrence rate than those treated with triple therapy comprised of surgery, TAC, and another intervention (13.7%; p = .099). CONCLUSION: Triple therapy using surgery plus radiation and/or TAC as one of the adjuvant treatment modalities may achieve the lowest recurrence rates for keloids.

Otolaryngology
Yaremchuk K. Why and When to Treat Snoring. *Otolaryngol Clin North Am* 2020; Epub ahead of print. PMID: 32336469. Full Text

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It is estimated that half of the adult population older than 60 years snores. This article discusses the many aspects of snoring, including impacts on bed partners, the individual who snores, and when and how to appropriately evaluate, diagnose, and treat the perpetrator. The goal is for clinicians to expand their knowledge regarding diagnosis and treatment of the phenomenon of snoring. It is estimated that half of the adult population over the age of 60 years of age snores. This chapter discusses snoring, including the impact on bed partners, the individual that snores and when and how to treat the snorer. The goal is for clinicians to expand their knowledge regarding diagnosis and treatment of patients who snores.

Pathology
Dedigama-Arachchige P, **Carskadon S**, **Li J**, **Loveless I**, **Alhamar M**, **Peabody JO**, **Stricker H**, **Chitale DA**, **Rogers CG**, **Menon M**, **Gupta NS**, Bismar TA, **Williamson SR**, and **Palanisamy N**. Clonal evaluation of prostate cancer molecular heterogeneity in biopsy samples by dual immunohistochemistry and dual RNA in situ hybridization. *Mod Pathol* 2020; Epub ahead of print. PMID: 32238875. Full Text

Department of Urology, Vattikuti Urology Institute, Henry Ford Health System, Detroit, MI, USA.
Department of Public Health Sciences, Henry Ford Health System, Detroit, MI, USA.
Department of Pathology, Henry Ford Health System, Detroit, MI, USA.
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Prostate cancer is frequently multifocal. Although there may be morphological variation, the genetic underpinnings of each tumor are not clearly understood. To assess the inter and intra tumor molecular heterogeneity in prostate biopsy samples, we developed a combined immunohistochemistry and RNA in situ hybridization method for the simultaneous evaluation of ERG, SPINK1, ETV1, and ETV4. Screening of 601 biopsy cores from 120 consecutive patients revealed multiple alterations in a mutually exclusive manner in 37% of patients, suggesting multifocal tumors with considerable genetic differences. Furthermore, the incidence of molecular heterogeneity was higher in African Americans patients compared with Caucasian American patients. About 47% of the biopsy cores with discontinuous tumor foci showed clonal differences with distinct molecular aberrations. ERG positivity occurred in low-grade cancer, whereas ETV4 expression was observed mostly in high-grade cancer. Further studies revealed correlation between the incidence of molecular markers and clinical and pathologic findings, suggesting potential implications for diagnostic pathology practice, such as defining dominant tumor nodules and discriminating juxtaposed but molecularly different tumors of different grade patterns.

Pathology
Jebastin JAS, **Perry KD**, **Chitale DA**, **Mott MP**, **Sanchez J**, Fritchie KJ, **Palanisamy N**, and **Williamson SR**. Atypical Lipomatous Tumor/Well-Differentiated Liposarcoma With Features Mimicking Spindle Cell Lipoma. *Int J Surg Pathol* 2020; 28(3):336-340. PMID: 31672072. Full Text

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Atypical lipomatous tumor/well-differentiated liposarcoma (ALT/WDL) and spindle cell lipoma are lipomatous tumors with distinct clinical, molecular, and prognostic features. Although histological and immunophenotypic features can overlap

between ALT/WDL and spindle cell lipoma, the oncogenesis and clinical behavior are markedly different. In borderline cases, molecular analysis for MDM2 or CDK4 amplification can aid in distinguishing ALT/WDL from spindle cell lipoma. Although dedifferentiated liposarcoma has been reported to harbor both MDM2 amplification and loss of the RB1 region, we are not aware of a reported RB1 loss in well-differentiated ALT/WDL. In this article, we present a 69-year-old woman with a lipomatous tumor in the gluteal region that histologically, immunohistochemically, and molecularly mimicked spindle cell lipoma (with positive immunohistochemical staining for CD34 and loss of the RB1 gene region), yet harbored amplification of MDM2 and CDK4 confirmed by fluorescence in situ hybridization, supporting classification as ALT/WDL. This case strengthens the argument that in atypical clinical contexts, molecular studies for MDM2/CDK4 should be considered in tumors resembling spindle cell lipoma.

Pathology

Roshandel D, Chen Z, Canty AJ, Bull SB, Natarajan R, Paterson AD, **Bhan A**, **Jones JK**, **Kruger D**, **Edwards PA**, **Remtema H**, **Angus E**, **Galprin A**, **McLellan M**, **Thomas A**, **Carey JD**, and **Whitehouse F**. DNA methylation age calculators reveal association with diabetic neuropathy in type 1 diabetes. *Clin Epigenetics* 2020; 12(1):52. PMID: 32248841. Request Article

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BACKGROUND: Many CpGs become hyper or hypo-methylated with age. Multiple methods have been developed by Horvath et al. to estimate DNA methylation (DNAm) age including Pan-tissue, Skin & Blood, PhenoAge, and GrimAge. Pan-tissue and Skin & Blood try to estimate chronological age in the normal population whereas PhenoAge and GrimAge use surrogate markers associated with mortality to estimate biological age and its departure from chronological age. Here, we applied Horvath's four methods to calculate and compare DNAm age in 499 subjects with type 1 diabetes (T1D) from the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) study using DNAm data measured by Illumina EPIC array in the whole blood. Association of the four DNAm ages with development of diabetic complications including cardiovascular diseases (CVD), nephropathy, retinopathy, and neuropathy, and their risk factors were investigated. RESULTS: Pan-tissue and GrimAge were higher whereas Skin & Blood and PhenoAge were lower than chronological age ($p < 0.0001$). DNAm age was not associated with the risk of CVD or retinopathy over 18-20 years after DNAm measurement. However, higher PhenoAge (beta = 0.023, p = 0.007) and GrimAge (beta = 0.029, p = 0.002) were associated with higher albumin excretion rate (AER), an indicator of diabetic renal disease, measured over time. GrimAge was also associated with development of both diabetic peripheral neuropathy (OR = 1.07, p = 9.24E-3) and cardiovascular autonomic neuropathy (OR = 1.06, p = 0.011). Both HbA1c (beta = 0.38, p = 0.026) and T1D duration (beta = 0.01, p = 0.043) were associated with higher PhenoAge. Employment (beta = - 1.99, p = 0.045) and leisure time (beta = - 0.81, p = 0.022) physical activity were associated with lower Pan-tissue and Skin & Blood, respectively. BMI (beta = 0.09, p = 0.048) and current smoking (beta = 7.13, p = 9.03E-50) were positively associated with Skin & Blood and GrimAge, respectively. Blood pressure, lipid levels, pulse rate, and alcohol consumption were not associated with DNAm age regardless of the method used. CONCLUSIONS: Various methods of measuring DNAm age are sub-optimal in detecting people at higher risk of developing diabetic complications although some work better than the others.

Pathology

Thanikachalam K, **Damarla V**, **Seixas T**, **Dobrosotskaya I**, **Wollner I**, **Kwon D**, **Winters K**, **Raoufi M**, **Li J**, **Siddiqui F**, and **Khan G**. Neoadjuvant Phase II Trial of Chemoradiotherapy in Patients With Resectable and Borderline Resectable Pancreatic Cancer. *Am J Clin Oncol* 2020; Epub ahead of print. PMID: 32251119. Full Text

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BACKGROUND: Pancreatic ductal adenocarcinoma is a largely incurable cancer. Surgical resection remains the only potential option for cure. Even in surgically resectable patients, only about 10% to 20% are long-term survivors. Emerging data suggest a role for neoadjuvant therapy to target occult micrometastatic disease. AIM: To report our institutional experience with a novel neoadjuvant chemoradiation (CRT) regimen in resectable and borderline resectable pancreatic cancer. MATERIALS AND METHODS: Patients were treated with 2 cycles of induction chemotherapy with FOLFOX and then received CRT with gemcitabine and intensity-modulated radiotherapy (IMRT). RESULTS: From April 2014 to June 2017, 24 patients were enrolled. Eighteen patients were borderline resectable and 6 patients were resectable. All patients received induction

chemotherapy with FOLFOX. Thirteen patients underwent pancreatectomy after CRT with a resection rate of 62%. R0 resection achieved in 11 patients (84.6%) and 2 patients had R1 resection (15.4%). For patients who underwent resection, the median progression-free survival (PFS) was 31 months, 1-year PFS rate was 69.2% (95% confidence interval [CI], 0.48-0.99), and 2-year PFS rate was 51.9% (95% CI, 0.3-0.89). Median overall survival (OS) was 34.8 months (95% CI, 1.045 to infinity), 1-year OS rate was 91.7% (95% CI, 0.77-1.0), and 2-year OS rate was 75% (95% CI, 0.54-1.0). Median CA 19-9 at screening for patients who underwent surgery was 659 (range, 18 to 2154), which decreased to 146.9 (range, 18 to 462) after CRT before resection. CONCLUSION: Neoadjuvant therapy for borderline resectable and resectable pancreatic ductal adenocarcinoma with CRT facilitated R0 resection in 84% patients who underwent surgery.

Pathology

White RJ, Jerjes-Sanchez C, Bohns Meyer GM, Pulido T, Sepulveda P, Wang KY, Grunig E, Hiremath S, Yu Z, Gangcheng Z, Yip WLJ, Zhang S, Khan A, Deng CQ, Grover R, Tapson VF, **Awdish R**, and **Cajigas H**. Combination Therapy with Oral Treprostinil for Pulmonary Arterial Hypertension. A Double-Blind Placebo-controlled Clinical Trial. *Am J Respir Crit Care Med* 2020; 201(6):707-717. PMID: 31765604. Full Text

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Department of Cardiology, National University Heart Centre, Singapore, Singapore.
Peking Union Medical College Hospital, Beijing, China.
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Rationale: Oral treprostinil improves exercise capacity in patients with pulmonary arterial hypertension (PAH), but the effect on clinical outcomes was unknown.Objectives: To evaluate the effect of oral treprostinil compared with placebo on time to first adjudicated clinical worsening event in participants with PAH who recently began approved oral monotherapy.Methods: In this event-driven, double-blind study, we randomly allocated 690 participants (1:1 ratio) with PAH to receive placebo or oral treprostinil extended-release tablets three times daily. Eligible participants were using approved oral monotherapy for over 30 days before randomization and had a 6-minute-walk distance 150 m or greater. The primary endpoint was the time to first adjudicated clinical worsening event: death; hospitalization due to worsening PAH; initiation of inhaled or parenteral prostacyclin therapy; disease progression; or unsatisfactory long-term clinical response.Measurements and Main Results: Clinical worsening occurred in 26% of the oral treprostinil group compared with 36% of placebo participants (hazard ratio, 0.74; 95% confidence interval, 0.56-0.97; P = 0.028). Key measures of disease status, including functional class, Borg dyspnea score, and N-terminal pro-brain natriuretic peptide, all favored oral treprostinil treatment at Week 24 and beyond. A noninvasive risk stratification analysis demonstrated that oral treprostinil-assigned participants had a substantially higher mortality risk at baseline but achieved a lower risk profile from Study Weeks 12-60. The most common adverse events in the oral treprostinil group were headache, diarrhea, flushing, nausea, and vomiting.Conclusions: In participants with PAH, addition of oral treprostinil to approved oral monotherapy reduced the risk of clinical worsening.Clinical trial registered with www.clinicaltrials.gov (NCT01560624).

Pathology

Williamson SR, Gill AJ, Argani P, Chen YB, Egevad L, Kristiansen G, Grignon DJ, and Hes O. Report From the International Society of Urological Pathology (ISUP) Consultation Conference on Molecular Pathology of Urogenital Cancers: III: Molecular Pathology of Kidney Cancer. *Am J Surg Pathol* 2020; Epub ahead of print. PMID: 32251007. Full Text

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Renal cell carcinoma (RCC) subtypes are increasingly being discerned via their molecular underpinnings. Frequently this can be correlated to histologic and immunohistochemical surrogates, such that only simple targeted molecular assays, or none at all, are needed for diagnostic confirmation. In clear cell RCC, VHL mutation and 3p loss are well known; however, other genes with emerging important roles include SETD2, BAP1, and PBRM1, among others. Papillary RCC type 2 is now known to include likely several different molecular entities, such as fumarate hydratase (FH) deficient RCC. In MIT family translocation RCC, an increasing number of gene fusions are now described. Some TFE3 fusion partners, such as NONO, GRIPAP1, RBMX, and RBM10 may show a deceptive fluorescence in situ hybridization result due to the proximity of the genes on the same chromosome. FH and succinate dehydrogenase deficient RCC have implications for patient counseling due to heritable syndromes and the aggressiveness of FH-deficient RCC. Immunohistochemistry is increasingly available and helpful for recognizing both. Emerging tumor types with strong evidence for distinct diagnostic entities include eosinophilic solid and cystic RCC and TFEB/VEGFA/6p21 amplified RCC. Other emerging entities that are less clearly understood include TCEB1 mutated RCC, RCC with ALK rearrangement, renal neoplasms with mutations of TSC2 or MTOR, and RCC with fibromuscular stroma. In metastatic RCC, the role of molecular studies is not entirely defined at present, although there may be an increasing role for genomic analysis related to specific therapy pathways, such as for tyrosine kinase or MTOR inhibitors.

Pathology
Yaguchi G, **Tang HJ**, **Deebajah M**, **Keeley J**, **Pantelic M**, **Williamson S**, **Gupta N**, **Peabody JO**, **Menon M**, **Dabaja A**, and Alanee S. The effect of multiplicity of PI-RADS 3 lesions on cancer detection rate of confirmatory targeted biopsy in patients diagnosed with prostate cancer and managed with active surveillance. *Urol Oncol* 2020; Epub ahead of print. PMID: 32265090. Full Text

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BACKGROUND AND OBJECTIVE: To determine the effect of multiplicity of prostate imaging reporting and data system assessment category 3 (PI-RADS 3) lesions on cancer detection rate (CDR) of confirmatory targeted biopsy of such lesion in patients diagnosed with prostate cancer and managed with active surveillance. METHODS: This study was conducted at a single academic institution. There were 91 men with >/= 1 PI-RADS 3 lesion detected through magnetic resonance imaging (MRI) after systematic prostate biopsy in the course of management of patients diagnosed with prostate cancer with active surveillance. We compared the CDRs based on targeted biopsy of PI-RADS 3 lesions that occurred (1) as solitary lesions, (2) as 1 of multiple PI-RADS 3 only lesions, or (3) with >/= 1 higher grade lesion. RESULTS: Median age was 65.0 years (interquartile range 59.5-70.0), median prostate specific antigen was 5.95 ng/ml (interquartile range 4.30-8.83), and median prostate specific antigen density was 0.161 ng/ml(2) (0.071-0.194). Forty-three men had solitary PI-RADS 3 lesions, 22 had multiple PI-RADS 3 only lesions, and 26 had multiple lesions with >/= 1 higher grade lesion. The overall CDR (Gleason score >/= 3+3) based on confirmatory MRI targeted biopsy in a given PI-RADS 3 lesion in each group was 23%, 45%, and 54%, respectively (P=0.0274). The CDRs for clinically significant disease (Gleason score >/= 3+4) were 16%, 32%, and 35%, respectively (P=0.1701). CONCLUSIONS: Coexisting lesions increase the CDR of confirmatory MRI targeted biopsy of PI-RADS 3 lesions in patients managed with active surveillance. Risk stratification algorithms for PI-RADS 3 lesion to guide biopsy and management decisions may consider including multiplicity of lesions.

Pharmacy
Dingman JS, **Smith ZR**, **Coba VE**, **Peters MA**, and **To L**. Argatroban dosing requirements in extracorporeal life support and other critically ill populations. *Thromb Res* 2020; 189:69-76. PMID: 32182522. Full Text

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Argatroban is a parenteral direct thrombin inhibitor that requires close monitoring to ensure safety and efficacy. Limited data exist to describe its effect in critically ill patients. This was a retrospective, single-center, cohort study that aimed to compare argatroban dosing requirements in those receiving extracorporeal life support (ECLS), continuous renal replacement therapy (CRRT), or neither. Organ dysfunction was assessed using a modified version of the Sequential Organ Failure Assessment (modSOFA) that incorporated the use of extracorporeal support systems. Eighty patients were included in the study (n = 20, 20, 40 in the ECLS, CRRT, and support-free groups, respectively). The majority of patients were Child-Pugh classification B (73%). Median modSOFA scores were higher in the ECLS (16.5) and CRRT (15.5) groups than in the support-free group (7.5) (P < .001). There was no difference in the primary outcome of first therapeutic argatroban dose between the three groups (0.5

mug/kg/min for each; IQRs 0.25-0.50, 0.11-0.50, and 0.25-0.50, respectively; P = .455). The ECLS group had the lowest mean (0.39 mug/kg/min), minimum (0.20 mug/kg/min), and final (0.43 mug/kg/min) doses. ECLS patients had more supratherapeutic aPTTs and dose changes overall, supporting the need for more frequent anticoagulation monitoring or dose reductions in this population. Total modSOFA score demonstrated a moderate inverse correlation with first therapeutic dose (dose = 0.54 - (modSOFA score x 0.012); R = -0.342, P = .002). Overall, initial argatroban doses of 0.3-0.5 mug/kg/min appear to achieve therapeutic aPTT values in the studied populations.

Pharmacy
Morrison AR, **Johnson JM**, **Ramesh M**, **Bradley P**, **Jennings J**, and **Smith ZR**. Letter to the Editor: Acute hypertriglyceridemia in patients with COVID-19 receiving tocilizumab. *J Med Virol* 2020; Epub ahead of print. PMID: 32314799. Full Text

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Tocilizumab is an interleukin-6 (IL-6) receptor antibody and is progressing as a viable and promising treatment option in patients with severe coronavirus disease 2019 (COVID-19). IL-6 is known to have both immunomodulatory and metabolic actions. In this letter we outline two cases of acute hypertriglyceridemia in patients with COVID-19 treated with tocilizumab: one with elevated biomarkers consistent with acute pancreatitis the other without. Given the paucity of robust clinical trial data for most COVID-19 pharmacotherapies at this time, clinicians should continue to remain steadfast in recognition of interventions that improve clinical outcomes and vigilant in monitoring for acute adverse effects that are difficult to detect in clinical trials with small sample sizes. The observations from our two cases highlight the complex, not fully elucidated interrelationship between elevated IL-6 and pharmacologic interventions impacting this pathway. Clinicians should consider monitoring for hypertriglyceridemia and acute pancreatitis as described with chronic tocilizumab use for rheumatoid arthritis in those receiving it for COVID-19.

Pharmacy
Wagner JL, Rhodes NJ, Scheetz MH, Bosso JA, Goff DA, Rybak MJ, and **Davis SL**. Opportunities for antibiotic stewardship among carbapenem-treated patients within 18 North American hospitals. *Int J Antimicrob Agents* 2020; Epub ahead of print. PMID: 32283176. Full Text

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Making a Difference in Infectious Diseases, P.O. Box 1604, Fairfield, CT 06825, U.S.A.

Adult inpatients treated with a carbapenem for >/= 24 hours were included. Outcomes evaluated included classification of therapy as empiric or definitive, discharge disposition, and 30-day readmission. Six hundred twenty-one patients were included, with 467 (75%) patients receiving a carbapenem empirically. Negative cultures occurred in 313 (67%) patients, and 93% of those were eligible for de-escalation of therapy. Of those discharged, 349 (56%) patients went home, and 72 (12%) patients expired. Thirty-day infection-related readmission occurred in 95 (17%) patients. This population represents a significant need for carbapenem stewardship. Institutional guidelines should focus on 4 common disease states (respiratory, genitourinary, intra-abdominal, and bloodstream), and diagnostic stewardship should be employed to aid in rapid de-escalation of carbapenem therapy. Additional studies aiming to identify stewardship techniques that may help to optimize carbapenem therapy and increase education about the importance of utilizing carbapenem-sparing regimens are needed.

Plastic Surgery
Worden A, **Yoho DJ**, **Houin H**, **Moquin K**, **Hamzavi I**, **Saab I**, and **Siddiqui A**. Factors Affecting Healing in the Treatment of Hidradenitis Suppurativa. *Ann Plast Surg* 2020; 84(4):436-440. PMID: 31688123. Full Text

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BACKGROUND: Hidradenitis suppurativa (HS) is a chronic debilitating condition. Treatment of HS depends on disease stage, goals of care, access to care, and frequency of symptoms. We present our experience with surgical treatment for patients with HS. METHODS: Patients were followed longitudinally for at least 2 years postsurgical intervention. Demographic data, participation in a multidisciplinary program, type of surgery, healing rates, and potential factors contributing to wound healing were retrospectively reviewed in all cases using multivariate analysis. RESULTS: Two hundred forty-eight patients met the inclusion criteria with a total of 810 involved sites. Overall, 59% of patients had Hurley stage 3 disease at the time of surgery. Healing rates of 80% were observed in stages 1 and 2, and 74% were observed in stage 3. Hurley stage was not a significant predictor of healing (P = 0.09). Surgical treatment consisted of 38% incision and drainage, 44% excision without closure, and 17% excision with primary closure. Incisional and excisional treatments healed 78% and 79%, respectively, at 2 years. Primarily repaired defects (grafts and flaps) were 68% healed at 2 years. Observed healing rates were uniform regardless of the number of sites involved (P = 0.959). Participation in the multidisciplinary program was the strongest predictor of healing (78% vs 45%, P = 0.004). Sex, age, body mass index, tobacco use, diabetes, presurgery hemoglobin, and family history of HS were statistically not significant. Continuation of immune modulating therapy within 2 weeks of surgery was a predictor of reduced healing (odds ratio, 0.23; P = 0.004), whereas holding biologics for at least 2 weeks was not significant (odds ratio, 1.99; P = 0.146). CONCLUSIONS: Participation in a multidisciplinary program is a strong predictor of long-term success when treating HS. Hurley score and number of involved sites did not correlate with successful healing after surgery. If taking biologics, we identified 2 weeks as an appropriate break from biologics before and after surgical intervention. Healing rates were highest with ablative procedures (incision and drainage, excision) alone.

Public Health Sciences
Bayard S, **Susick L**, Kyei I, **Chen Y**, Davis MB, Gyan K, and Newman LA. Brief report: Global health initiatives and breast oncology capacity-building in Africa. *Am J Surg* 2020; 219(4):563-565. PMID: 32008719. Full Text

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INTRODUCTION: Global health initiatives provide exciting opportunities for capacity-building in low- and middle-income countries but data regarding how African clinicians characterize the most effective partnerships are lacking. METHODS: We surveyed attendees at two "Breast Cancer in Africa" symposia sponsored through a surgeon-led global breast cancer research collaborative. Respondents ranked their preferences for needs from American global health partnerships. RESULTS: 399 African attendees responded (170 at the 2017 Ghana conference; 229 at the 2018 Ethiopia conference). Physicians comprised 41.1% of respondents; nurses 20.1% and medical students 27.6%. Ancillary hospital staff comprised the remaining 11.2%. Among clinicians, 75.7% ranked educational/training programs or donation of medical supplies as the highest-priority needs compared to only 20.4% ranking direct monetary support as the highest-priority need (P < 0.0001). CONCLUSIONS: Our survey study found that African clinicians prioritize training programs and donation of medical/hospital supplies above direct monetary support as their highest-value needs from global health initiatives.

Public Health Sciences
Darvishi P, Batchala PP, Patrie JT, **Poisson LM**, Lopes MB, Jain R, Fadul CE, Schiff D, and Patel SH. Prognostic Value of Preoperative MRI Metrics for Diffuse Lower-Grade Glioma Molecular Subtypes. *AJNR Am J Neuroradiol* 2020; Epub ahead of print. PMID: 32327434. Full Text

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From the Departments of Radiology and Medical Imaging (P.D., P.P.B., S.H.P.) shp4k@virginia.edu.

BACKGROUND AND PURPOSE: Despite the improved prognostic relevance of the 2016 WHO molecular-based classification of lower-grade gliomas, variability in clinical outcome persists within existing molecular subtypes. Our aim was to determine prognostically significant metrics on preoperative MR imaging for lower-grade gliomas within currently defined molecular categories. MATERIALS AND METHODS: We undertook a retrospective analysis of 306 patients with lower-grade gliomas accrued from an institutional data base and The Cancer Genome Atlas. Two neuroradiologists in consensus analyzed

preoperative MRIs of each lower-grade glioma to determine the following: tumor size, tumor location, number of involved lobes, corpus callosum involvement, hydrocephalus, midline shift, eloquent cortex involvement, ependymal extension, margins, contrast enhancement, and necrosis. Adjusted hazard ratios determined the association between MR imaging metrics and overall survival per molecular subtype, after adjustment for patient age, patient sex, World Health Organization grade, and surgical resection status. RESULTS: For isocitrate dehydrogenase (IDH) wild-type lower-grade gliomas, tumor size (hazard ratio, 3.82; 95% CI, 1.94-7.75; P < .001), number of involved lobes (hazard ratio, 1.70; 95% CI, 1.28-2.27; P < .001), hydrocephalus (hazard ratio, 4.43; 95% CI, 1.12-17.54; P = .034), midline shift (hazard ratio, 1.16; 95% CI, 1.03-1.30; P = .013), margins (P = .031), and contrast enhancement (hazard ratio, 0.34; 95% CI, 0.13-0.90; P = .030) were associated with overall survival. For IDH-mutant 1p/19q-codeleted lower-grade gliomas, tumor size (hazard ratio, 2.85; 95% CI, 1.06-7.70; P = .039) and ependymal extension (hazard ratio, 6.34; 95% CI, 1.07-37.59; P = .042) were associated with overall survival. CONCLUSIONS: MR imaging metrics offers prognostic information for patients with lower-grade gliomas within molecularly defined classes, with the greatest prognostic value for IDH wild-type lower-grade gliomas.

Public Health Sciences

Dedigama-Arachchige P, **Carskadon S**, **Li J**, **Loveless I**, **Alhamar M**, **Peabody JO**, **Stricker H**, **Chitale DA**, **Rogers CG**, **Menon M**, **Gupta NS**, Bismar TA, **Williamson SR**, and **Palanisamy N**. Clonal evaluation of prostate cancer molecular heterogeneity in biopsy samples by dual immunohistochemistry and dual RNA in situ hybridization. *Mod Pathol* 2020; Epub ahead of print. PMID: 32238875. Full Text

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Prostate cancer is frequently multifocal. Although there may be morphological variation, the genetic underpinnings of each tumor are not clearly understood. To assess the inter and intra tumor molecular heterogeneity in prostate biopsy samples, we developed a combined immunohistochemistry and RNA in situ hybridization method for the simultaneous evaluation of ERG, SPINK1, ETV1, and ETV4. Screening of 601 biopsy cores from 120 consecutive patients revealed multiple alterations in a mutually exclusive manner in 37% of patients, suggesting multifocal tumors with considerable genetic differences. Furthermore, the incidence of molecular heterogeneity was higher in African Americans patients compared with Caucasian American patients. About 47% of the biopsy cores with discontinuous tumor foci showed clonal differences with distinct molecular aberrations. ERG positivity occurred in low-grade cancer, whereas ETV4 expression was observed mostly in high-grade cancer. Further studies revealed correlation between the incidence of molecular markers and clinical and pathologic findings, suggesting potential implications for diagnostic pathology practice, such as defining dominant tumor nodules and discriminating juxtaposed but molecularly different tumors of different grade patterns.

Public Health Sciences

Laughlin-Tommaso SK, Lu D, Thomas L, Diamond MP, Wallace K, **Wegienka G**, Vines AI, Anchan RM, Wang T, Maxwell GL, Jacoby V, Marsh EE, Spies JB, Nicholson WK, Stewart EA, and Myers ER. Short-term quality of life after myomectomy for uterine fibroids from the COMPARE-UF Fibroid Registry. *Am J Obstet Gynecol* 2020; 222(4):345.e341-345.e322. PMID: 31678093. Full Text

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BACKGROUND: Uterine fibroids may decrease quality of life in a significant proportion of affected women. Myomectomy offers a uterine-sparing treatment option for patients with uterine fibroids that can be performed abdominally, laparoscopically (with or without robotic assistance), and hysteroscopically. Quality of life information using validated measures for different myomectomy routes, especially hysteroscopic myomectomy, is limited. OBJECTIVE: To compare women's perception of their short-term health-related quality of life measures and reported time to return to usual activities and return to work for different routes of myomectomy. MATERIALS AND METHODS: Comparing Options for Management: Patient-centered Results for Uterine Fibroids (COMPARE-UF) is a prospective nationwide fibroid registry that enrolled premenopausal women seeking treatment for uterine fibroids at 8 clinical sites. For this analysis, we included women undergoing hysteroscopic, abdominal, or laparoscopic myomectomy who completed the postprocedure questionnaire scheduled between 6 and 12 weeks after surgery. Health-related quality of life outcomes, such as pain, anxiety, and return to usual activitie, were assessed for each route. The hysteroscopic myomectomy group had large differences in demographics, fibroid number, and uterine size compared to the other groups; thus, a direct comparison of quality of life measures was performed only for abdominal and laparoscopic approaches after propensity weighting. Propensity weighting was done using 24 variables that included demographics, quality of life baseline measures, and fibroid and uterine measurements. RESULTS: A total of 1206 women from 8 COMPARE-UF sites underwent myomectomy (338 hysteroscopic, 519 laparoscopic, and 349 abdominal). All women had substantial improvement in short-term health-related quality of life and symptom severity scores, which was not different among groups. Average symptom severity scores decreased about 30 points in each group. Return to usual activities averaged 0 days (interquartile range, 0-14 days) for hysteroscopic myomectomy, 21 days (interquartile range, 14-28 days) for laparoscopic myomectomy, and 28 days (interquartile range, 14-35 days) for abdominal myomectomy. After propensity adjustment, quality of life outcomes in the laparoscopic and abdominal myomectomy groups were similar except for more anxiety in the laparoscopic myomectomy group and slightly more pain in the abdominal myomectomy group. After propensity weighting, return to usual activities favored laparoscopic compared to abdominal procedures; median time was the same at 21 days, but the highest quartile of women in the abdominal group needed an additional week of recovery (interquartile range,14.0-28.0 for laparoscopic versus 14.0-35.0 for abdominal, $P < .01$). Time to return to work was also longer in the abdominal arm (median, 22 days; interquartile range, 14-40 days, versus median, 42; interquartile range, 27-56). CONCLUSION: Women who underwent myomectomy had substantial improvement in health-related quality of life, regardless of route of myomectomy. After propensity weighting, abdominal myomectomy was associated with a nearly 2-week longer time to return to work than laparoscopic myomectomy.

Public Health Sciences
Lyons AB, Peacock A, McKenzie SA, **Jacobsen G**, Naik HB, Shi VY, **Hamzavi IH**, and Hsiao JL. Retrospective Cohort Study of Pregnancy Outcomes in Hidradenitis Suppurativa. *Br J Dermatol* 2020; Epub ahead of print. PMID: 32333790. Full Text

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Hidradenitis suppurativa (HS) disproportionately affects women of childbearing age; however, there has been a paucity of literature in the field of HS and pregnancy.(1) The objective of this study was to examine pregnancy complications, pregnancy outcomes, and neonatal outcomes in patients with HS.

Public Health Sciences
Ownby DR, **Havstad S**, **Wegienka G**, and **Johnson CC**. Allergic Sensitization Does Not Differ Between Childhood- and Adolescent-Onset Asthma in Women. *J Allergy Clin Immunol* 2020; Epub ahead of print. PMID: 32311392. Full Text

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Public Health Sciences
Snyder JM, **Pawloski JA**, and **Poisson LM**. Developing Real-world Evidence-Ready Datasets: Time for Clinician Engagement. *Curr Oncol Rep* 2020; 22(5):45. PMID: 32297007. Full Text

Department of Neurosurgery, Hermelin Brain Tumor Center, Henry Ford Hospital, 2799 West Grand Boulevard, Detroit, MI, 48202, USA. jsnyder5@hfhs.org.
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PURPOSE OF REVIEW: Real-world data (RWD) applications in healthcare that support learning health systems and pragmatic clinical trials are gaining momentum, largely due to legislation supporting real-world evidence (RWE) for drug approvals. Clinical notes are thought to be the cornerstone of RWD applications, particularly for conditions with limited effective treatments, extrapolation of treatments from other conditions, or heterogenous disease biology and clinical phenotypes. RECENT FINDINGS: Here, we discuss current issues in applying RWD captured at the point-of-care and provide a framework for clinicians to engage in RWD collection. To achieve clinically meaningful results, RWD must be reliably captured using consistent terminology in the description of our patients. RWD complements traditional clinical trials and research by informing the generalizability of results, generating new hypotheses, and creating a large data network for scientific discovery. Effective clinician engagement in the development of RWD applications is necessary for continued progress in the field.

Public Health Sciences
Spradling PR, Xing J, **Rupp LB**, Moorman AC, **Gordon SC**, **Lu M**, Teshale EH, Boscarino JA, Schmidt MA, Daida YG, and Holmberg SD. Low Uptake of Direct-acting Antiviral Therapy Among Hepatitis C Patients With Advanced Liver Disease and Access to Care, 2014-2017. *J Clin Gastroenterol* 2020; Epub ahead of print. PMID: 32250999. Full Text

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GOALS: To determine the proportion and characteristics of adults with hepatitis C at health care organizations in 4 US states who initiated direct-acting antivirals (DAAs). BACKGROUND: There are almost no data to assess the penetrance of treatment of the hepatitis C population in general US health care settings. STUDY: We conducted a prospective observational study using electronic clinical, pharmacy, and mortality data to determine the fraction of patients who initiated DAAs between January 2014 and December 2017, by start date and regimen. We used stepwise multivariate logistic regression analysis to identify sociodemographic and clinical characteristics associated with receipt of DAAs. RESULTS: Of 8823 patients, 2887 (32.7%) received DAAs. Quarterly (Q) uptake ranged from 1.1% in Q3 2014 to a high of 5.6% in Q2 2015. Characteristics associated with receipt of DAAs included age 51 to 70 years, higher income, pre-2014 treatment failure, and higher noninvasive fibrosis score (FIB4); however, over one half of patients with FIB4 scores >3.25, consistent with severe liver disease, were not treated. A lower likelihood of initiation was associated with Medicaid coverage. Of 5936 patients who did not initiate treatment, 911 (15.3%) had died and 2774 (46.7%) had not had a clinical encounter in >/=12 months by the end of the study. Fewer than 1% of DAA prescriptions originated from nonspecialty providers. CONCLUSIONS: During 4 calendar years of follow-up, one third of patients initiated DAAs. Large fractions of untreated patients had advanced liver disease, died, or were lost to follow-up. Even among patients in integrated health care systems, receipt of DAAs was limited.

Public Health Sciences
Su WK, Lehto MR, Degnan DD, Yih Y, Duffy VG, and DeLaurentis P. Healthcare Professionals Risk Assessments for Alert Overrides in High-Risk IV Infusions Using Simulated Scenarios. *Risk Anal* 2020; Epub ahead of print. PMID: 32339316. Request Article

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This study aimed to use healthcare professionals' assessments to calculate expected risk of intravenous (IV) infusion harm for simulated high-risk medications that exceed soft limits and to investigate the impact of relevant risk factors. We designed 30 infusion scenarios for four high-risk medications, propofol, morphine, insulin, and heparin, infused in adult intensive care unit (AICU) and adult medical and surgical care unit (AMSU). A total of 20 pharmacists and 5 nurses provided their assessed

expected risk of harm in each scenario. Descriptive statistics, analysis of variance with least square mean, and post hoc test were conducted to test the effects of field limit type, soft (SoftMax), and hard maximum drug limit types (HardMax), and care area-medication combination on risk of harm. The results showed that overdosing scenarios with continuous and bolus dose limit types were assessed with significantly higher risks than those of bolus dose rate type. An overdose infusion in AICU over a large SoftMax was assessed to be of higher risk than over a small one, but not in AMSU. For overdose infusions with three levels of drug amount, greater drug amount in AICU and AMSU was assessed to have higher risk, except insignificant risk difference between the infusions with higher and moderate drug amount in AMSU. This study obtained expected risk for simulated high-risk IV infusions and found that different field limit and SoftMax types can affect expected risk based on healthcare professionals' perspectives. The findings will be regarded as benchmarks for validating risk quantification models in future research.

Public Health Sciences

Thanikachalam K, **Damarla V**, **Seixas T**, **Dobrosotskaya I**, **Wollner I**, **Kwon D**, **Winters K**, **Raoufi M**, **Li J**, **Siddiqui F**, and **Khan G**. Neoadjuvant Phase II Trial of Chemoradiotherapy in Patients With Resectable and Borderline Resectable Pancreatic Cancer. *Am J Clin Oncol* 2020; Epub ahead of print. PMID: 32251119. Full Text

Division of Hematology and Medical Oncology.
Cancer Care Specialists of Illinois.
Division of Surgical Oncology.
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Division of Radiation Oncology, Detroit, MI.

BACKGROUND: Pancreatic ductal adenocarcinoma is a largely incurable cancer. Surgical resection remains the only potential option for cure. Even in surgically resectable patients, only about 10% to 20% are long-term survivors. Emerging data suggest a role for neoadjuvant therapy to target occult micrometastatic disease. AIM: To report our institutional experience with a novel neoadjuvant chemoradiation (CRT) regimen in resectable and borderline resectable pancreatic cancer. MATERIALS AND METHODS: Patients were treated with 2 cycles of induction chemotherapy with FOLFOX and then received CRT with gemcitabine and intensity-modulated radiotherapy (IMRT). RESULTS: From April 2014 to June 2017, 24 patients were enrolled. Eighteen patients were borderline resectable and 6 patients were resectable. All patients received induction chemotherapy with FOLFOX. Thirteen patients underwent pancreatectomy after CRT with a resection rate of 62%. R0 resection achieved in 11 patients (84.6%) and 2 patients had R1 resection (15.4%). For patients who underwent resection, the median progression-free survival (PFS) was 31 months, 1-year PFS rate was 69.2% (95% confidence interval [CI], 0.48-0.99), and 2-year PFS rate was 51.9% (95% CI, 0.3-0.89). Median overall survival (OS) was 34.8 months (95% CI, 1.045 to infinity), 1-year OS rate was 91.7% (95% CI, 0.77-1.0), and 2-year OS rate was 75% (95% CI, 0.54-1.0). Median CA 19-9 at screening for patients who underwent surgery was 659 (range, 18 to 2154), which decreased to 146.9 (range, 18 to 462) after CRT before resection. CONCLUSION: Neoadjuvant therapy for borderline resectable and resectable pancreatic ductal adenocarcinoma with CRT facilitated R0 resection in 84% patients who underwent surgery.

Pulmonary and Critical Care Medicine

Morrison AR, **Johnson JM**, **Ramesh M**, **Bradley P**, **Jennings J**, and **Smith ZR**. Letter to the Editor: Acute hypertriglyceridemia in patients with COVID-19 receiving tocilizumab. *J Med Virol* 2020; Epub ahead of print. PMID: 32314799. Full Text

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Tocilizumab is an interleukin-6 (IL-6) receptor antibody and is progressing as a viable and promising treatment option in patients with severe coronavirus disease 2019 (COVID-19). IL-6 is known to have both immunomodulatory and metabolic actions. In this letter we outline two cases of acute hypertriglyceridemia in patients with COVID-19 treated with tocilizumab: one with elevated biomarkers consistent with acute pancreatitis the other without. Given the paucity of robust clinical trial data for most COVID-19 pharmacotherapies at this time, clinicians should continue to remain steadfast in recognition of interventions that improve clinical outcomes and vigilant in monitoring for acute adverse effects that are difficult to detect in clinical trials with small sample sizes. The observations from our two cases highlight the complex, not fully elucidated interrelationship between elevated IL-6 and pharmacologic interventions impacting this pathway. Clinicians should consider monitoring for hypertriglyceridemia and acute pancreatitis as described with chronic tocilizumab use for rheumatoid arthritis in those receiving it for COVID-19. This article is protected by copyright. All rights reserved.

Pulmonary and Critical Care Medicine

White RJ, Jerjes-Sanchez C, Bohns Meyer GM, Pulido T, Sepulveda P, Wang KY, Grunig E, Hiremath S, Yu Z, Gangcheng Z, Yip WLJ, Zhang S, Khan A, Deng CQ, Grover R, Tapson VF, **Awdish R**, and **Cajigas H**. Combination Therapy with Oral

Treprostinil for Pulmonary Arterial Hypertension. A Double-Blind Placebo-controlled Clinical Trial. *Am J Respir Crit Care Med* 2020; 201(6):707-717. PMID: 31765604. Full Text

Division of Pulmonary and Critical Care Medicine and the Mary M. Parkes Center, University of Rochester Medical Center, Rochester, New York.
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Pontifica Universidad Catolica de Chile, Santiago, Chile.
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Ruby Hall Clinic, Grant Medical Foundation, Pune, India.
Department of Cardiology, Xiangya Hospital of Central South University, Changsha, China.
Wuhan Asia Heart Hospital, Wuhan Shi, China.
Department of Cardiology, National University Heart Centre, Singapore, Singapore.
Peking Union Medical College Hospital, Beijing, China.
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Rationale: Oral treprostinil improves exercise capacity in patients with pulmonary arterial hypertension (PAH), but the effect on clinical outcomes was unknown.Objectives: To evaluate the effect of oral treprostinil compared with placebo on time to first adjudicated clinical worsening event in participants with PAH who recently began approved oral monotherapy.Methods: In this event-driven, double-blind study, we randomly allocated 690 participants (1:1 ratio) with PAH to receive placebo or oral treprostinil extended-release tablets three times daily. Eligible participants were using approved oral monotherapy for over 30 days before randomization and had a 6-minute-walk distance 150 m or greater. The primary endpoint was the time to first adjudicated clinical worsening event: death; hospitalization due to worsening PAH; initiation of inhaled or parenteral prostacyclin therapy; disease progression; or unsatisfactory long-term clinical response.Measurements and Main Results: Clinical worsening occurred in 26% of the oral treprostinil group compared with 36% of placebo participants (hazard ratio, 0.74; 95% confidence interval, 0.56-0.97; P = 0.028). Key measures of disease status, including functional class, Borg dyspnea score, and N-terminal pro-brain natriuretic peptide, all favored oral treprostinil treatment at Week 24 and beyond. A noninvasive risk stratification analysis demonstrated that oral treprostinil-assigned participants had a substantially higher mortality risk at baseline but achieved a lower risk profile from Study Weeks 12-60. The most common adverse events in the oral treprostinil group were headache, diarrhea, flushing, nausea, and vomiting.Conclusions: In participants with PAH, addition of oral treprostinil to approved oral monotherapy reduced the risk of clinical worsening.Clinical trial registered with www.clinicaltrials.gov (NCT01560624).

Radiation Oncology

Ellis MM, **Jones LR**, **Siddiqui F**, **Sunkara PR**, and **Ozog DM**. The Efficacy of Surgical Excision Plus Adjuvant Multimodal Therapies in the Treatment of Keloids: A Systematic Review and Meta-Analysis. *Dermatol Surg* 2020; Epub ahead of print. PMID: 32224709. Full Text

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BACKGROUND: Research evaluating the efficacy of multimodal therapy for the treatment of keloids has reported combination regimens are most effective. OBJECTIVE: To compare recurrence rates for keloids treated with surgery plus one adjuvant intervention (dual therapy) versus surgery plus 2 or more adjuvant interventions (triple therapy). MATERIALS AND METHODS: Systematic literature review and meta-analysis of combination treatment for keloids. RESULTS: After full-text review, we included 60 articles representing 5,547 keloids: 5,243 received dual therapy, 259 received triple therapy, and 45 received quadruple therapy (the latter 2 groups were combined for analysis). The difference in recurrence rates between dual (19%) and triple therapy (11.2%) was not significant (p = .343). However, the difference in recurrence rates between dual therapy using surgery and radiation (18.7%) and triple therapy using surgery, radiation, and a third intervention (7.7%) was significant (p = .002). The differences for surgery and intralesional triamcinolone (TAC) showed trends toward significance, because keloids treated with dual therapy (21.7%) had a higher recurrence rate than those treated with triple therapy comprised of surgery, TAC, and another intervention (13.7%; p = .099). CONCLUSION: Triple therapy using surgery plus radiation and/or TAC as one of the adjuvant treatment modalities may achieve the lowest recurrence rates for keloids.

Radiation Oncology

Sood A, **Keeley J**, **Palma-Zamora I**, **Arora S**, **Dalela D**, **Olson P**, **Hanna R**, **Cotter D**, **Jeong W**, **Elshaikh M**, **Rogers CG**, **Peabody JO**, **Menon M**, and **Abdollah F**. Ten-year disease progression and mortality rates in men who experience

biochemical recurrence versus persistence after radical prostatectomy and undergo salvage radiation therapy: A post-hoc analysis of RTOG 9601 trial data. *Urol Oncol* 2020; Epub ahead of print. PMID: 32229186. Full Text

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Department of Radiation Oncology, Henry Ford Hospital, Detroit, MI.

PURPOSE: To compare local/metastatic disease progression and overall mortality rates in men with node-negative prostate cancer at radical prostatectomy (RP) that experience biochemical recurrence vs. persistence postoperatively and undergo salvage radiation therapy (sRT). MATERIALS AND METHODS: Data on 760 men who participated in the RTOG 9601 trial were extracted using the NCTN data archive platform. Patients were stratified into biochemical recurrence (nadir-PSA </=0.4 ng/ml) or persistence (nadir-PSA >0.4 ng/ml) groups, based on the cut-off reported in the original trial. Inverse probability of treatment weighting (IPTW) methodology was utilized to minimize the baseline differences among groups. Competing-risk and Kaplan-Meier analyses estimated the impact of prostate-specific antigen (PSA) persistence vs. recurrence on local and metastatic disease progression and overall-mortality in the IPTW-adjusted model; a 2-sided P < 0.05 was considered significant. RESULTS: All patients received sRT, and about 50% of the patients in either group received concomitant antiandrogen therapy (P=0.951). The median follow-up was 12 years. After IPTW, the 2 groups were well-matched with standardized mean differences approximately 10%. In the IPTW-adjusted cohort, the 10-year local and metastatic disease occurrence rates were 3.2% vs. 1.4% (Gray's P=0.0001) and 28.6% vs. 10.1% (Gray's P < 0.0001) in patients with persistent vs. recurrent PSA, respectively. Similarly, the 10-year overall-mortality rates were 24.9% vs. 11.9% (Log-rank P=0.029), respectively. CONCLUSIONS: Patients with biochemical persistence after RP are approximately 2.5 times more likely to experience local/metastatic failure and death, compared to patients with biochemical recurrence after RP, despite equivalent sRT with/without antiandrogen therapy use. These data may facilitate patient counseling and shared treatment selection.

Radiation Oncology

Thanikachalam K, **Damarla V**, **Seixas T**, **Dobrosotskaya I**, **Wollner I**, **Kwon D**, **Winters K**, **Raoufi M**, **Li J**, **Siddiqui F**, and **Khan G**. Neoadjuvant Phase II Trial of Chemoradiotherapy in Patients With Resectable and Borderline Resectable Pancreatic Cancer. *Am J Clin Oncol* 2020; Epub ahead of print. PMID: 32251119. Full Text

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Division of Pathology, Henry Ford Health System.
Division of Radiation Oncology, Detroit, MI.

BACKGROUND: Pancreatic ductal adenocarcinoma is a largely incurable cancer. Surgical resection remains the only potential option for cure. Even in surgically resectable patients, only about 10% to 20% are long-term survivors. Emerging data suggest a role for neoadjuvant therapy to target occult micrometastatic disease. AIM: To report our institutional experience with a novel neoadjuvant chemoradiation (CRT) regimen in resectable and borderline resectable pancreatic cancer. MATERIALS AND METHODS: Patients were treated with 2 cycles of induction chemotherapy with FOLFOX and then received CRT with gemcitabine and intensity-modulated radiotherapy (IMRT). RESULTS: From April 2014 to June 2017, 24 patients were enrolled. Eighteen patients were borderline resectable and 6 patients were resectable. All patients received induction chemotherapy with FOLFOX. Thirteen patients underwent pancreatectomy after CRT with a resection rate of 62%. R0 resection achieved in 11 patients (84.6%) and 2 patients had R1 resection (15.4%). For patients who underwent resection, the median progression-free survival (PFS) was 31 months, 1-year PFS rate was 69.2% (95% confidence interval [CI], 0.48-0.99), and 2-year PFS rate was 51.9% (95% CI, 0.3-0.89). Median overall survival (OS) was 34.8 months (95% CI, 1.045 to infinity), 1-year OS rate was 91.7% (95% CI, 0.77-1.0), and 2-year OS rate was 75% (95% CI, 0.54-1.0). Median CA 19-9 at screening for patients who underwent surgery was 659 (range, 18 to 2154), which decreased to 146.9 (range, 18 to 462) after CRT before resection. CONCLUSION: Neoadjuvant therapy for borderline resectable and resectable pancreatic ductal adenocarcinoma with CRT facilitated R0 resection in 84% patients who underwent surgery.

Research Administration

Jamali-Dinan SS, **Soltanian-Zadeh H**, **Bowyer SM**, Almohri H, Dehghani H, Elisevich K, and Nazem-Zadeh MR. A Combination of Particle Swarm Optimization and Minkowski Weighted K-Means Clustering: Application in Lateralization of Temporal Lobe Epilepsy. *Brain Topogr* 2020; Epub ahead of print. PMID: 32347472. Full Text

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K-Means is one of the most popular clustering algorithms that partitions observations into nonoverlapping subgroups based on a predefined similarity metric. Its drawbacks include a sensitivity to noisy features and a dependency of its resulting clusters upon the initial selection of cluster centroids resulting in the algorithm converging to local optima. Minkowski weighted K-Means (MWK-Means) addresses the issue of sensitivity to noisy features, but is sensitive to the initialization of clusters, and so the algorithm may similarly converge to local optima. Particle Swarm Optimization (PSO) uses a globalized search method to solve this issue. We present a hybrid Particle Swarm Optimization (PSO) + MWK-Means clustering algorithm to address all the above problems in a single framework, while maintaining benefits of PSO and MWK Means methods. This study investigated the utility of this approach in lateralizing the epileptogenic hemisphere for temporal lobe epilepsy (TLE) cases using magnetoencephalography (MEG) coherence source imaging (CSI) and diffusion tensor imaging (DTI). Using MEG-CSI, we analyzed preoperative resting state MEG data from 17 adults TLE patients with Engel class I outcomes to determine coherence at 54 anatomical sites and compared the results with 17 age- and gender-matched controls. Fiber-tracking was performed through the same anatomical sites using DTI data. Indices of both MEG coherence and DTI nodal degree were calculated. A PSO + MWK-Means clustering algorithm was applied to identify the side of temporal lobe epileptogenicity and distinguish between normal and TLE cases. The PSO module was aimed at identifying initial cluster centroids and assigning initial feature weights to cluster centroids and, hence, transferring to the MWK-Means module for the final optimal clustering solution. We demonstrated improvements with the use of the PSO + MWK-Means clustering algorithm compared to that of K-Means and MWK-Means independently. PSO + MWK-Means was able to successfully distinguish between normal and TLE in 97.2% and 82.3% of cases for DTI and MEG data, respectively. It also lateralized left and right TLE in 82.3% and 93.6% of cases for DTI and MEG data, respectively. The proposed optimization and clustering methodology for MEG and DTI features, as they relate to focal epileptogenicity, would enhance the identification of the TLE laterality in cases of unilateral epileptogenicity.

Rheumatology

Yousif PA, **Moshrefi H**, **Meysami A**, and **Alkhatib AH**. Lupus-Induced Vasculitis and Multiple Organ Dysfunction Syndrome as the First Presentation of Systemic Lupus Erythematosus (SLE) in Pregnancy. *Am J Case Rep* 2020; 21:e921299. PMID: 32284523. Request Article

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BACKGROUND Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by autoantibody production leading to inflammation in multiple organs; it commonly affects young women in their child-bearing years. Clinical manifestations are diverse and range from mild arthritis to diffuse alveolar hemorrhage (DAH). DAH is a rare and devastating complication of SLE that carries a mortality rate of up to 50%, despite aggressive therapy. CASE REPORT A 21-year-old primigravida at 16 weeks gestation presents with a productive cough, rash, sore throat, and high-grade fever. Chest x-ray suggested multifocal pneumonia. Patient deteriorated despite antibiotics and intravenous (IV) fluids. She developed worsening anemia, leukopenia, and thrombocytopenia. Autoimmune workup was positive for Coombs, antinuclear antibody, anti-smith antibody, and hypocomplementemia. Skin biopsy was consistent with SLE. SLE vasculitis was suspected. She required mechanical intubation for rapid respiratory deterioration, with CT thorax suggesting ARDS. Bronchoscopy was done and confirmed DAH. Her course was further complicated with retinopathy and acute pancreatitis associated with SLE. She was treated with IV steroids, IV cyclophosphamide, and plasmapheresis, with significant clinical improvement and successful extubation. She delivered a healthy baby at 32 weeks gestation. CONCLUSIONS Early recognition and initiation of treatment is critical to survival in DAH and requires a high index of clinical suspicion. Treatment includes high-dose steroids, cyclophosphamide, and plasma exchange. Pregnancy increases the risk of adverse outcome in SLE. Seven cases of DAH in pregnant patients with SLE have been reported. Here, we report a catastrophic presentation of DAH, acute pancreatitis, and retinopathy in a pregnant patient with newly diagnosed SLE.

Rheumatology
Yousif PA, **Moshrefi HR**, **Mohamed MA**, and **Meysami A**. A Rare and Fatal Case of Hemophagocytic Lymphohistiocytosis Associated with Sarcoidosis. *Am J Case Rep* 2020; 21:e921306. PMID: 32315294. Request Article

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BACKGROUND Sarcoidosis is a systemic inflammatory disorder characterized by a classic pathologic feature of non-caseating granulomas involving any organ system. Hemophagocytic lymphohistiocytosis (HLH) is a catastrophic cytokine surge characterized by dysregulation of the macrophage response, which can be rapidly fatal. Recognition of HLH has been increasing over the past decade. HLH can present with features of sepsis that can make the diagnosis challenging and requires high clinical suspicion. CASE REPORT We report a case of a 48-year-old African American male with a past medical history of sarcoidosis infiltrating the lymph nodes, liver, and bone marrow with initial presentation of abdominal pain, nausea, vomiting, and weight loss of 100 pounds over 8 months. Sepsis was suspected, but the patient clinically deteriorated with vancomycin and cefepime. Fevers, bone marrow biopsy, anemia, thrombocytopenia, elevated ferritin, and elevated soluble receptor interleukin 2 confirmed HLH. The patient was treated with etoposide and dexamethasone with poor response and died from cardiac arrest. CONCLUSIONS Sarcoidosis associated with HLH is an extremely rare phenomenon with only 10 cases reported in the literature. Early clinical suspicion can be challenging as this condition is a sepsis-mimicker. To reduce mortality, prompt initiation of therapy is a key determinant in patients who are clinically deteriorating despite treatment for sepsis.

Sleep Medicine
Ivgy-May N, Hajak G, van Osta G, Braat S, Chang Q, and **Roth T**. Efficacy and safety of esmirtazapine in adult outpatients with chronic primary insomnia: a randomized, double-blind placebo-controlled study, and open-label extension. *J Clin Sleep Med* 2020; Epub ahead of print. PMID: 32351205. Full Text

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STUDY OBJECTIVES: Esmirtazapine (1.5-4.5 mg) has demonstrated short-term sleep-promoting effects in non-elderly outpatients with chronic insomnia. This Phase 3, randomized, double-blind study (NCT00631657) and its open-label extension (NCT00750919) investigated efficacy and safety of long-term esmirtazapine treatment in adult outpatients with chronic insomnia. METHODS: Participants were randomized to receive esmirtazapine 4.5 mg or placebo for 6 months; those receiving esmirtazapine were then re-randomized to esmirtazapine or placebo for an additional 7 days. Participants could enter the 6-month open-label extension with esmirtazapine 4.5 mg. The primary objective of the double-blind study was to assess long-term efficacy of esmirtazapine versus placebo on self-reported total sleep time. Assessing long-term safety and tolerability were secondary and primary objectives of the double-blind and extension studies, respectively. RESULTS: Overall, 457 participants received treatment in the double-blind study (esmirtazapine, n=342; placebo, n=115) and 184 participants (prior esmirtazapine, n=136; prior placebo, n=48) received esmirtazapine in the extension. In the double-blind study, a 48.7-min increase in average nightly total sleep time was observed for esmirtazapine versus placebo (95% confidence interval 35.0, 62.5; P<.0001) at Months 4-6. There was no evidence of residual effects on next-day alertness or daytime functioning, and no evidence of rebound insomnia or withdrawal symptoms upon treatment discontinuation. Esmirtazapine was generally well tolerated; somnolence and weight gain were the most common adverse events. CONCLUSIONS: Esmirtazapine improved sleep duration versus placebo over at least 6 months. There was no evidence of next-day residual effects, or of withdrawal symptoms or rebound insomnia following abrupt treatment discontinuation. CLINICAL TRIAL REGISTRATION: "A 6-Month Efficacy and Safety Study of Org 50081 in Adult Patients With Chronic Primary Insomnia (21106/P05701/MK-8265-002)" (NCT00631657; https://clinicaltrials.gov/ct2/show/NCT00631657) and "Twenty-six Week Extension Trial of Org 50081 (Esmirtazapine) in Outpatients With Chronic Primary Insomnia (176003/P05721/MK-8265-007)" (NCT00750919; https://clinicaltrials.gov/ct2/show/NCT00750919).

Sleep Medicine
Weaver TE, **Drake CL**, Benes H, Stern T, Maynard J, Thein SG, Andry JM, Sr., Hudson JD, Chen D, Carter LP, Bron M, Lee L, Black J, and Bogan RK. Effects of Solriamfetol on Quality of Life Measures From a 12-Week Phase 3 Randomized Trial. *Ann Am Thorac Soc* 2020; Epub ahead of print. PMID: 32353246. Full Text

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RATIONALE: Excessive daytime sleepiness in patients with obstructive sleep apnea is associated with substantial burden of illness. OBJECTIVE: To assess solriamfetol, a dopamine/norepinephrine reuptake inhibitor, treatment effects on daily functioning, health-related quality of life, and work productivity in participants with obstructive sleep apnea and excessive daytime sleepiness as additional outcomes in a 12-week phase 3 trial (www.ClinicalTrials.gov identifier: NCT02348606). METHODS: Participants (N=476) were randomized to solriamfetol 37.5, 75, 150, or 300 milligrams, or placebo. Outcome measures included Functional Outcomes of Sleep Questionnaire short version, Work Productivity and Activity Impairment questionnaire for Specific Health Problem, and 36-Item Short Form Health Survey version 2. A mixed-effects model with repeated measures was used for comparisons to placebo. RESULTS: Demographics, baseline disease characteristics, daily functioning, health-related quality of life, and work productivity were similar across groups. At week 12, increased functioning and decreased impairment were observed with solriamfetol 150 and 300 milligrams (mean difference from placebo [95% confidence interval]): Functional Outcomes of Sleep Questionnaire total score (1.22 [0.57, 1.88]) and (1.47 [0.80, 2.13], respectively), overall work impairment (-11.67 [-19.66, -3.69] and -11.75 [-19.93, -3.57], respectively) activity impairment (-10.42 [-16.37, -4.47] and -10.51 [-16.59, -4.43], respectively), physical component summary (2.07 [0.42, 3.72] and 1.91 [0.22, 3.59], respectively), and mental component summary (150 mg only: 2.05 [0.14, 3.96]). Common adverse events were headache, nausea, decreased appetite, and anxiety. CONCLUSIONS: Solriamfetol improved measures of functioning, quality of life, and work productivity in participants with obstructive sleep apnea and excessive daytime sleepiness. Safety was consistent with previous studies. Clinical trial registered with ClinicalTrials.gov (NCT02348606).

Surgery

Bendix SD, **Peterson EL**, **Kabbani LS**, **Weaver MR**, and **Lin JC**. The Impact of Endovenous Ablation Assessment Based on Great Saphenous Vein Size, Gender, Clinical Severity, and Patient Reported Outcomes. *J Vasc Surg Venous Lymphat Disord* 2020; Epub ahead of print. PMID: 32353593. Full Text

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OBJECTIVE: Policies of insurance carriers have used truncal vein size as a criteria for coverage. The objective of this study was to compare the effect of great saphenous vein (GSV) size > 5 mm versus < 5 mm on patient presentation and clinical outcomes. METHODS: Patients in a national cohort were prospectively captured in the Vascular Quality Initiative (VQI) Varicose Vein Registry (VVR). From January 2015 to October 2017, the VQI VVR database was queried for all patients undergoing varicose vein procedures. Clinical, Etiology, Anatomy, and Pathophysiology (CEAP) classification, Venous Clinical Severity Score (VCSS), and patient-reported outcomes (PROs) were compared between GSV size < 5 mm (group 1) versus size > 5 mm (group 2) before and after the procedures. Two-sample Wilcoxon test was performed to assess the difference between the two groups as defined by GSV size. To assess for improvement after procedure in this population, a matched-pairs signed-rank Wilcoxon test was performed for each group separately. RESULTS: During the study period, 5757 vein ablation procedures were performed for GSV: 770 GSV size < 5 mm and 4987 size > 5 mm. Group 1 were more likely female (81.7% vs 68.4%, P=0.001) and older age (56.8 years vs 55.6 years, P=0.012). CEAP clinical classes were more advanced in group 2 compared to group 1 (P=0.001). Maximal GSV diameter in group 2 was significantly higher (8.32 mm vs 3.86 mm, P=0.001). 64% of group 2 underwent RF thermal ablation compared to 59.2% of group 1 (P=0.001). There were no mortalities in either group. Group 2 had more complications post-procedure (0.6% vs 0%, P=0.027), required post-operative anticoagulation (8.8% vs 5%, P=0.001), developed partial recanalization rate (0.8% vs 0.3%, P=0.001), and missed more work days (2.32 days vs 1.6 days) as compared to group 1. Similar rate of hematoma developed in both groups, but a higher rate of paresthesia in group 1. Both groups had improvement in their VCSS and HASTI scores. The degree of symptomatic improvement between the groups was similar. CONCLUSIONS: All patients demonstrate improvement in both clinical outcomes and patient-reported outcomes after endovenous ablation regardless of size. Patients with preoperative GSV size > 5 mm have similar improvement in their symptomatology but sustain an increased complication rate. Patients with smaller vein size should not be denied intervention or coverage based on size criteria.

Surgery
Bergquist JR, **Li AY**, Chang EM, Scott GD, Dua MM, and Visser BC. Nearing the Summit: Associating Liver Partitioning and Portal Ligation for Staged Hepatectomy (ALPPS) in Progressive Carcinoid Disease. *Dig Dis Sci* 2020; Epub ahead of print. PMID: 32307614. Full Text

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Surgery
Dingman JS, **Smith ZR**, **Coba VE**, **Peters MA**, and **To L**. Argatroban dosing requirements in extracorporeal life support and other critically ill populations. *Thromb Res* 2020; 189:69-76. PMID: 32182522. Full Text

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Argatroban is a parenteral direct thrombin inhibitor that requires close monitoring to ensure safety and efficacy. Limited data exist to describe its effect in critically ill patients. This was a retrospective, single-center, cohort study that aimed to compare argatroban dosing requirements in those receiving extracorporeal life support (ECLS), continuous renal replacement therapy (CRRT), or neither. Organ dysfunction was assessed using a modified version of the Sequential Organ Failure Assessment (modSOFA) that incorporated the use of extracorporeal support systems. Eighty patients were included in the study (n = 20, 20, 40 in the ECLS, CRRT, and support-free groups, respectively). The majority of patients were Child-Pugh classification B (73%). Median modSOFA scores were higher in the ECLS (16.5) and CRRT (15.5) groups than in the support-free group (7.5) (P < .001). There was no difference in the primary outcome of first therapeutic argatroban dose between the three groups (0.5 mug/kg/min for each; IQRs 0.25-0.50, 0.11-0.50, and 0.25-0.50, respectively; P = .455). The ECLS group had the lowest mean (0.39 mug/kg/min), minimum (0.20 mug/kg/min), and final (0.43 mug/kg/min) doses. ECLS patients had more supratherapeutic aPTTs and dose changes overall, supporting the need for more frequent anticoagulation monitoring or dose reductions in this population. Total modSOFA score demonstrated a moderate inverse correlation with first therapeutic dose (dose = 0.54 - (modSOFA score x 0.012); R = -0.342, P = .002). Overall, initial argatroban doses of 0.3-0.5 mug/kg/min appear to achieve therapeutic aPTT values in the studied populations.

Surgery
Rteil A, **Draxler M**, **Al Adas Z**, **Mohammad F**, **Kavousi Y**, and **Kabbani L**. Progressive stenosis of a popliteal artery stent graft by laminated thrombus. *J Vasc Surg Cases Innov Tech* 2020; 6(2):189-194. PMID: 32322774. Full Text

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We present a case of failed popliteal artery aneurysm repair using a Viabahn stent graft (W. L. Gore & Associates, Flagstaff, Ariz) due to laminated thrombus formation. A 75-year-old man presented with a symptomatic popliteal artery aneurysm. He was treated with a Viabahn stent graft. On follow-up, the patient complained of lower extremity claudication, and duplex ultrasound examination showed a focal intrastent stenosis. A computed tomography scan showed a significant stenosis within the stent graft, at the level of the knee joint creases. The patient underwent superficial femoral artery to distal popliteal surgery. This case report aims to expand on the mechanism of stent graft failure in popliteal aneurysms.

Surgery
Shah R, Borrebach JD, Hodges JC, Varley PR, Wisniewski MK, Shinall MC, Jr., Arya S, Johnson J, Nelson JB, Youk A, Massarweh NN, Johanning JM, and Hall DE. Validation of the Risk Analysis Index for Evaluating Frailty in Ambulatory Patients. *J Am Geriatr Soc* 2020; Epub ahead of print. PMID: 32310317. Full Text

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BACKGROUND: Frailty is a marker of dependency, disability, hospitalization, and mortality in community-dwelling older adults. However, existing tools for measuring frailty are too cumbersome for rapid point-of-care assessment. The Risk Analysis Index (RAI) of frailty is validated in surgical populations, but its performance outside surgical populations is unknown. OBJECTIVE: Validate the RAI in ambulatory patients. DESIGN, SETTING, AND PARTICIPANTS: Observational cohort study of outpatient surgical clinics within the University of Pittsburgh Medical Center Healthcare System between July 1, 2016, and December 31, 2016. Frailty was assessed using the RAI. Current Procedural Terminology codes following RAI assessment identified patients with and without minor office-based procedures (eg, joint injection, laryngoscopy). MAIN OUTCOMES AND MEASURES: All-cause 1-year mortality, assessed by stratified Cox proportional hazard models. RESULTS: Of 28,059 patients, 13,861 were matched to a minor, office-based procedure and 14,198 did not undergo any procedure. The mean (SD) age was 56.7 (17.2) years; women constituted 15,797 (56.3%) of the cohort. Median time (interquartile range 25th-75th percentile) to measure RAI was 30 (22-47) seconds. Mortality among the frail was two to five times that of patients with normal RAI scores. For example, the hazard ratio for frail ambulatory patients without a minor procedure was 3.69 (95% confidence interval [CI] = 2.51-5.41), corresponding to 30-, 180-, and 365-day mortality rates of 2.9%, 11.2%, and 17.4%, respectively, compared to 0.3%, 2.3%, and 4.0% among patients with normal RAI scores. Discrimination of mortality (overall, and censored at 30, 180, and 365 days) was excellent, ranging from c = 0.838 (95% CI = 0.773-0.902) for 30-day mortality after minor procedures to c = 0.909 (95% CI = 0.855-0.964) without a procedure. CONCLUSION: RAI is a valid, easily administered tool for point-of-care frailty assessment in ambulatory populations that may help clinicians and patients make better informed decisions about care choices-especially among patients considered high risk with a potentially limited life span.

Surgery

Thanikachalam K, **Damarla V**, **Seixas T**, **Dobrosotskaya I**, **Wollner I**, **Kwon D**, **Winters K**, **Raoufi M**, **Li J**, **Siddiqui F**, and **Khan G**. Neoadjuvant Phase II Trial of Chemoradiotherapy in Patients With Resectable and Borderline Resectable Pancreatic Cancer. *Am J Clin Oncol* 2020; Epub ahead of print. PMID: 32251119. Full Text

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BACKGROUND: Pancreatic ductal adenocarcinoma is a largely incurable cancer. Surgical resection remains the only potential option for cure. Even in surgically resectable patients, only about 10% to 20% are long-term survivors. Emerging data suggest a role for neoadjuvant therapy to target occult micrometastatic disease. AIM: To report our institutional experience with a novel neoadjuvant chemoradiation (CRT) regimen in resectable and borderline resectable pancreatic cancer. MATERIALS AND METHODS: Patients were treated with 2 cycles of induction chemotherapy with FOLFOX and then received CRT with gemcitabine and intensity-modulated radiotherapy (IMRT). RESULTS: From April 2014 to June 2017, 24 patients were enrolled. Eighteen patients were borderline resectable and 6 patients were resectable. All patients received induction chemotherapy with FOLFOX. Thirteen patients underwent pancreatectomy after CRT with a resection rate of 62%. R0 resection achieved in 11 patients (84.6%) and 2 patients had R1 resection (15.4%). For patients who underwent resection, the median progression-free survival (PFS) was 31 months, 1-year PFS rate was 69.2% (95% confidence interval [CI], 0.48-0.99), and 2-year PFS rate was 51.9% (95% CI, 0.3-0.89). Median overall survival (OS) was 34.8 months (95% CI, 1.045 to infinity), 1-year OS rate was 91.7% (95% CI, 0.77-1.0), and 2-year OS rate was 75% (95% CI, 0.54-1.0). Median CA 19-9 at screening for patients who underwent surgery was 659 (range, 18 to 2154), which decreased to 146.9 (range, 18 to 462) after CRT before resection. CONCLUSION: Neoadjuvant therapy for borderline resectable and resectable pancreatic ductal adenocarcinoma with CRT facilitated R0 resection in 84% patients who underwent surgery.

Surgery

Worden A, **Yoho DJ**, **Houin H**, **Moquin K**, **Hamzavi I**, **Saab I**, and **Siddiqui A**. Factors Affecting Healing in the Treatment of Hidradenitis Suppurativa. *Ann Plast Surg* 2020; 84(4):436-440. PMID: 31688123. Full Text

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BACKGROUND: Hidradenitis suppurativa (HS) is a chronic debilitating condition. Treatment of HS depends on disease stage, goals of care, access to care, and frequency of symptoms. We present our experience with surgical treatment for patients with HS. METHODS: Patients were followed longitudinally for at least 2 years postsurgical intervention. Demographic data, participation in a multidisciplinary program, type of surgery, healing rates, and potential factors contributing to wound healing were retrospectively reviewed in all cases using multivariate analysis. RESULTS: Two hundred forty-eight patients met the inclusion criteria with a total of 810 involved sites. Overall, 59% of patients had Hurley stage 3 disease at the time of surgery. Healing rates of 80% were observed in stages 1 and 2, and 74% were observed in stage 3. Hurley stage was not a significant predictor of healing (P = 0.09). Surgical treatment consisted of 38% incision and drainage, 44% excision without closure, and 17% excision with primary closure. Incisional and excisional treatments healed 78% and 79%, respectively, at 2 years. Primarily repaired defects (grafts and flaps) were 68% healed at 2 years. Observed healing rates were uniform regardless of the number of sites involved (P = 0.959). Participation in the multidisciplinary program was the strongest predictor of healing (78% vs 45%, P = 0.004). Sex, age, body mass index, tobacco use, diabetes, presurgery hemoglobin, and family history of HS were statistically not significant. Continuation of immune modulating therapy within 2 weeks of surgery was a predictor of reduced healing (odds ratio, 0.23; P = 0.004), whereas holding biologics for at least 2 weeks was not significant (odds ratio, 1.99; P = 0.146). CONCLUSIONS: Participation in a multidisciplinary program is a strong predictor of long-term success when treating HS. Hurley score and number of involved sites did not correlate with successful healing after surgery. If taking biologics, we identified 2 weeks as an appropriate break from biologics before and after surgical intervention. Healing rates were highest with ablative procedures (incision and drainage, excision) alone.

Urology

Abdelsalam RA, Khalifeh I, Box A, Kalantarian M, Ghosh S, Abou-Ouf H, Lotfi T, Shahait M, **Palanisamy N**, and Bismar TA. Molecular characterization of prostate cancer in Middle Eastern population highlights differences with Western populations with prognostic implication. *J Cancer Res Clin Oncol* 2020; Epub ahead of print. PMID: 32350606. Full Text

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BACKGROUND: To investigate the incidence and prognostication of ERG, PTEN and SPINK1 protein expressions in prostate cancer cohort of Middle Eastern descent in comparison to published data from Western population. METHODS: Immunohistochemistry for ERG, PTEN and SPINK1 was performed in a cohort of localized PCA (n = 340). The data were correlated to pathological and clinical outcomes and compared to Western populations. RESULTS: ERG expression and PTEN loss were noted in 123/288 (42.7%) and 91/297 (30.6%) of patients, respectively. SPINK1 expression was assessed in a subset of cases, noted in 6/150 (4%) of patients. Only ERG expression was associated with grade groups, being more common in the lower grade groups (1-3 vs 4-5; p = 0.04). In contrast to the Western population, PTEN loss foci were more likely to be ERG negative, observed in 81% of tumor foci and patients with PTEN neg/ERG pos were more likely to exhibit biochemical recurrence (OR 2.831; 95% CI 1.10-726, p = 0.03). This association remained significant in multivariate analysis (OR 2.68; 95% CI 0.98-7.33, p = 0.05), after adjusting for GG, path stage and surgical margin. CONCLUSION: This study documents significant differences in key molecular events in PCA in Middle Eastern population compared to Western populations that could explain differences in PCA incidence, progression and prognostication. ERG, PTEN and SPINK1 genomic alteration occur less frequently and the enrichment of ERG for PTEN loss is not observed. Additionally, patients with combined PTEN loss/ERG positive are at highest risk for BCR vs North American Caucasian population where PTEN loss alone seems to be associated with the worst clinical outcome. The data presented here further support differences in clonal evolution between Middle Eastern and Western population in relation to PCA and add further insight to understanding PCA molecular pathways.

Urology

Bhandari M, Nallabasannagari AR, Reddiboina M, Porter JR, **Jeong W**, Mottrie A, Dasgupta P, Challacombe B, Abaza R, Rha KH, Parekh DJ, Ahlawat R, Capitanio U, Yuvaraja TB, Rawal S, Moon DA, Buffi's NM, Sivaraman A, Maes KK, Porpiglia F, Gautam G, Turkeri L, Meyyazhgan KR, Patil P, **Menon M**, and **Rogers C**. Predicting intraoperative and postoperative consequential events using machine learning techniques in patients undergoing robotic partial nephrectomy (RPN): Vattikuti Collective Quality Initiative (VCQI) database study. *BJU Int* 2020; Epub ahead of print. PMID: 32315504. Full Text

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OBJECTIVE: To predict intraoperative events (IOE) and postoperative events (POE) consequential to the derailment of the ideal clinical course of patient recovery. MATERIAL AND METHODS: Vattikuti Collective Quality Initiative (VCQI), a multi-institutional dataset of patients who underwent Robotic Partial Nephrectomy for kidney tumors. Machine Learning (ML) models were constructed to predict IOE, and POE using Logistic Regression, Random Forest, and Neural Networks. The models to predict IOE used patient demographics and preoperative data. In addition to the above, intraoperative data was used to predict POE. Performance on the test dataset was assessed using Area Under Receiver Operating Curve (AUC-ROC) and Area Under Precision-Recall Curve (PR-AUC). RESULTS: The rate of IOE and POE was 5.62% and 20.98%, respectively. Models for predicting IOE were constructed using data from 1690 patients and 38 variables; the best model had AUC-ROC of 0.858 (95% CI, 0.762, 0.936), and PR-AUC of 0.590 (95% CI, 0.400, 0.759). Models for predicting POE were trained using data from 1406 patients and 59 variables; the best model had AUC-ROC of 0.875 (95% CI, 0.834, 0.913), and PR-AUC 0.706 (95% CI, 0.610, 0.790). CONCLUSIONS: The performance of the ML models in this study is encouraging. Further validation in a multi-institutional clinical setting with larger datasets would be necessary to establish their clinical value. ML models can be used to predict significant events during and after surgery with good accuracy, paving the way for application in clinical practice to predict and intervene at an opportune time to avert complications and improve patient outcomes.

Urology
Chandrashekar DS, Chakravarthi B, Robinson AD, Anderson JC, Agarwal S, Balasubramanya SAH, Eich ML, Bajpai AK, Davuluri S, Guru MS, Guru AS, Naik G, Della Manna DL, Acharya KK, **Carskadon S**, Manne U, Crossman DK, Ferguson JE, Grizzle WE, **Palanisamy N**, Willey CD, Crowley MR, Netto GJ, Yang ES, Varambally S, and Sonpavde G. Therapeutically actionable PAK4 is amplified, overexpressed, and involved in bladder cancer progression. *Oncogene* 2020; Epub ahead of print. PMID: 32231273. Full Text

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Muscle-invasive bladder carcinomas (MIBCs) are aggressive genitourinary malignancies. Metastatic urothelial carcinoma of the bladder is generally incurable by current chemotherapy and leads to early mortality. Recent studies have identified molecular subtypes of MIBCs with different sensitivities to frontline therapy, suggesting tumor heterogeneity. We have performed multi-omic profiling of the kinome in bladder cancer patients with the goal of identify therapeutic targets. Our analyses revealed amplification, overexpression, and elevated kinase activity of P21 (RAC1) activated kinase 4 (PAK4) in a subset of Bladder cancer (BLCA). Using bladder cancer cells, we confirmed the role of PAK4 in BLCA cell proliferation and invasion. Furthermore, we observed that a PAK4 inhibitor was effective in curtailing growth of BLCA cells. Transcriptomic analyses identified elevated expression of another kinase, protein tyrosine kinase 6 (PTK6), upon treatment with a PAK4 inhibitor and RNA interference of PAK4. Treatment with a combination of kinase inhibitors (vandetanib and dasatinib) showed enhanced sensitivity compared with either drug alone. Thus, PAK4 may be therapeutically actionable for a subset of MIBC patients with amplified and/or overexpressed PAK4 in their tumors. Our results also indicate that combined inhibition of PAK4 and PTK6 may overcome resistance to PAK4. These observations warrant clinical investigations with selected BLCA patients.

Urology

Dedigama-Arachchige P, **Carskadon S**, **Li J**, **Loveless I**, **Alhamar M**, **Peabody JO**, **Stricker H**, **Chitale DA**, **Rogers CG**, **Menon M**, **Gupta NS**, Bismar TA, **Williamson SR**, and **Palanisamy N**. Clonal evaluation of prostate cancer molecular heterogeneity in biopsy samples by dual immunohistochemistry and dual RNA in situ hybridization. *Mod Pathol* 2020; Epub ahead of print. PMID: 32238875. Full Text

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Prostate cancer is frequently multifocal. Although there may be morphological variation, the genetic underpinnings of each tumor are not clearly understood. To assess the inter and intra tumor molecular heterogeneity in prostate biopsy samples, we developed a combined immunohistochemistry and RNA in situ hybridization method for the simultaneous evaluation of ERG, SPINK1, ETV1, and ETV4. Screening of 601 biopsy cores from 120 consecutive patients revealed multiple alterations in a mutually exclusive manner in 37% of patients, suggesting multifocal tumors with considerable genetic differences. Furthermore, the incidence of molecular heterogeneity was higher in African Americans patients compared with Caucasian American patients. About 47% of the biopsy cores with discontinuous tumor foci showed clonal differences with distinct molecular aberrations. ERG positivity occurred in low-grade cancer, whereas ETV4 expression was observed mostly in high-grade cancer. Further studies revealed correlation between the incidence of molecular markers and clinical and pathologic findings, suggesting potential implications for diagnostic pathology practice, such as defining dominant tumor nodules and discriminating juxtaposed but molecularly different tumors of different grade patterns.

Urology

Hussein AA, Elsayed AS, Aldhaam NA, Jing Z, **Peabody JO**, Wijburg CJ, Wagner A, Canda AE, Khan MS, Scherr D, Schanne F, Maatman TJ, Kim E, Mottrie A, Aboumohamed A, Gaboardi F, Pini G, Kaouk J, Yuh B, Rha KH, Hemal A, Palou Redorta J, Badani K, Saar M, Stockle M, Richstone L, Roupret M, Balbay D, Dasgupta P, **Menon M**, and Guru KA. A Comparative Propensity-Score Matched Analysis of Perioperative Outcomes of Intracorporeal versus Extracorporeal Urinary Diversion after Robot-Assisted Radical Cystectomy: Results from the International Robotic Cystectomy Consortium. *BJU Int* 2020; Epub ahead of print. PMID: 32306494. Full Text

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INTRODUCTION AND BACKGROUND: Randomized controlled trials comparing open and robot-assisted radical cystectomy (RARC) have mainly focused on the extirpative portion of the procedure rather than the urinary diversion approach. There is paucity of data comparing intracorporeal (ICUD) and extracorporeal urinary diversion (ECUD) following RARC, and published data were mostly subject to selection bias. METHODS: Retrospective review of the prospectively maintained International Robotic Cystectomy Consortium (IRCC) database. A total of 972 patients from 27 institutions who underwent RARC were included. Propensity score matching was utilized to match patients based on age, gender, BMI, ASA score, Charlson comorbidity index (CCI) score, prior radiation and abdominal surgery, receipt of neoadjuvant chemotherapy, and clinical staging. Matched cohorts were compared. Multivariate stepwise logistic and linear regression models were fit to evaluate variables associated with receiving ICUD, operative time, 90-d high grade complications (Clavien Dindo Classification >/=3) and 90-d readmissions after RARC. RESULTS: Utilization of ICUD increased from 0% in 2005 to 95% in 2018. ICUD patients demonstrated more overall complications (66% vs 58%, p=0.01), and readmissions (27% vs 17%, p=0.01) but not high-grade complications (21% vs 24%, p=0.22). A more recent cystectomy era and ileal conduit diversion were associated with receiving ICUD. Higher BMI, ASA >/=3, and receiving a neobladder were associated with longer operative times. Shorter operative time was associated with male gender, older age, ICUD and centers with higher annual average cystectomy volume. Longer ICU stay was associated with 90-d high grade complications. Higher CCI score, prior radiation therapy, neoadjuvant chemotherapy and ICUD were associated with higher risk of 90-d readmissions. CONCLUSIONS: Utilization of ICUD has increased over the past decade. ICUD was associated with more overall complications and readmissions compared to ECUD but not high grade complications.

Urology
Jebastin JAS, **Perry KD**, **Chitale DA**, **Mott MP**, **Sanchez J**, Fritchie KJ, **Palanisamy N**, and **Williamson SR**. Atypical Lipomatous Tumor/Well-Differentiated Liposarcoma With Features Mimicking Spindle Cell Lipoma. *Int J Surg Pathol* 2020; 28(3):336-340. PMID: 31672072. Full Text

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Atypical lipomatous tumor/well-differentiated liposarcoma (ALT/WDL) and spindle cell lipoma are lipomatous tumors with distinct clinical, molecular, and prognostic features. Although histological and immunophenotypic features can overlap between ALT/WDL and spindle cell lipoma, the oncogenesis and clinical behavior are markedly different. In borderline cases, molecular analysis for MDM2 or CDK4 amplification can aid in distinguishing ALT/WDL from spindle cell lipoma. Although dedifferentiated liposarcoma has been reported to harbor both MDM2 amplification and loss of the RB1 region, we are not aware of a reported RB1 loss in well-differentiated ALT/WDL. In this article, we present a 69-year-old woman with a lipomatous tumor in the gluteal region that histologically, immunohistochemically, and molecularly mimicked spindle cell lipoma (with positive immunohistochemical staining for CD34 and loss of the RB1 gene region), yet harbored amplification of MDM2 and CDK4 confirmed by fluorescence in situ hybridization, supporting classification as ALT/WDL. This case strengthens the argument that in atypical clinical contexts, molecular studies for MDM2/CDK4 should be considered in tumors resembling spindle cell lipoma.

Urology
Monga J, **Subramani D**, **Bharathan A**, and **Ghosh J**. Pharmacological and genetic targeting of 5-lipoxygenase interrupts c-Myc oncogenic signaling and kills enzalutamide-resistant prostate cancer cells via apoptosis. *Sci Rep* 2020; 10(1):6649. PMID: 32313135. Full Text

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Much of the morbidity and mortality due to prostate cancer happen because of castration-resistant prostate cancer (CRPC) which invariably develops after anti-androgenic therapy. FDA-approved enzalutamide is commonly prescribed for CRPC which works by blocking androgen receptor function. However, even after initial good response, enzalutamide-resistant prostate cancer (ERPC) develops which eventually leads to widespread metastasis. Management of ERPC is extremely difficult

because available therapeutic regimen cannot effectively kill and eliminate ERPC cells. Though the mechanism behind enzalutamide-resistance is not properly understood, over-activation of c-Myc has been found to be a common event which plays an important role in the maintenance and progression of ERPC phenotype. However, direct-targeting of c-Myc poses special problem because of its non-enzymatic nature and certain amount of c-Myc activity is needed by non-cancer cells as well. Thus, c-Myc has emerged as an elusive target which needs to be managed by novel agents and strategies in a cancer-specific way. We investigated the effects of pharmacological and genetic inhibition of 5-lipoxygenase (5-Lox) on cell proliferation, apoptosis and invasive potential of enzalutamide-resistant prostate cancer cells. Transcriptional activity of c-Myc was analyzed by DNA-binding, luciferase-assays, and expression of c-Myc-target genes. We found that 5-Lox regulates c-Myc signaling in enzalutamide-resistant prostate cancer cells and inhibition of 5-Lox by Quiflapon/MK591 or shRNA interrupts oncogenic c-Myc signaling and kills ERPC cells by triggering caspase-mediated apoptosis. Interestingly, MK591 does not affect normal, non-cancer cells in the same experimental conditions. Our findings indicate that inhibition of 5-Lox may emerge as a promising new approach to effectively kill ERPC cells sparing normal cells and suggest that development of a long-term curative therapy of prostate cancer may be possible by killing and eliminating ERPC cells with suitable 5-Lox-inhibitors.

Urology
Sood A, **Keeley J**, **Palma-Zamora I**, **Arora S**, **Dalela D**, **Olson P**, **Hanna R**, **Cotter D**, **Jeong W**, **Elshaikh M**, **Rogers CG**, **Peabody JO**, **Menon M**, and **Abdollah F**. Ten-year disease progression and mortality rates in men who experience biochemical recurrence versus persistence after radical prostatectomy and undergo salvage radiation therapy: A post-hoc analysis of RTOG 9601 trial data. *Urol Oncol* 2020; Epub ahead of print. PMID: 32229186. Full Text

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PURPOSE: To compare local/metastatic disease progression and overall mortality rates in men with node-negative prostate cancer at radical prostatectomy (RP) that experience biochemical recurrence vs. persistence postoperatively and undergo salvage radiation therapy (sRT). MATERIALS AND METHODS: Data on 760 men who participated in the RTOG 9601 trial were extracted using the NCTN data archive platform. Patients were stratified into biochemical recurrence (nadir-PSA </=0.4 ng/ml) or persistence (nadir-PSA >0.4 ng/ml) groups, based on the cut-off reported in the original trial. Inverse probability of treatment weighting (IPTW) methodology was utilized to minimize the baseline differences among groups. Competing-risk and Kaplan-Meier analyses estimated the impact of prostate-specific antigen (PSA) persistence vs. recurrence on local and metastatic disease progression and overall-mortality in the IPTW-adjusted model; a 2-sided $P < 0.05$ was considered significant. RESULTS: All patients received sRT, and about 50% of the patients in either group received concomitant antiandrogen therapy (P=0.951). The median follow-up was 12 years. After IPTW, the 2 groups were well-matched with standardized mean differences approximately 10%. In the IPTW-adjusted cohort, the 10-year local and metastatic disease occurrence rates were 3.2% vs. 1.4% (Gray's P=0.0001) and 28.6% vs. 10.1% (Gray's $P < 0.0001$) in patients with persistent vs. recurrent PSA, respectively. Similarly, the 10-year overall-mortality rates were 24.9% vs. 11.9% (Log-rank P=0.029), respectively. CONCLUSIONS: Patients with biochemical persistence after RP are approximately 2.5 times more likely to experience local/metastatic failure and death, compared to patients with biochemical recurrence after RP, despite equivalent sRT with/without antiandrogen therapy use. These data may facilitate patient counseling and shared treatment selection.

Urology
Turner KA, **Rambhatla A**, Schon S, Agarwal A, Krawetz SA, Dupree JM, and Avidor-Reiss T. Male infertility is a women's health issue—research and clinical evaluation of male infertility is needed. *Cells* 2020; 9(4). PMID: Not assigned. Request Article

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Infertility is a devastating experience for both partners as they try to conceive. Historically, when a couple could not conceive, the woman has carried the stigma of infertility; however, men and women are just as likely to contribute to the couple's infertility. With the development of assisted reproductive technology (ART), the treatment burden for male and unexplained infertility has fallen mainly on women. Equalizing this burden requires reviving research on male infertility to both improve treatment options and enable natural conception. Despite many scientific efforts, infertility in men due to sperm dysfunction is mainly diagnosed by a semen analysis. The semen analysis is limited as it only examines general sperm properties such as concentration, motility, and morphology. A diagnosis of male infertility rarely includes an assessment of internal sperm components such as DNA, which is well documented to have an impact on infertility, or other components such as RNA and centrioles, which are beginning to be adopted. Assessment of these components is not typically included in current diagnostic testing because available treatments are limited. Recent research has expanded our understanding of sperm biology and

suggests that these components may also contribute to the failure to achieve pregnancy. Understanding the sperm's internal components, and how they contribute to male infertility, would provide avenues for new therapies that are based on treating men directly for male infertility, which may enable less invasive treatments and even natural conception.

Urology
Yaguchi G, **Tang HJ**, **Deebajah M**, **Keeley J**, **Pantelic M**, **Williamson S**, **Gupta N**, **Peabody JO**, **Menon M**, **Dabaja A**, and Alanee S. The effect of multiplicity of PI-RADS 3 lesions on cancer detection rate of confirmatory targeted biopsy in patients diagnosed with prostate cancer and managed with active surveillance. *Urol Oncol* 2020; Epub ahead of print. PMID: 32265090. Full Text

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BACKGROUND AND OBJECTIVE: To determine the effect of multiplicity of prostate imaging reporting and data system assessment category 3 (PI-RADS 3) lesions on cancer detection rate (CDR) of confirmatory targeted biopsy of such lesion in patients diagnosed with prostate cancer and managed with active surveillance. METHODS: This study was conducted at a single academic institution. There were 91 men with >/= 1 PI-RADS 3 lesion detected through magnetic resonance imaging (MRI) after systematic prostate biopsy in the course of management of patients diagnosed with prostate cancer with active surveillance. We compared the CDRs based on targeted biopsy of PI-RADS 3 lesions that occurred (1) as solitary lesions, (2) as 1 of multiple PI-RADS 3 only lesions, or (3) with >/= 1 higher grade lesion. RESULTS: Median age was 65.0 years (interquartile range 59.5-70.0), median prostate specific antigen was 5.95 ng/ml (interquartile range 4.30-8.83), and median prostate specific antigen density was 0.161 ng/ml(2) (0.071-0.194). Forty-three men had solitary PI-RADS 3 lesions, 22 had multiple PI-RADS 3 only lesions, and 26 had multiple lesions with >/= 1 higher grade lesion. The overall CDR (Gleason score >/= 3+3) based on confirmatory MRI targeted biopsy in a given PI-RADS 3 lesion in each group was 23%, 45%, and 54%, respectively (P=0.0274). The CDRs for clinically significant disease (Gleason score >/= 3+4) were 16%, 32%, and 35%, respectively (P=0.1701). CONCLUSIONS: Coexisting lesions increase the CDR of confirmatory MRI targeted biopsy of PI-RADS 3 lesions in patients managed with active surveillance. Risk stratification algorithms for PI-RADS 3 lesion to guide biopsy and management decisions may consider including multiplicity of lesions.

Conference Abstracts

Cardiology/Cardiovascular Research
Alrayes H, **Radjef R**, and **Tita C**. Cardiogenic shock: A bittersweet diagnosis. *Journal of the American College of Cardiology* 2020; 75(11):2476.

Background Sweet's syndrome (SS), also known as febrile neutrophilic dermatosis, is a rare reactive phenomenon characterized by a pattern of clinical symptoms with physical and pathologic manifestations. We present a case of SS with cardiac, dermatologic, and neurologic manifestations. Case A 73-year-old female presented with slurred speech for several hours, along with preceding fevers and flu-like symptoms. Initial stroke and infectious workups were negative. A transthoracic echocardiogram (TTE) was unremarkable. Two days later, she became tachypneic with pulmonary edema on chest X-ray. A repeat TTE showed an EF of 30% with global hypokinesis. A left heart catheterization revealed no obstructive coronary artery disease. She was intubated and an Impella CP was placed with Dobutamine for concerns of cardiogenic shock. She remained febrile with altered mentation despite an unremarkable infectious workup. ESR and CRP were elevated to 45mm/hr and 19.2mg/dL, respectively. WBC was elevated to 13,400 with a 92% neutrophil predominance. Several days after admission, pink papules on the patient's lower extremities were discovered, biopsied, and revealed neutrophilic dermatitis with negative infectious stains. Decision-making This patient fulfilled two major criteria required for the diagnosis of SS, including the abrupt onset of painful erythematous nodules, and histopathologic evidence of dense neutrophilic infiltrate without evidence of leukocytoclastic vasculitis. She met two of the four minor criteria, including pyrexia and at least three abnormal laboratory values (elevated ESR > 20mm/hr, positive CRP, >8000 leukocytes, >70% neutrophils). Given the fulfillment of her criteria and lack of an alternative etiology behind her shock, the patient was started on 1mg/kg of prednisone daily. She had rapid improvement in her skin papules, mentation, and cardiogenic shock, with discontinuation of her Impella CP and Dobutamine within 24 hours. Repeat TTE showed an EF of 53%. Conclusion This case highlights SS as a rare cause of cardiogenic shock and encephalitis and illustrates the importance of maintaining a broad differential diagnosis when determining the etiology of cardiogenic shock.

Cardiology/Cardiovascular Research
Bernardo M, **Jafri S**, and **Ananthasubramaniam K**. Challenges in imaging complex pericardial effusions: Incremental value of multimodality imaging. *Journal of the American College of Cardiology* 2020; 75(11):3395.

Background Pericardial effusion can be a common finding, but loculated fluid collections may be missed and require more of a focused examination with complementary imaging studies. Case A 60 years old female with metastatic lung cancer was sent to the emergency room after chest CT completed by her oncologist showed a large (15 × 9 × 7 cm) ring-enhancing lesion causing mass effect to the heart and left lung. She denied complaints of chest pain, palpitations, dyspnea, or syncope. An echocardiogram was completed to further ascertain anatomic delineation and tissue characterization of this lesion. Decision-making In this case, chest CT provides advantages of better evaluating pericardial thickness, extracardiac anatomy and possible tissue content. On the other hand, echocardiography avoids radiation and contrast exposure, can be completed at bedside in critical patients, and shows dynamic information of intracardiac structures. Together, they helped to confirm diagnosis of a loculated pericardial effusion likely due to malignancy in this patient. Conclusion Multimodality imaging is integral for correct diagnosis and appropriate management of cardiovascular conditions, especially that of pericardial diseases. Initial imaging may fail to provide adequate information on anatomic origin of masses or fluid collection. Therefore, pericardial effusion especially loculated effusions, may be misconstrued as pericardial tumors or cysts, extracardiac complex masses, or loculated pleural effusions. [Figure presented]

Cardiology/Cardiovascular Research
Butera B, **Modi K**, **Cowger JA**, and **Russell C**. Eosinophilic myocarditis in a patient with biopsy proven systemic sarcoidosis who was referred for bradycardia. *Journal of the American College of Cardiology* 2020; 75(11):3098.

Background Eosinophilic myocarditis (EM) is an understudied and often missed diagnosis whose constellation of symptoms are frequently attributed to other morbidities. Case A 57-year-old woman with mediastinal lymphadenopathy (Figure 1A), uveitis, celiac lymph node biopsy in 2013 demonstrating noncaseating granulomas and a questionable prior diagnosis of hypereosinophilic syndrome presented to establish care for dizziness and bradycardia (Figure 1B). She had a stroke in 2004 with an echocardiographic diagnosis of left ventricular (LV) thrombus (Figure 1C-D) for which she was prescribed coumadin. She exhibited a pruritic maculopapular skin rash on several areas of her body (Figure 1E-F) and laboratory tests showed a history of peripheral eosinophilia. Decision-making There was concern for cardiac sarcoidosis or undiagnosed EM. A cardiac MRI demonstrated thickening of the LV apex (Figure G-H) with corresponding sub endocardial perfusion defect and late gadolinium enhancement, without LV thrombus. These findings were consistent with late stage myocardial fibrosis from EM. Reliance on the single imaging modality of echocardiogram resulted in past misdiagnosis of thrombus and delayed therapy of myocardial fibrosis in this patient. Conclusion This case highlights the need for awareness of EM and the importance of considering alternative or additional diagnoses in patients with complex past medical histories. An association of sarcoidosis and EM has not yet been reported in the literature. [Figure presented]

Cardiology/Cardiovascular Research
Fram G, **Hudson MP**, **McCord J**, **Moyer M**, **Jacobsen G**, and **Nowak RM**. Utility of gender-specific HS-troponin I cut-points for AMI diagnosis. *Journal of the American College of Cardiology* 2020; 75(11):64.

Background Circulating concentrations of high sensitivity cardiac troponin I (hs-cTnI) are higher in men than women during normal conditions and acute coronary syndromes. There is clinical uncertainty whether gender-specific vs. single gender-neutral hs-cTnI cut-off values more effectively diagnose acute myocardial infarction (AMI). Methods Emergency department patients with suspected coronary ischemia and no ST-segment elevation underwent clinical evaluation plus serial hs-cTnI testing (Abbott Architect, 99th percentile women 16 ng/L, men 34 ng/L) at baseline, 1 hour, and 3 hours. Final diagnosis of AMI was centrally adjudicated by 2 independent cardiologists using the Fourth Universal Definition of AMI, clinical information, and serial hs-cTnI results. We compared the diagnostic accuracy of a single, general hs-cTnI cut-point of >26.0 ng/L, versus gender-specific cut-points (>16.0 ng/l for females and >34.0 ng/l for males) to diagnose AMI. Results The study population included 569 patients (48% female) with an adjudicated AMI diagnosis in 42 patients (7.4%). A single, general hs-cTnI cut-off value demonstrated a sensitivity of 97.6%, specificity of 87.3%, positive predictive value (PPV) of 38.0%, and negative predictive value (NPV) of 99.8% for AMI diagnosis. Gender-specific cut-off values did not change AMI diagnosis in any male patients and identified 1 additional female AMI patient. Additionally, among females there were 17 more false positives (FP), and among males there were 9 less FPs. Gender-specific hs-cTnI criteria demonstrated a sensitivity of 100%, specificity of 85.8%, PPV 35.9%, and NPV 100% for AMI diagnosis. There was no significant difference in sensitivity, specificity, PPV, or NPV using the gender-specific versus the general cut-point values ($p = 1.000$, $p = 0.471$, $p = 0.748$, and $p = 1.000$ respectively). Conclusion Our study reveals no significant AMI diagnostic difference using a single, gender-neutral hs-cTnI cut-point versus separate gender-specific hs-cTnI criteria. Emergency Department and Cardiology providers may implement hs-cTnI testing algorithms with single, gender-neutral cut-off values to diagnose or exclude AMI.

Cardiology/Cardiovascular Research
Gorgis S, **Demertzis Z**, **Malette K**, **Fram G**, **Dobesh K**, **Keteyian S**, **Alaswad K**, **Basir M**, and **Brawner C**. Percutaneous coronary revascularization is associated with higher exercise capacity after myocardial infarction. *Journal of the American College of Cardiology* 2020; 75(11):220.

Background Cardiopulmonary exercise testing (CPET) is a valuable tool to assess exercise tolerance and prognosis in heart failure. Limited studies have evaluated its clinical utility in patients with myocardial infarction (MI). The purpose of this study was to evaluate exercise capacity in post-MI patients based on whether they received percutaneous coronary intervention (PCI) or were treated with medical therapy. Methods We retrospectively identified patients who completed a CPET within 1 year after an acute MI. A general linear mixed model was developed to compare peak oxygen uptake (VO2) between patients who did and did not receive PCI with adjustments for age, sex, ST-elevation MI (STEMI), and presence of chronic total occlusion (CTO). A sub-analysis was performed in patients with CTO. Results Between April 2002 and March 2019, 436 patients (age= 57±11 years; 65% male; 63% white; 40% STEMI; 30% CTO; 70% PCI) completed a CPET within 1 year post-MI. Among 175 patients who suffered a STEMI, 84% underwent PCI. Among 261 patients who suffered a non-STEMI, 61% underwent PCI. There was significant variability of PCI performed between sex, race, MI type, and age (P<0.05). As shown in the Table, PCI was associated with significantly higher adjusted peak VO2 among the entire cohort and the subgroup of patients with CTO (n=130). Conclusion Among patients who suffer an acute MI, PCI is associated with higher exercise capacity as determined by peak VO2. This effect was larger in patients who present with CTO. [Figure presented]

Cardiology/Cardiovascular Research
Gorgis S, **Dhillon D**, **Mishra K**, **Saleh A**, **Basir M**, and **Fuller B**. Aggressive acute coronary thrombosis in ulcerative colitis flare. *Journal of the American College of Cardiology* 2020; 75(11):3302.

Background Thromboembolic disease is a well-recognized complication of Ulcerative Colitis (UC), but coronary involvement is rare. Chest pain in UC flare should raise suspicion for acute coronary thrombosis. Case A 46 year old male with UC was admitted after 3 weeks of bloody diarrhea despite treatment with prednisone. He also reported severe refractory chest pain. ECG showed ST-segment elevation myocardial infarction in inferior/lateral leads. Emergent left heart catheterization (LHC) revealed a large thrombus in mid left anterior descending (LAD) artery with distal embolization. Aspiration thrombectomy was unsuccessful. A drug eluting stent (DES) was placed in mid-LAD. Intracoronary vasodilators improved distal coronary flow. The patient was continued on DAPT. Five days later, his chest pain recurred. Decision-making LHC showed acute in-stent thrombosis. Two DES were placed in overlapping fashion to proximal-mid LAD with PTCA on the diagonal. Persistent thrombus was treated with balloon inflations. The patient continued to be symptomatic, so an intra-aortic balloon bump (IABP) was placed. He was continued on DAPT. Hemodynamics and chest pain improved in next 2 days, and IABP was removed. Conclusion Acute coronary thrombosis in pro-inflammatory states are challenging to treat, since both the underlying condition and treatment of UC are pro-thrombotic. Close monitoring and consideration of mechanical support devices may improve coronary perfusion while controlling the underlying flare. [Figure presented]

Cardiology/Cardiovascular Research
Nowak RM, **Christenson RH**, **Jacobsen G**, **Apple F**, **McCord J**, **Limkakeng A**, **Singer A**, **Peacock WF**, and **DeFilippi CR**. High sensitivity troponin values rapidly rule-out myocardial infarction and allow for ed discharge in a higher risk patient population compared to contemporary practice. *Journal of the American College of Cardiology* 2020; 75(11):66.

Background The multicenter High Sensitivity Cardiac Troponin I (hs-cTnI) study (HIGH-US) reported a 1 hour hs-cTnI algorithm in the Emergency Department (ED) rule-out rate of 50.4% for AMI (negative predictive value 99.7%) and 30 day incidence of AMI/death of 0.2%. We sought to determine factors associated with ED discharge versus observation/inpatient placements in these patients. Methods 2113 consenting adults were enrolled from 2015-2016 in 29 medical centers with suspicion for AMI. Baseline and 1 hour plasma samples were analyzed using the Siemens Atellica hs-cTnI assay (overall 99th %ile 45.0 ng/L). AMI diagnosis was independently adjudicated using local contemporary troponin assays and 30 day clinical information. Clinical variables used to aid in disposition decision making were compared in AMI ruled out patients. Results 1020 (48.3%) individuals were ruled out in for AMI in 1 hour. Of these 584 (57.3%) were discharged home while 436 (42.7%) were placed in observation/inpatient beds. The latter group were older with more hypertension, diabetes, smoking, heart or renal failure, personal or family history of coronary artery disease, prior AMI or revascularization and other vascular diseases (Table). Conclusion ED physicians were less likely to discharge home patients ruled out for AMI if they had traditional risk factors for CAD. Compared to contemporary practice hs-cTnI use allows more patients with higher risk clinical profiles to be discharged home than based on traditional assessments. [Figure presented]

Cardiology/Cardiovascular Research
Patel A, **Grafton G**, **Tita C**, Hannawi B, **Selektor Y**, **Chamogeorgakis T**, **Apostolou D**, **Lanfear DE**, **Williams CT**, **Nemeh HW**, and **Cowger JA**. Survival and Predictors of Mortality in Patients Undergoing RVAD Explant in IMACS. *Journal of Heart and Lung Transplantation* 2020; 39(4):S25-S26.

Purpose: Survival in patients requiring RVAD support is known to be poor. However, outcomes in those undergoing subsequent RVAD explant and predictors of mortality remain unknown. Methods: Of 16482 patients in IMACS, 723 patients had an isolated RVAD (n=29) or BiVAD (n=694) in place. Using Kaplan Meier methods, survival was estimated for the LVAD-only cohort and within the subgroup of RVAD/BiVAD patients with and without RVAD explant. Correlates of mortality in the RVAD explant group were identified with Cox multivariable regression. Results: Within

the BiVAD group, 240 patients (33%) had an RVAD explant. Of these, 221 (92%) were performed for RV recovery, 17 (7.1%) for device malfunction and 2 (0.8%) were for other reasons. Survival at 1Y was 53±2.0% in the BiVAD group vs. 82±0.3% in LVAD-only patients (p<0.0001). Within the BiVAD group, patients undergoing RVAD explant had equivalent survival (1Y=54±2.5%) to those with ongoing BiVAD support (1Y=52±3.4%, p=0.54). BiVAD patients who died after RVAD explant were older, more likely to be BTT, and had higher preimplant creatinine (table). On multivariable analysis, older age, higher preimplant pulmonary systolic pressure, explant for RVAD dysfunction, and BTT indication predicted death after RVAD explant (table). Within the subgroup of BTT BiVAD (n=51) patients undergoing RVAD explant, survival was only 62% at 3 months. Conclusion: Patients undergoing RVAD explant, even for RV-recovery, have very poor survival. Patients who are transplant eligible with signs of RVAD dysfunction should be given urgent listing status. Rather than RVAD explant, BTT patients with signs of RV recovery may be better served with transplant.

Cardiology/Cardiovascular Research
Sabbah HN, **Gupta RC**, and **Singh-Gupta V**. Marked deterioration of mitochondrial function in failing cardiomyocytes exposed to hypoxic conditions. *Journal of the American College of Cardiology* 2020; 75(11):697.

Background Clinical presentation of acute heart failure (HF) defined as new-onset or worsening of chronic HF, includes symptoms or signs of congestion and volume overload. Understanding the underlying pathophysiological mechanisms related to congestion is essential for offering better treatment to these patients. Congestion can cause dyspnea as well as hypoxia often at the organ level. We and others have shown that under normoxic (NX) conditions, cardiac mitochondria (MITO) are dysfunctional in HF leading to energy deprivation and contributing to progressive LV dysfunction. This study tested the hypothesis that exposure of failing cardiomyocytes to hypoxia (HX) elicits further worsening of MITO function. Methods Cardiomyocytes were isolated from the LV free wall of 4 normal (NL) dogs and 7 dogs with HF produced by intracoronary microembolizations (LV ejection fraction <30%). A standard collagenase-based enzymatic process was used for isolation that yielded ~70% viable rod-shaped cardiomyocytes that excluded trypan blue. Equal aliquots of cardiomyocytes from NL and HF dogs were incubated for 1 hour at 37°C under NX conditions (room air) and under HX conditions (95% N2 +5% CO2). At the end of incubation, MITO ADP-stimulated state-3 respiration (ADPresp) was measured using a Strathklein respirometer and MITO maximum rate of ATP synthesis (ATPsyn) was measured using the bioluminescent ApoSENSOR assay kit. Results Under NX conditions, ADPresp and ATPsyn in HF cardiomyocytes were decreased to levels down to only 40% of NL cardiomyocytes (ADPresp: 167±10 vs. 470±38 nAtom Oxygen/min/mg protein, p<0.05; ATPsyn: 19±1 vs. 46±1 RFU/µg protein, p<0.05). Exposure of HF cardiomyocytes to HX elicited a further decrease of ADPresp and ATPsyn to levels down to only 20% of NL (ADPresp: 111±14 nAtom Oxygen/min/mg protein; ATPsyn: 10±5 RFU/µg protein). Conclusion Exposure of failing cardiomyocytes to HX conditions, even for short periods of time, can deliver a crippling insult to MITO function that can potentially lead to a critical state of cardiac energy deprivation with adverse consequences on LV function.

Cardiology/Cardiovascular Research
Sabbah HN, **Gupta RC**, **Singh-Gupta V**, **Zhang K**, and **Xu J**. Beta-3 adrenergic receptors are upregulated in left ventricular myocardium of dogs with chronic heart failure. *Journal of the American College of Cardiology* 2020; 75(11):696.

Background β-adrenergic receptors (ARs) belong to the superfamily of membrane proteins known as G-protein-coupled receptors. There are four subtypes of β-ARs-β1-AR, β2-AR, β3-AR and the β4-AR. The β1-AR is found primarily in the heart and comprises 75-80% of the β-ARs in the heart. The β2-ARs are also found in the heart and represent ~20% of total cardiac ARs. The β3-ARs are found minimally in the heart. The β4-AR is considered a low affinity state of the β1-AR, which awaits genetic and pharmacologic characterization. When stimulated, β1-ARs elicit a cAMP-dependent increase of contractility whereas stimulation of β2-ARs elicit cAMP-independent increase of contractility. In contrast, stimulation of the β3-ARs inhibits cardiac contraction. Heart Failure (HF) is associated with a near 50% reduction of β1-ARs and no change in the expression of β2-ARs. In this study, we examined mRNA and protein levels β3-ARs in LV myocardium of normal (NL) dogs and dogs with chronic HF (LV ejection fraction ≤35%). Methods Studies were performed in LV tissue obtained from 7 NL dogs and 7 dogs with HF produced by intracoronary microembolizations. mRNA expression of β3-ARs and GAPDH was measured in all dogs using real-time PCR. Protein level of β3-ARs and GAPDH was measured in SDS-extracts of LV tissue prepared from all dogs and subjected to Western blotting coupled with chemiluminescence detection and bands were quantified in densitometric units. Results There were no significant differences in levels of GAPDH mRNA and protein between NL dogs and HF dogs. mRNA expression of β3-ARs normalized to GAPDH was increased 3.1 fold in HF dogs compared to NL dogs. Protein levels of β3-ARs normalized to GAPDH were also markedly and significantly increased (~3.6 fold) in HF dogs compared to NL dogs 0.82 ± 0.05 vs. 0.23 ± 0.02, p<0.05). Conclusion β3-ARs expression and protein levels are markedly upregulated in LV myocardium of dogs with HF. This maladaptation, through its signaling pathway, likely contributes to the reduced LV function seen in HF. The results support recent observations of improved LV function in dogs with HF treated with β3-ARs blockers.

Cardiology/Cardiovascular Research
Swanson B, **Brooks K**, **Bajwa F**, **Fadel R**, and **Parikh S**. Novel echocardiographic assessment of right ventricular function utilizing dynamic base to apex fractional shortening. *Journal of the American College of Cardiology* 2020; 75(11):1689.

Background The right ventricle (RV) has a unique geometry and mechanical function that make it hard to evaluate by transthoracic echocardiography (TTE). Tricuspid annular plane systolic excursion (TAPSE) is commonly utilized for RV function assessment but is limited since it evaluates the RV base independent of the motion of the rest of the heart. We evaluated a novel measurement of RV base to apex fractional shortening (BAFS) between systole and diastole, which accounts for global cardiac motion, to see if it could accurately assess RV function. Methods We screened patients with cardiac MRI (CMR) between 06/2018 to 07/2019 in our system for presence of TTE within 1 month of CMR and chose 120 to evaluate. We excluded any studies without TAPSE, apical 4 chamber view or with incomplete CMR data. We reviewed studies and calculated RV BAFS by measuring distance from RV base to RV apex in diastole and systole and calculating relative change. We documented recorded TAPSE from TTE and RV Ejection Fraction (RVEF) from CMR. We then compared RV BAFS values from studies with RVEF >55% to those with RVEF <45%. Results Of the 120 TTEs and CMRs reviewed, 89 were included for interpretation. When comparing studies with RVEF <45% to those with RVEF >55%, the average RV BAFS was 15% vs. 24% (P<0.005). This correlated with TAPSE, which had average values of 1.7 vs 2.1 (cm) respectively. Utilizing a specific cut off for RV BAFS of <18% was associated with a 76% specificity and 69% sensitivity for predicting RVEF <45%. We found RV BAFS to be easily obtainable across multiple investigators with good reproducibility. Conclusion The RV continues to be a difficult chamber to evaluate by TTE. Other potential parameters, such as TAPSE, Fractional area change and 3D echocardiography are all limited by requiring adequate image acquisition that cannot be obtained on every patient. A new metric that is reliably obtainable could greatly aid in day to day evaluation of RV function. This study demonstrates that RV BAFS has excellent correlation with RV assesment by CMR, has the potential to be a specific marker of RV dysfunction and can be easily performed on standard TTE images available to all echocardiography labs.

Cardiology/Cardiovascular Research

Swanson B, **Salgia R**, **El-Bashir J**, and **Parikh S**. Accuracy of agitated saline contrast echocardiography for assessment of intracardiac shunting in preoperative liver transplant patients. *Journal of the American College of Cardiology* 2020; 75(11):1600.

Background Patent Foramen Ovale (PFO) is a common clinical condition that is found in up to 20% of adults. Transthoracic Echocardiography (TTE) with agitated saline contrast imaging (ASCi) has become the screening test of choice for PFO with reported sensitivity of 99% and specificity of 85%. Exclusion of significant atrial level shunt is important prior to liver transplant but patients with end stage liver disease (ESLD) can be difficult to evaluate with ASCi given a high prevalence of intra-pulmonary shunting. We sought to evaluate if ASCi can accurately predict presence of atrial level shunting in patients with ESLD prior to transplant. Methods We performed a retrospective chart review of patients in our health system who underwent liver transplant between January 2016 and March of 2019. We screened for TTE with ASCi that was positive for presence of left sided microbubbles who also had a transesophageal echocardiogram (TEE). TTEs were reviewed and categorized as large if there were more than 20 left sided bubbles and early if they appeared within 5 cardiac cycles following opacification of right atrium. TEEs were then reviewed for presence of a PFO or atrial septal defect. Results Of the initial 317 patients that were screened, 124 had TTEs with ASCi performed of which, 51 (41%) were positive for shunt with rest or provocation. Of those, 25 (49%) had an adequate TEE performed in our system, of which 5 (20%) were found to have a PFO. Early vs. late positivity was not significantly associated with presence of PFO (19%vs 22% [p=0.84]) and of patients with early and large positive studies only 23% (3 of 13) had a PFO. Conclusion Our finding of only 20% of positive ASCi studies being associated with PFO is substantially lower than reported in prior literature. Furthermore, there does not seem to be any significant benefit utilizing early positivity or size of shunt to differentiate between PFO and intra-pulmonary shunting in ESLD patients. High prevalence of concomitant hepatopulmonary syndrome as well as high-flow states renders traditional measures of shunt localization and categorization inaccurate. These findings suggest that ASCi lacks adequate positive predictive value to assess for PFO in patients with ESLD.

Emergency Medicine

Fram G, **Hudson MP**, **McCord J**, **Moyer M**, **Jacobsen G**, and **Nowak RM**. Utility of gender-specific HS-troponin I cut-points for AMI diagnosis. *Journal of the American College of Cardiology* 2020; 75(11):64.

Background Circulating concentrations of high sensitivity cardiac troponin I (hs-cTnI) are higher in men than women during normal conditions and acute coronary syndromes. There is clinical uncertainty whether gender-specific vs. single gender-neutral hs-cTnI cut-off values more effectively diagnose acute myocardial infarction (AMI). Methods Emergency department patients with suspected coronary ischemia and no ST-segment elevation underwent clinical evaluation plus serial hs-cTnI testing (Abbott Architect, 99th percentile women 16 ng/L, men 34 ng/L) at baseline, 1 hour, and 3 hours. Final diagnosis of AMI was centrally adjudicated by 2 independent cardiologists using the Fourth Universal Definition of AMI, clinical information, and serial hs-cTnI results. We compared the diagnostic accuracy of a single, general hs-cTnI cut-point of >26.0 ng/L, versus gender-specific cut-points (>16.0 ng/l for females and >34.0 ng/l for males) to diagnose AMI. Results The study population included 569 patients (48% female) with an adjudicated AMI diagnosis in 42 patients (7.4%). A single, general hs-cTnI cut-off value demonstrated a sensitivity of 97.6%, specificity of 87.3%, positive predictive value (PPV) of 38.0%, and negative predictive value (NPV) of 99.8% for AMI diagnosis. Gender-specific cut-off values did not change AMI diagnosis in any male patients and identified 1 additional female AMI patient. Additionally, among females there were 17 more false positives (FP), and among males there were 9 less FPs. Gender-specific hs-cTnI criteria demonstrated a sensitivity of 100%, specificity of

85.8%, PPV 35.9%, and NPV 100% for AMI diagnosis. There was no significant difference in sensitivity, specificity, PPV, or NPV using the gender-specific versus the general cut-point values (p = 1.000, p = 0.471, p = 0.748, and p = 1.000 respectively). Conclusion Our study reveals no significant AMI diagnostic difference using a single, gender-neutral hs-cTnI cut-point versus separate gender-specific hs-cTnI criteria. Emergency Department and Cardiology providers may implement hs-cTnI testing algorithms with single, gender-neutral cut-off values to diagnose or exclude AMI.

Emergency Medicine
Nowak RM, **Christenson RH**, **Jacobsen G**, **Apple F**, **McCord J**, **Limkakeng A**, **Singer A**, **Peacock WF**, and **DeFilippi CR**. High sensitivity troponin values rapidly rule-out myocardial infarction and allow for ed discharge in a higher risk patient population compared to contemporary practice. *Journal of the American College of Cardiology* 2020; 75(11):66.

Background The multicenter High Sensitivity Cardiac Troponin I (hs-cTnI) study (HIGH-US) reported a 1 hour hs-cTnI algorithm in the Emergency Department (ED) rule-out rate of 50.4% for AMI (negative predictive value 99.7%) and 30 day incidence of AMI/death of 0.2%. We sought to determine factors associated with ED discharge versus observation/inpatient placements in these patients. Methods 2113 consenting adults were enrolled from 2015-2016 in 29 medical centers with suspicion for AMI. Baseline and 1 hour plasma samples were analyzed using the Siemens Atellica hs-cTnI assay (overall 99th %ile 45.0 ng/L). AMI diagnosis was independently adjudicated using local contemporary troponin assays and 30 day clinical information. Clinical variables used to aid in disposition decision making were compared in AMI ruled out patients. Results 1020 (48.3%) individuals were ruled out in for AMI in 1 hour. Of these 584 (57.3%) were discharged home while 436 (42.7%) were placed in observation/inpatient beds. The latter group were older with more hypertension, diabetes, smoking, heart or renal failure, personal or family history of coronary artery disease, prior AMI or revascularization and other vascular diseases (Table). Conclusion ED physicians were less likely to discharge home patients ruled out for AMI if they had traditional risk factors for CAD. Compared to contemporary practice hs-cTnI use allows more patients with higher risk clinical profiles to be discharged home than based on traditional assessments. [Figure presented]

Gastroenterology
Konel J, **Kitajima T**, Arevalo L, Murray N, **Pietrowsky T**, **Venkat D**, **Gonzalez H**, **Samaniego M**, **Abouljoud M**, and **Nagai S**. Assessment of sarcopenia and obesity by bioelectrical impedance analysis in transplant and hepatobiliary populations. *American Journal of Transplantation* 2020; 20:56.

J. Konel, Wayne State University, School of Medicine, Detroit, MI, United States

Bioelectrical impedance analysis (BIA) can measure body composition, including assessment of sarcopenia and obesity. This study aimed to evaluate the clinical utility of BIA in transplant and hepatobiliary populations. Methods: We conducted a single-center study of 60 patients (5 living donor candidates, 10 early postoperative, 7 benign liver disease, 14 chronic kidney disease, 5 early cirrhosis, 7 post-transplant, 6 early malignancy, and 6 advanced malignancy). Sarcopenia was defned as a calculated whole-body muscle mass (kg)/body surface area below the 25th percentile. Obesity was defned as fat percentage of >25% and >30% in males and females, respectively. Patients were categorized into 4 groups: (1) not sarcopenic/not obese, (2) sarcopenic/not obese, (3) not sarcopenic/obese, and (4) sarcopenic/obese. Clinical characteristics and BIA measurements were compared. Results: Among the 60 participants, 28 were not sarcopenic/not obese, 1 was sarcopenic/not obese, 17 were not sarcopenic/obese, and 14 were sarcopenic/obese. There were no signifcant diferences in BMI, albumin, total protein, and absolute lymphocyte count. Sarcopenic/obese patients showed signifcantly lower Karnofsky score (median 55% [IQR, 50-82.5%]), compared to not sarcopenic/obese patients (median 80% [IQR, 60-92.5%], p = 0.037). All advanced malignancy patients were either sarcopenic/not obese or sarcopenic/obese. Conclusion: Sarcopenic-obesity patients showed signifcantly lower performance status than obese patients without sarcopenia. BIA may be useful tool in identifying high-risk patients and improving surgical outcomes.

Gastroenterology
Long CW, Yi-Hsiang H, Young-Suk L, Edward JG, Hoon AS, Owen TTY, Jeong H, Josun HA, Magdy E, Chi-Yi C, Wei-Wen S, John F, Anuj G, Leland YJ, Shalini S, Belinda J, Shuyuan M, **Syed-Mohammed J**, and Harry LAJ. Efficacy and safety of switching to tenofovir alafenamide (TAF) in virally-suppressed chronic hepatitis B patients (CHB) with renal impairment: Week 24 results. *Hepatology International* 2020; 14:S35.

C.W. Long, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan

Introduction: TAF, a tenofovir prodrug, has demonstrated noninferior efficacy to TDF with superior bone and renal safety in virallysuppressed CHB patients with eGFR (by Cockcroft-Gault; eGFRCG) ≥50 mL/min when switched from TDF. Objectives: To evaluate the efficacy and safety of switching to TAF in virally suppressed, renally-impaired, CHB patients. Methods: In this Phase 2 study, renally-impaired CHB patients taking TDF and/or other oral antivirals for ≥48 weeks and virally suppressed for ≥6 months with HBV DNA<20 IU/mL at screening were enrolled into 2 cohorts: (1) moderate-severe renal impairment (eGFRCG 15-<60 mL/min; N = 78) and (2) End Stage Renal Disease (eGFRCG<15 mL/min; N = 15) patients on chronic

hemodialysis . All patients were switched to TAF 25 mg QD for 96 weeks. Co-primary endpoints were proportion with HBV DNA<20 IU/mL and adverse events (AEs)/lab abnormalities at Week 24. Secondary safety endpoints included changes in hip/ and spine bone mineral density (BMD), and in eGFRCG. Results: All patients on treatment at Week 24 maintained HBV DNA<20 IU/mL and 88% had normal ALT levels. Relative to baseline levels, switching to TAF from TDF resulted in increases in hip/spine BMD, decreases in bone turnover markers, as well as increases in eGFRCG and decreases in renal tubular markers. TAF was well tolerated with few having Grade 3 or 4 AEs. Conclusions: In renally-impaired CHB patients, including ESRD patients on hemodialysis, viral suppression was well-maintained, and the bone and renal safety were improved 24 weeks after switching from TDF to TAF.

Gastroenterology

Swanson B, **Salgia R**, **El-Bashir J**, and **Parikh S**. Accuracy of agitated saline contrast echocardiography for assessment of intracardiac shunting in preoperative liver transplant patients. *Journal of the American College of Cardiology* 2020; 75(11):1600.

Background Patent Foramen Ovale (PFO) is a common clinical condition that is found in up to 20% of adults. Transthoracic Echocardiography (TTE) with agitated saline contrast imaging (ASCi) has become the screening test of choice for PFO with reported sensitivity of 99% and specificity of 85%. Exclusion of significant atrial level shunt is important prior to liver transplant but patients with end stage liver disease (ESLD) can be difficult to evaluate with ASCi given a high prevalence of intra-pulmonary shunting. We sought to evaluate if ASCi can accurately predict presence of atrial level shunting in patients with ESLD prior to transplant. Methods We performed a retrospective chart review of patients in our health system who underwent liver transplant between January 2016 and March of 2019. We screened for TTE with ASCi that was positive for presence of left sided microbubbles who also had a transesophageal echocardiogram (TEE). TTEs were reviewed and categorized as large if there were more than 20 left sided bubbles and early if they appeared within 5 cardiac cycles following opacification of right atrium. TEEs were then reviewed for presence of a PFO or atrial septal defect. Results Of the initial 317 patients that were screened, 124 had TTEs with ASCi performed of which, 51 (41%) were positive for shunt with rest or provocation. Of those, 25 (49%) had an adequate TEE performed in our system, of which 5 (20%) were found to have a PFO. Early vs. late positivity was not significantly associated with presence of PFO (19%vs 22% [p=0.84]) and of patients with early and large positive studies only 23% (3 of 13) had a PFO. Conclusion Our finding of only 20% of positive ASCi studies being associated with PFO is substantially lower than reported in prior literature. Furthermore, there does not seem to be any significant benefit utilizing early positivity or size of shunt to differentiate between PFO and intra-pulmonary shunting in ESLD patients. High prevalence of concomitant hepatopulmonary syndrome as well as high-flow states renders traditional measures of shunt localization and categorization inaccurate. These findings suggest that ASCi lacks adequate positive predictive value to assess for PFO in patients with ESLD.

Graduate Medical Education

Bernardo M, **Jafri S**, and **Ananthasubramaniam K**. Challenges in imaging complex pericardial effusions: Incremental value of multimodality imaging. *Journal of the American College of Cardiology* 2020; 75(11):3395.

Background Pericardial effusion can be a common finding, but loculated fluid collections may be missed and require more of a focused examination with complementary imaging studies. Case A 60 years old female with metastatic lung cancer was sent to the emergency room after chest CT completed by her oncologist showed a large (15 × 9 × 7 cm) ring-enhancing lesion causing mass effect to the heart and left lung. She denied complaints of chest pain, palpitations, dyspnea, or syncope. An echocardiogram was completed to further ascertain anatomic delineation and tissue characterization of this lesion. Decision-making In this case, chest CT provides advantages of better evaluating pericardial thickness, extracardiac anatomy and possible tissue content. On the other hand, echocardiography avoids radiation and contrast exposure, can be completed at bedside in critical patients, and shows dynamic information of intracardiac structures. Together, they helped to confirm diagnosis of a loculated pericardial effusion likely due to malignancy in this patient. Conclusion Multimodality imaging is integral for correct diagnosis and appropriate management of cardiovascular conditions, especially that of pericardial diseases. Initial imaging may fail to provide adequate information on anatomic origin of masses or fluid collection. Therefore, pericardial effusion especially loculated effusions, may be misconstrued as pericardial tumors or cysts, extracardiac complex masses, or loculated pleural effusions. [Figure presented]

Internal Medicine

Alrayes H, **Radjef R**, and **Tita C**. Cardiogenic shock: A bittersweet diagnosis. *Journal of the American College of Cardiology* 2020; 75(11):2476.

Background Sweet's syndrome (SS), also known as febrile neutrophilic dermatosis, is a rare reactive phenomenon characterized by a pattern of clinical symptoms with physical and pathologic manifestations. We present a case of SS with cardiac, dermatologic, and neurologic manifestations. Case A 73-year-old female presented with slurred speech for several hours, along with preceding fevers and flu-like symptoms. Initial stroke and infectious workups were negative. A transthoracic echocardiogram (TTE) was unremarkable. Two days later, she became tachypneic with pulmonary edema on chest X-ray. A repeat TTE showed an EF of 30% with global hypokinesis. A left heart catheterization revealed no obstructive coronary artery

disease. She was intubated and an Impella CP was placed with Dobutamine for concerns of cardiogenic shock. She remained febrile with altered mentation despite an unremarkable infectious workup. ESR and CRP were elevated to 45mm/hr and 19.2mg/dL, respectively. WBC was elevated to 13,400 with a 92% neutrophil predominance. Several days after admission, pink papules on the patient's lower extremities were discovered, biopsied, and revealed neutrophilic dermatitis with negative infectious stains. Decision-making This patient fulfilled two major criteria required for the diagnosis of SS, including the abrupt onset of painful erythematous nodules, and histopathologic evidence of dense neutrophilic infiltrate without evidence of leukocytoclastic vasculitis. She met two of the four minor criteria, including pyrexia and at least three abnormal laboratory values (elevated ESR > 20mm/hr, positive CRP, >8000 leukocytes, >70% neutrophils). Given the fulfillment of her criteria and lack of an alternative etiology behind her shock, the patient was started on 1mg/kg of prednisone daily. She had rapid improvement in her skin papules, mentation, and cardiogenic shock, with discontinuation of her Impella CP and Dobutamine within 24 hours. Repeat TTE showed an EF of 53%. Conclusion This case highlights SS as a rare cause of cardiogenic shock and encephalitis and illustrates the importance of maintaining a broad differential diagnosis when determining the etiology of cardiogenic shock.

Internal Medicine
Butera B, **Modi K**, **Cowger JA**, and **Russell C**. Eosinophilic myocarditis in a patient with biopsy proven systemic sarcoidosis who was referred for bradycardia. *Journal of the American College of Cardiology* 2020; 75(11):3098.

Background Eosinophilic myocarditis (EM) is an understudied and often missed diagnosis whose constellation of symptoms are frequently attributed to other morbidities. Case A 57-year-old woman with mediastinal lymphadenopathy (Figure 1A), uveitis, celiac lymph node biopsy in 2013 demonstrating noncaseating granulomas and a questionable prior diagnosis of hypereosinophilic syndrome presented to establish care for dizziness and bradycardia (Figure 1B). She had a stroke in 2004 with an echocardiographic diagnosis of left ventricular (LV) thrombus (Figure 1C-D) for which she was prescribed coumadin. She exhibited a pruritic maculopapular skin rash on several areas of her body (Figure 1E-F) and laboratory tests showed a history of peripheral eosinophilia. Decision-making There was concern for cardiac sarcoidosis or undiagnosed EM. A cardiac MRI demonstrated thickening of the LV apex (Figure G-H) with corresponding sub endocardial perfusion defect and late gadolinium enhancement, without LV thrombus. These findings were consistent with late stage myocardial fibrosis from EM. Reliance on the single imaging modality of echocardiogram resulted in past misdiagnosis of thrombus and delayed therapy of myocardial fibrosis in this patient. Conclusion This case highlights the need for awareness of EM and the importance of considering alternative or additional diagnoses in patients with complex past medical histories. An association of sarcoidosis and EM has not yet been reported in the literature. [Figure presented]

Internal Medicine
Fram G, **Hudson MP**, **McCord J**, **Moyer M**, **Jacobsen G**, and **Nowak RM**. Utility of gender-specific HS-troponin I cut-points for AMI diagnosis. *Journal of the American College of Cardiology* 2020; 75(11):64.

Background Circulating concentrations of high sensitivity cardiac troponin I (hs-cTnI) are higher in men than women during normal conditions and acute coronary syndromes. There is clinical uncertainty whether gender-specific vs. single gender-neutral hs-cTnI cut-off values more effectively diagnose acute myocardial infarction (AMI). Methods Emergency department patients with suspected coronary ischemia and no ST-segment elevation underwent clinical evaluation plus serial hs-cTnI testing (Abbott Architect, 99th percentile women 16 ng/L, men 34 ng/L) at baseline, 1 hour, and 3 hours. Final diagnosis of AMI was centrally adjudicated by 2 independent cardiologists using the Fourth Universal Definition of AMI, clinical information, and serial hs-cTnI results. We compared the diagnostic accuracy of a single, general hs-cTnI cut-point of >26.0 ng/L, versus gender-specific cut-points (>16.0 ng/l for females and >34.0 ng/l for males) to diagnose AMI. Results The study population included 569 patients (48% female) with an adjudicated AMI diagnosis in 42 patients (7.4%). A single, general hs-cTnI cut-off value demonstrated a sensitivity of 97.6%, specificity of 87.3%, positive predictive value (PPV) of 38.0%, and negative predictive value (NPV) of 99.8% for AMI diagnosis. Gender-specific cut-off values did not change AMI diagnosis in any male patients and identified 1 additional female AMI patient. Additionally, among females there were 17 more false positives (FP), and among males there were 9 less FPs. Gender-specific hs-cTnI criteria demonstrated a sensitivity of 100%, specificity of 85.8%, PPV 35.9%, and NPV 100% for AMI diagnosis. There was no significant difference in sensitivity, specificity, PPV, or NPV using the gender-specific versus the general cut-point values ($p = 1.000$, $p = 0.471$, $p = 0.748$, and $p = 1.000$ respectively). Conclusion Our study reveals no significant AMI diagnostic difference using a single, gender-neutral hs-cTnI cut-point versus separate gender-specific hs-cTnI criteria. Emergency Department and Cardiology providers may implement hs-cTnI testing algorithms with single, gender-neutral cut-off values to diagnose or exclude AMI.

Internal Medicine
Gorgis S, **Demertzis Z**, **Malette K**, **Fram G**, **Dobesh K**, **Keteyian S**, **Alaswad K**, **Basir M**, and **Brawner C**. Percutaneous coronary revascularization is associated with higher exercise capacity after myocardial infarction. *Journal of the American College of Cardiology* 2020; 75(11):220.

Background Cardiopulmonary exercise testing (CPET) is a valuable tool to assess exercise tolerance and prognosis in heart failure. Limited studies have evaluated its clinical utility in patients with myocardial infarction (MI). The purpose of this study

was to evaluate exercise capacity in post-MI patients based on whether they received percutaneous coronary intervention (PCI) or were treated with medical therapy. Methods We retrospectively identified patients who completed a CPET within 1 year after an acute MI. A general linear mixed model was developed to compare peak oxygen uptake (VO2) between patients who did and did not receive PCI with adjustments for age, sex, ST-elevation MI (STEMI), and presence of chronic total occlusion (CTO). A sub-analysis was performed in patients with CTO. Results Between April 2002 and March 2019, 436 patients (age= 57±11 years; 65% male; 63% white; 40% STEMI; 30% CTO; 70% PCI) completed a CPET within 1 year post-MI. Among 175 patients who suffered a STEMI, 84% underwent PCI. Among 261 patients who suffered a non-STEMI, 61% underwent PCI. There was significant variability of PCI performed between sex, race, MI type, and age (P<0.05). As shown in the Table, PCI was associated with significantly higher adjusted peak VO2 among the entire cohort and the subgroup of patients with CTO (n=130). Conclusion Among patients who suffer an acute MI, PCI is associated with higher exercise capacity as determined by peak VO2. This effect was larger in patients who present with CTO. [Figure presented]

Internal Medicine
Gorgis S, **Dhillon D**, **Mishra K**, **Saleh A**, **Basir M**, and **Fuller B**. Aggressive acute coronary thrombosis in ulcerative colitis flare. *Journal of the American College of Cardiology* 2020; 75(11):3302.

Background Thromboembolic disease is a well-recognized complication of Ulcerative Colitis (UC), but coronary involvement is rare. Chest pain in UC flare should raise suspicion for acute coronary thrombosis. Case A 46 year old male with UC was admitted after 3 weeks of bloody diarrhea despite treatment with prednisone. He also reported severe refractory chest pain. ECG showed ST-segment elevation myocardial infarction in inferior/lateral leads. Emergent left heart catheterization (LHC) revealed a large thrombus in mid left anterior descending (LAD) artery with distal embolization. Aspiration thrombectomy was unsuccessful. A drug eluting stent (DES) was placed in mid-LAD. Intracoronary vasodilators improved distal coronary flow. The patient was continued on DAPT. Five days later, his chest pain recurred. Decision-making LHC showed acute in-stent thrombosis. Two DES were placed in overlapping fashion to proximal-mid LAD with PTCA on the diagonal. Persistent thrombus was treated with balloon inflations. The patient continued to be symptomatic, so an intra-aortic balloon bump (IABP) was placed. He was continued on DAPT. Hemodynamics and chest pain improved in next 2 days, and IABP was removed. Conclusion Acute coronary thrombosis in pro-inflammatory states are challenging to treat, since both the underlying condition and treatment of UC are pro-thrombotic. Close monitoring and consideration of mechanical support devices may improve coronary perfusion while controlling the underlying flare. [Figure presented]

Internal Medicine
Khan BSA, **Reddy S**, **Zakhour S**, **Sallam O**, and **Shaban H**. Clostridium difficile peritonitis in PD: Transmural migration or intestinal perforation? *American Journal of Kidney Diseases* 2020; 75(4):595-596.

Diuretics are an important component of guideline-directed treatment of resistant hypertension. However, the ideal diuretic regimen has not been defined. We hypothesize that the BP response to a diuretic is dependent on the type of diuretic used. In this study, we aim to identify any differences in BP response between the most commonly prescribed diuretics: hydrochlorothiazide (HCTZ), chlorthalidone, spironolactone and loop diuretics. Data from clinic visits of adults referred to the Hypertension Specialty Clinic at the University of Alabama at Birmingham were analyzed. Fellows trained to follow the American Heart Association guidelines measured each office BP. Anti-hypertensive medications with dosing were captured at each clinic visit. The association between office BP and type of diuretic used was assessed using a mixed linear model, which accounted for multiple clinic visits per patient and allowed for covariate adjustment. The study population consisted of 386 patients with 1043 visits; 156 out of 386 (40%) patients were Black and 227 out of 386 (59%) were women. A typical patient was 61 years old and obese (median BMI 31 kg/m^2) with an initial BP of 154/83 mm Hg (mean) while taking 4 (median) classes of antihypertensive medications. Over the course of a median of 3 visits, the office BP dropped by 15.3 ± 25 mm Hg (mean ± std). After adjusting for age, sex, class of antihypertensive medication, and race, diuretic use and ACEi/ARB use were independently associated with office systolic BP (F value 11.6, p 0.0007 and F value 12.4, p 0.0005, respectively). When diuretics were further subcategorized as chlorthalidone, hydrochlorothiazide, loop diuretic, and spironolactone, only chlorthalidone and spironolactone were associated with office systolic BP (F value 27.5, $p < 0.0001$ and F value 8.9, $p < 0.0029$, respectively). In the adjusted model, an increase in chlorthalidone dose by 12.5mg is associated with a 4.13 mm Hg reduction in office systolic BP. In our hypertension specialty clinic, diuretic use was associated with BP reduction in the treatment of resistant hypertension. After covariate adjustment in a mixed linear model, chlorthalidone was identified as the principal diuretic responsible for blood pressure reduction. Loop diuretics and HCTZ were not associated with BP reductions.

Nephrology
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Nephrology

Srour K, **Khan BSA**, and **Novak J**. Starvation ketoacidosis in patient with muscular dystrophy. *American Journal of Kidney Diseases* 2020; 75(4):640-640.

Few treatment options are avaiable to delay renal replacement therapy for young patients with Type 2 Diabetes and eGFRs approaching End Stage Renal Disease. We describe an ongoing Phase II trial utilizing Neo-Kidney AugmentTM percutaneously injected into kidneys with Pre-Stage 5 T2DM CKD with intent to delay renal replacement therapy. REGEN-003 is a multi-center, non-randomized prospective, openlabel, single-arm study recruiting 10 patients (NCT03270956). Inclusion criteria include T2DM subjects age 30-65 years, eGFR 14 - 20 mL/min/1.73m3, and managed hypertension and HbA1c. Primary objective is safety of NKA injected in one recipient kidney and procedure and/or product related adverse events through 24 months. The method of renal NKA delivery is by real-time image guided percutaneous targeted injection into the subject's kidney with small caliber atraumatic needles in an outpatient setting with moderate sedation. NKA is composed of expanded autologous homologous selected renal cells obtained by kidney biopsy. Trial completion is expected early 2020. Of 6 enrolled subjects to date, mean age is 55.8 years, 66.7% female, 50% Non-Hispanic/Latino. Baseline eGFR, serum creatinine and ACR are shown below. All 6 subjects have undergone renal biopsy, 4 have received injections. There have been no cell product or injection related adverse events to date. 1 subject developed a post biopsy hematoma however successfully underwent NKA injection. Biomarkers measured Baseline values (S.D.) Number eGFR (mean) 22.27 mL/min (7.99) 5 sCreatinine (mean) 3.14 (0.47) 5 ACR (geometric mean) 1391.0 mg/g (911.1) 3 This active Phase 2 trial of pre-stage 5 DKD using novel imaged guided percutaneous targeted autologous homologous cell injection into the kidney offers potential for preservation of renal function and delay of renal replacement therapy.

Nephrology

Srour K, **Lakshmikanth J**, **Chitturi C**, and **Faber M**. C3 glomerulonephritis; a rare complication of cll. *American Journal of Kidney Diseases* 2020; 75(4):640-640.

Kidney disease develops in chronic lymphocytic leukemia (CLL) patients via multiple mechanisms including infiltration, obstruction, tumor lysis syndrome, and glomerular disease. We present a rare case of C3 glomerulonephritis (C3GN) associated with pulmonary renal syndrome that we believe was an autoimmune manifestation of CLL. A 76-year-old male with a 15-year history of SLL/CLL, DVT, HTN, DM and Stage 3 CKD developed SOB and dry cough. At ED presentation he was in respiratory distress with BIPAP-resistant hypoxia requiring intubation. Labs included Cr 7.1 mg/dL, K 5.7 mEq/L and uric acid 12.2 mg/dL CXR showed vascular congestion. Prior to developing anuria urine sediment showed RBC casts. Bronchoscopy DAH, consistent with a pulmonary renal syndrome. Patient was started on plasmapheresis, high-dose steroids and CRRT. Autoimmune workup including ANA, anti-GBM and ANCA was negative. Kidney biopsy showed diffuse proliferative and sclerosing glomerulonephritis with lymphocytic infiltrates consistent with involvement by patient's known CD5+, CD23+ B-cell lymphoproliferative disorder. IF showed diffuse C3 staining. Steroids and plasmapheresis were continued. Renal function improved and dialysis discontinued, with Cr at last follow up 1.9. Chemotherapy for CLL has been ordered. We present a case of C3GN and DAH secondary to CLL autoimmune etiology, a rare complication of CLL which usually affects the kidney by infiltration and by toxicity of the CLL treatment. Due to the rarity of the disease, there is no standard of care treatment but this patient initially responded well to steroids and plasmapheresis. Recent case reports suggest improved outcomes of CLL-associated C3GN when CLL is treated. CLL is a rare cause of C3GN. A

high suspicion of the disease and early intervention with immunosuppression is the key in treating such condition. Chemotherapy for CLL is expected to improve the patient's long-term renal outcome.

Nephrology
Zasuwa G, **Frinak S**, **Uduman J**, and **Yee J**. Automated alert of sustained low-efficiency dialysis (sled) machines. *American Journal of Kidney Diseases* 2020; 75(4):661-661.

SLED machines are used to treat critically ill patients with kidney failure for prolong intervals. Technicians surveil machines every 2 hours. If alarms occur during therapy, nursing staff mute the alarm and notify dedicated technicians. However, alarms may be ignored, thereby permitting machines to remain in "error" mode for hours, potentially compromising patient care. Targeted alarm-based surveillance of SLED machines would optimize therapy. In 2017, SLED machines were linked by WIFI to the hospital private phone network (ASCOM) to develop an automated alarm system. When an alarm occurred, the machine computer sent an email to a dedicated Outlook SLED email account for subsequent transmission to ASCOM MailGate. This system next created an "alarm" text message on ASCOM phones provided by technicians. Response times to machine alamrs by technicians decreased significantly after system implementation. No additional training was feasible with WIFI- and ASCOM-based architectures.

Nephrology
Zasuwa G, **Frinak S**, and **Yee J**. Improving detection of symptomatic, asymptomatic intradialytic hypotension (AIDH), during hemodialysis (HD) with guided automated blood pressure (BP). *American Journal of Kidney Diseases* 2020; 75(4):661-661.

IDH is an HD complication associated with patient morbidity and mortality. IDH detection eneables early intervention that may reduce complications. We explored the hypothesis that the continuous intra-access pressure (IAP) measurements using the Vas-Alert algorithm (VA) can detect IDH during HD and initiate a blood pressure (BP) measurement. Undetected A/IDH was defined as a systolic BP (SBP) decline of 40 mmHg from the predialysis SBP and an intradialytic SBP <100 mmHg. Fresenius T2 dialysis machines (n=24) with CLiC devices that asses blood volume changes had software (LabVIEW) installed to calculate IAP at 20psec intervals from DM data. IAP was determined by hematocrit (default value, 0.34) and venous pressure (VP) by VA from 3470 treatments among 291 patients over 36 days. Electronic health records and dialysis machine data were merged. IAP curves and slopes were correlated with A/IDH.

Neurosurgery
Raffee S, **Griffin M**, **Massie L**, **Basheer A**, **Tundo K**, **Brown A**, **Air E**, and **Atiemo H**. Lower urinary tract symptoms in women with spinal pathologies: a prospective prevalence study. *Neurourology and Urodynamics* 2020; 39:S198-S199.

Introduction: The relationship between spinal pathologies and lower urinary tract symptoms (LUTS) is largely unknown. The incidence of LUTS in patients with lumbar disk disease has been estimated to be between 27% and 92%. Further, the effect of spine surgery on lower urinary tract symptoms has not been definitively established. The objective of this study was to determine the prevalence of urinary dysfunction among female patients with spinal pathologies and to evaluate the effects of spinal surgery on these symptoms using validated questionnaires. Methods: After IRB approval, women with lower spine complaints were identified in the neurosurgery clinic. Patients were asked to fill out the Pelvic Floor Distress Inventory (PFDI-20) and Pelvic Floor Impact Questionnaire (PFIQ-7) at their initial visit. Exclusion criteria included primary spinal pathology in the cervical spine. If the patient elected to undergo spine surgery after their initial evaluation, questionnaires were obtained at 6 weeks and 6 months postoperatively. Patient demographics, medical and surgical history were obtained through a review of the electronic medical record. Results: A total of 169 patients were recruited between April 2017 and July 2019. See Table 1. At baseline, 72.7% answered "yes" to at least one question on the Urinary Distress Inventory (UDI-6). The average score was 23.5/100. Those with higher UDI-6 scores were strongly correlated to higher Urinary Impact Questionnaire (UIQ-7) score (Pearson correlation coefficient= 0.69). Colorectal-Anal Distress Inventory (CRADI-8) was also evaluated with 64.3% presenting with some level of bowel complaints. The average score was only 14.4/100. Higher baseline UDI-6 and CRADI-8 scores were observed for patients with a history of a prior hysterectomy, use of stool softeners, and a spinal pathology including L3 ($P < 0.05$). Postoperative questionnaires were obtained from 22 women at 6 weeks and 8 women at 6 months, with the average UDI-6 scores being 19.9/100 and 31.2/100, respectively. Conclusion: Though the majority of women presented with some level of urinary bother, quality of life impact appeared low. More significant bother was seen in patients that had L3 spinal involvement at their initial assessment. At this point, there was no demonstrable influence of surgery on urinary symptoms, though the number of patients followed postoperatively was small.

Nursing
Brazelton T. A Program Evaluation of the Hospital Elder Life Program in a Community Teaching Hospital. *Journal of the American Geriatrics Society* 2020; 68:S205-S205.

BACKGROUND/OBJECTIVES The growing population of older adults and the numerous negative outcomes associated with delirium challenges health systems to provide specialized older adult care. One intervention that has been shown to have positive effects on older adults is the Hospital Elder Life Program (HELP) which utilizes volunteers to help prevent delirium and immobility. This project sought to answer the following questions: What was the effect of HELP volunteers on clinical outcomes (rate of patient falls, use of patient sitters and length of stay) and what was the associated financial impact? METHODS This project was a retrospective program outcomes evaluation. Charts of patients that were 70 years and older admitted to the Neurology/Stroke Unit, at community-based teaching hospital in Metro-Detroit Michigan between February 2017 and May 2018 were reviewed. The time frame includes 8 months pre-implementation of HELP volunteers and 8 months post-implementation. Descriptive statistics was used to describe fall rates. The Wilcoxon rank test was used to analyze length of stay and patient sitter hours. A study site statistician conducted the analysis of data using Statistical Analysis System. The financial services department assisted in obtaining information regarding the financial impact of falls, patient sitter hours, and length of stay. RESULTS A total of 1670 patients were included in the review. Falls decreased from 15 during the pre-implementation period to 9 falls post implementation. Average length of stay decreased from 4.1 days to 3.9 days (p= 0.027). Total patient sitter hours decreased from 4,210.10 hours to 3,742.70 hours, for a difference of 475.40 hours (p= 0.80). The estimated cost of a fall, with or without injury, while hospitalized was unable to be obtained from the financial department. In the post-implementation study period, HELP volunteers on one nursing unit showed minimum cost savings of $48,053.05 through the reduction of length of stay and use of patient sitters. CONCLUSION The results of this project are consistent with literature, concluding that volunteer visits from the HELP positively impacts patient outcomes and reduces financial costs and substantiates the need to sustain and expand the current program.

Nursing

Fram G, **Hudson MP**, **McCord J**, **Moyer M**, **Jacobsen G**, and **Nowak RM**. Utility of gender-specific HS-troponin I cut-points for AMI diagnosis. *Journal of the American College of Cardiology* 2020; 75(11):64.

Background Circulating concentrations of high sensitivity cardiac troponin I (hs-cTnI) are higher in men than women during normal conditions and acute coronary syndromes. There is clinical uncertainty whether gender-specific vs. single gender-neutral hs-cTnI cut-off values more effectively diagnose acute myocardial infarction (AMI). Methods Emergency department patients with suspected coronary ischemia and no ST-segment elevation underwent clinical evaluation plus serial hs-cTnI testing (Abbott Architect, 99th percentile women 16 ng/L, men 34 ng/L) at baseline, 1 hour, and 3 hours. Final diagnosis of AMI was centrally adjudicated by 2 independent cardiologists using the Fourth Universal Definition of AMI, clinical information, and serial hs-cTnI results. We compared the diagnostic accuracy of a single, general hs-cTnI cut-point of >26.0 ng/L, versus gender-specific cut-points (>16.0 ng/l for females and >34.0 ng/l for males) to diagnose AMI. Results The study population included 569 patients (48% female) with an adjudicated AMI diagnosis in 42 patients (7.4%). A single, general hs-cTnI cut-off value demonstrated a sensitivity of 97.6%, specificity of 87.3%, positive predictive value (PPV) of 38.0%, and negative predictive value (NPV) of 99.8% for AMI diagnosis. Gender-specific cut-off values did not change AMI diagnosis in any male patients and identified 1 additional female AMI patient. Additionally, among females there were 17 more false positives (FP), and among males there were 9 less FPs. Gender-specific hs-cTnI criteria demonstrated a sensitivity of 100%, specificity of 85.8%, PPV 35.9%, and NPV 100% for AMI diagnosis. There was no significant difference in sensitivity, specificity, PPV, or NPV using the gender-specific versus the general cut-point values ($p = 1.000$, $p = 0.471$, $p = 0.748$, and $p = 1.000$ respectively). Conclusion Our study reveals no significant AMI diagnostic difference using a single, gender-neutral hs-cTnI cut-point versus separate gender-specific hs-cTnI criteria. Emergency Department and Cardiology providers may implement hs-cTnI testing algorithms with single, gender-neutral cut-off values to diagnose or exclude AMI.

Obstetrics, Gynecology, and Women's Health

Raffee S, **Griffin M**, **Massie L**, **Basheer A**, **Tundo K**, **Brown A**, **Air E**, and **Atiemo H**. Lower urinary tract symptoms in women with spinal pathologies: a prospective prevalence study. *Neurourology and Urodynamics* 2020; 39:S198-S199.

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Otolaryngology

Leonard-Murali S, **Ivanics T**, **Nasser H**, **Tang A**, and **Singer M**. Intraoperative nerve monitoring in thyroidectomies for malignancy: Does it matter? *Annals of Surgical Oncology* 2020; 27:S58.

S. Leonard-Murali, Henry Ford Hospital, Department of Surgery, Detroit, MI, United States

Introduction: Recurrent laryngeal nerve injury (RLNI) and postoperative hypocalcemia are potential complications of thyroidectomy, especially in cases of malignancy. Intraoperative nerve monitoring (IONM) remains controversial. We sought to evaluate the impact of IONM on these complications using a national dataset. Methods: The American College of Surgeons National Surgical Quality Improvement Program thyroidectomy targeted dataset was queried for patients who underwent open thyroidectomies from 2016 through 2017. Primary outcomes were 30-day readmission (RA), 30-day hypocalcemic events (HCE), and RLNI. Patients were grouped by IONM use. Demographic, clinicopathologic, intraoperative, and postoperative variables were compared. Univariate and multivariable logistic regression models were constructed to evaluate associations of variables with each primary outcome, measured by adjusted odds ratios (AOR) and 95% confidence intervals (95CI). Subgroup analysis with similar methods was performed on patients with malignant pathology. Significance was established at p<0.05. Results: A total of 9527 patients were identified, 3558 (37.3%) without IONM, and 5969 (62.7%) with. The IONM group had higher BMI (31.0±7.8 kg/m2 vs 30.3±7.7 kg/m2; p<0.001), more benign pathology (38.9% vs 35.4%; p<0.001), more use of vessel sealing devices (73.6% vs 57.9%; p<0.001), and more neck dissections (28.1% vs 18.9%; p<0.001). By multivariable analysis, IONM was not associated with RA, but was protective against HCE (AOR=0.81, 95CI=0.68-0.96; p=0.013) and RLNI (AOR=0.83, 95CI=0.69-0.98; p=0.033). Malignant pathology was a risk factor for HCE (AOR=1.21, 95CI=1.01-1.45; p=0.038) and RLNI (AOR=1.22, 95CI=1.02-1.46; p=0.034). In the subgroup analysis of patients with malignancy (5943/9527, 62.4%), IONM continued to be protective against HCE (AOR=0.73, 95CI=0.60-0.90; p=0.003) and RLNI (AOR=0.76, 95CI=0.62-0.94; p=0.012). Conclusion: Malignancy was a risk factor for HCE and RLNI. IONM was protective against HCE and RLNI. both overall, and in the malignant subgroup. This suggests that patients undergoing thyroidectomy may benefit from treatment at centers that offer IONM, especially if the indication is malignancy.

Public Health Sciences

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Public Health Sciences

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Introduction: Recurrent laryngeal nerve injury (RLNI) and postoperative hypocalcemia are potential complications of thyroidectomy, especially in cases of malignancy. Intraoperative nerve monitoring (IONM) remains controversial. We sought to evaluate the impact of IONM on these complications using a national dataset. Methods: The American College of Surgeons National Surgical Quality Improvement Program thyroidectomy targeted dataset was queried for patients who underwent open thyroidectomies from 2016 through 2017. Primary outcomes were 30-day readmission (RA), 30-day hypocalcemic events (HCE), and RLNI. Patients were grouped by IONM use. Demographic, clinicopathologic, intraoperative, and postoperative variables were compared. Univariate and multivariable logistic regression models were constructed to evaluate associations of variables with each primary outcome, measured by adjusted odds ratios (AOR) and 95% confidence intervals (95CI). Subgroup analysis with similar methods was performed on patients with malignant pathology. Significance was established at $p<0.05$. Results: A total of 9527 patients were identified, 3558 (37.3%) without IONM, and 5969 (62.7%) with. The IONM group had higher BMI (31.0±7.8 kg/m2 vs 30.3±7.7 kg/m2; $p<0.001$), more benign pathology (38.9% vs 35.4%; $p<0.001$), more use of vessel sealing devices (73.6% vs 57.9%; $p<0.001$), and more neck dissections (28.1% vs 18.9%; $p<0.001$). By multivariable analysis, IONM was not associated with RA, but was protective against HCE (AOR=0.81, 95CI=0.68-0.96; p=0.013) and RLNI (AOR=0.83, 95CI=0.69-0.98; p=0.033). Malignant pathology was a risk factor for HCE (AOR=1.21, 95CI=1.01-1.45; p=0.038) and RLNI (AOR=1.22, 95CI=1.02-1.46; p=0.034). In the subgroup analysis of patients with malignancy (5943/9527, 62.4%), IONM continued to be protective against HCE (AOR=0.73, 95CI=0.60-0.90; p=0.003) and RLNI (AOR=0.76, 95CI=0.62-0.94; p=0.012). Conclusion: Malignancy was a risk factor for HCE and RLNI. IONM was protective against HCE and RLNI. both overall, and in the malignant subgroup. This suggests that patients undergoing thyroidectomy may benefit from treatment at centers that offer IONM, especially if the indication is malignancy.

Public Health Sciences
Nasser H, **Bensenhaver J**, Antonelli L, **Susick LL**, **Divine G**, and **Petersen L**. Breast cancer patients are interested in telemedicine. *Annals of Surgical Oncology* 2020; 27:S162-S163.

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

Introduction: Telemedicine is enhancing or replacing many aspects of traditional in-office healthcare. The role of telemedicine in the complex care of breast cancer (BC) patients remains unclear. Methods: Via a survey at their initial BC appointment, patients self-reported demographics such as age, race, distance from hospital and education level. Patients answered ten Likert questions about perceptions of telemedicine. Wilcoxon signed rank tests assessed whether overall the respondents reported more or less than neutral interest or concerns due to each of the ten considerations. Wilcoxon rank sum tests and Spearman's rank correlations were used for univariate analysis to assess if responses varied by patient characteristic. Multiple regression assessed for associations. Results: 51 female BC patients completed the survey. 31 patients were White, 19 were <60, and 17 lived over 20 miles from the hospital. 30 patients answered telemedicine could save time, 34 answered telemedicine could improve their access to care, and 35 answered telemedicine could decrease wait time, with Likert responses of '4'/Agree or '5'/ Strongly Agree. No significant associations were observed between interest in telemedicine (gauged by responses to the Likert score questions) and respondent characteristics. The questions that were associated with greater interest in telemedicine had to do with easier access, less waiting time and reduced exposure to infectious diseases. Each of these variables had a median Likert response of '4'/Agree with signed rank test p-values ≤0.010. The question which denoted the most concern about telemedicine involved the use of technology, although the median for that question was '3'/neutral. Finally, the overall median of the directionally aligned Likert responses was 3.4 partway between neutral and agree (indicating more interest/less concern). The signed rank test p-value for this average was 0.009. Conclusions: BC patients are interested in telemedicine. Since age, race, distance from hospital, and education level, are not predictors of interest in telemedicine, providers can consider offering these opportunities to everyone, as healthcare continues to become more personalized.

Public Health Sciences
Nowak RM, **Christenson RH**, **Jacobsen G**, **Apple F**, **McCord J**, **Limkakeng A**, **Singer A**, **Peacock WF**, and **DeFilippi CR**. High sensitivity troponin values rapidly rule-out myocardial infarction and allow for ed discharge in a higher risk patient population compared to contemporary practice. *Journal of the American College of Cardiology* 2020; 75(11):66.

Background The multicenter High Sensitivity Cardiac Troponin I (hs-cTnI) study (HIGH-US) reported a 1 hour hs-cTnI algorithm in the Emergency Department (ED) rule-out rate of 50.4% for AMI (negative predictive value 99.7%) and 30 day incidence of AMI/death of 0.2%. We sought to determine factors associated with ED discharge versus observation/inpatient placements in these patients. Methods 2113 consenting adults were enrolled from 2015-2016 in 29 medical centers with suspicion for AMI. Baseline and 1 hour plasma samples were analyzed using the Siemens Atellica hs-cTnI assay (overall 99th %ile 45.0 ng/L). AMI diagnosis was independently adjudicated using local contemporary troponin assays and 30 day clinical information. Clinical variables used to aid in disposition decision making were compared in AMI ruled out patients. Results 1020 (48.3%) individuals were ruled out in for AMI in 1 hour. Of these 584 (57.3%) were discharged home while 436 (42.7%) were placed in observation/inpatient beds. The latter group were older with more hypertension, diabetes, smoking, heart or

renal failure, personal or family history of coronary artery disease, prior AMI or revascularization and other vascular diseases (Table). Conclusion ED physicians were less likely to discharge home patients ruled out for AMI if they had traditional risk factors for CAD. Compared to contemporary practice hs-cTnI use allows more patients with higher risk clinical profiles to be discharged home than based on traditional assessments.

Surgery

Gorgis S, **Demertzis Z**, **Malette K**, **Fram G**, **Dobesh K**, **Keteyian S**, **Alaswad K**, **Basir M**, and **Brawner C**. Percutaneous coronary revascularization is associated with higher exercise capacity after myocardial infarction. *Journal of the American College of Cardiology* 2020; 75(11):220.

Background Cardiopulmonary exercise testing (CPET) is a valuable tool to assess exercise tolerance and prognosis in heart failure. Limited studies have evaluated its clinical utility in patients with myocardial infarction (MI). The purpose of this study was to evaluate exercise capacity in post-MI patients based on whether they received percutaneous coronary intervention (PCI) or were treated with medical therapy. Methods We retrospectively identified patients who completed a CPET within 1 year after an acute MI. A general linear mixed model was developed to compare peak oxygen uptake (VO2) between patients who did and did not receive PCI with adjustments for age, sex, ST-elevation MI (STEMI), and presence of chronic total occlusion (CTO). A sub-analysis was performed in patients with CTO. Results Between April 2002 and March 2019, 436 patients (age= 57±11 years; 65% male; 63% white; 40% STEMI; 30% CTO; 70% PCI) completed a CPET within 1 year post-MI. Among 175 patients who suffered a STEMI, 84% underwent PCI. Among 261 patients who suffered a non-STEMI, 61% underwent PCI. There was significant variability of PCI performed between sex, race, MI type, and age (P<0.05). As shown in the Table, PCI was associated with significantly higher adjusted peak VO2 among the entire cohort and the subgroup of patients with CTO (n=130). Conclusion Among patients who suffer an acute MI, PCI is associated with higher exercise capacity as determined by peak VO2. This effect was larger in patients who present with CTO. [Figure presented]

Surgery

Konel J, **Kitajima T**, Arevalo L, Murray N, **Pietrowsky T**, **Venkat D**, **Gonzalez H**, **Samaniego M**, **Abouljoud M**, and **Nagai S**. Assessment of sarcopenia and obesity by bioelectrical impedance analysis in transplant and hepatobiliary populations. *American Journal of Transplantation* 2020; 20:56.

J. Konel, Wayne State University, School of Medicine, Detroit, MI, United States

Bioelectrical impedance analysis (BIA) can measure body composition, including assessment of sarcopenia and obesity. This study aimed to evaluate the clinical utility of BIA in transplant and hepatobiliary populations. Methods: We conducted a single-center study of 60 patients (5 living donor candidates, 10 early postoperative, 7 benign liver disease, 14 chronic kidney disease, 5 early cirrhosis, 7 post-transplant, 6 early malignancy, and 6 advanced malignancy). Sarcopenia was defned as a calculated whole-body muscle mass (kg)/body surface area below the 25th percentile. Obesity was defned as fat percentage of >25% and >30% in males and females, respectively. Patients were categorized into 4 groups: (1) not sarcopenic/not obese, (2) sarcopenic/not obese, (3) not sarcopenic/obese, and (4) sarcopenic/obese. Clinical characteristics and BIA measurements were compared. Results: Among the 60 participants, 28 were not sarcopenic/not obese, 1 was sarcopenic/not obese, 17 were not sarcopenic/obese, and 14 were sarcopenic/obese. There were no signifcant diferences in BMI, albumin, total protein, and absolute lymphocyte count. Sarcopenic/obese patients showed signifcantly lower Karnofsky score (median 55% [IQR, 50-82.5%]), compared to not sarcopenic/obese patients (median 80% [IQR, 60-92.5%], p = 0.037). All advanced malignancy patients were either sarcopenic/not obese or sarcopenic/obese. Conclusion: Sarcopenic-obesity patients showed signifcantly lower performance status than obese patients without sarcopenia. BIA may be useful tool in identifying high-risk patients and improving surgical outcomes.

Surgery

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Surgery

Patel A, **Grafton G**, **Tita C**, Hannawi B, **Selektor Y**, **Chamogeorgakis T**, **Apostolou D**, **Lanfear DE**, **Williams CT**, **Nemeh HW**, and **Cowger JA**. Survival and Predictors of Mortality in Patients Undergoing RVAD Explant in IMACS. *Journal of Heart and Lung Transplantation* 2020; 39(4):S25-S26.

Purpose: Survival in patients requiring RVAD support is known to be poor. However, outcomes in those undergoing subsequent RVAD explant and predictors of mortality remain unknown. Methods: Of 16482 patients in IMACS, 723 patients had an isolated RVAD (n=29) or BiVAD (n=694) in place. Using Kaplan Meier methods, survival was estimated for the LVAD-only cohort and within the subgroup of RVAD/BiVAD patients with and without RVAD explant. Correlates of mortality in the RVAD explant group were identified with Cox multivariable regression. Results: Within the BiVAD group, 240 patients (33%) had an RVAD explant. Of these, 221 (92%) were performed for RV recovery, 17 (7.1%) for device malfunction and 2 (0.8%) were for other reasons. Survival at 1Y was 53±2.0% in the BiVAD group vs. 82±0.3% in LVAD-only patients (p<0.0001). Within the BiVAD group, patients undergoing RVAD explant had equivalent survival (1Y=54±2.5%) to those with ongoing BiVAD support (1Y=52±3.4%, p=0.54). BiVAD patients who died after RVAD explant were older, more likely to be BTT, and had higher preimplant creatinine (table). On multivariable analysis, older age, higher preimplant pulmonary systolic pressure, explant for RVAD dysfunction, and BTT indication predicted death after RVAD explant (table). Within the subgroup of BTT BiVAD (n=51) patients undergoing RVAD explant, survival was only 62% at 3 months. Conclusion: Patients undergoing RVAD explant, even for RV-recovery, have very poor survival. Patients who are transplant eligible with signs of RVAD dysfunction should be given urgent listing status. Rather than RVAD explant, BTT patients with signs of RV recovery may be better served with transplant.

Urology

Baumgarten L, **Irish V**, **Raffee S**, and **Atiemo H**. Utilization of third line therapy in the urologic management of patients with multiple sclerosis. *Neurourology and Urodynamics* 2020; 39:S197-S198.

Introduction: Multiple sclerosis (MS) is a demyelinating neurologic condition affecting approximately 2 million people worldwide. Lower urinary tract symptoms (LUTS) affect up to 50%-90% of MS patients. Urodynamic (UD) evaluation for these patients often shows evidence of Neurogenic Detrusor Overactivity (NDO). Treatment strategies include behavioral and physical therapy, oral medications, and third line therapies (intravesical botox, Interstim, PTNS). We sought to characterize MS patients with NDO, measure changes in urinary quality of life with treatment, and evaluate for any factors predictive of progression to third line therapies. Methods: Using a prospectively collected, routinely updated database of MS patients within a single neuro-urologist practice between 2013-2019, patient demographics, UD data, treatment variables, and pre- and posttreatment patient-reported questionnaire responses were recorded. We present descriptive characteristics of the patients with NDO within this cohort. We grouped these patients into two groups: those who progress to third line therapy and those who remain on medical therapy. We evaluate for any differences in UD characteristics between these groups and compare the degree of change in symptom and quality of life scores. Urodynamic and quality of life data were compared using chi-square and Wilcoxon rank sum statistics, respectively. Results: Our cohort of 182 patients with MS, averages 55 years of age, is 84% female and 45% Caucasian. Nearly 50% of these patients are diagnosed with relapsing remitting MS. Eighty percent of our patients underwent UD, with findings showing detrusor sphincter dyssynergia (DSD) in 24% and NDO in 45% (66 patients). Nearly 40% of patients with NDO progress to third line therapy with intravesical botox being the most common in our cohort (89%). As seen in the Table, there were no demographic or UD factors predictive of progressing to third line therapy. However, patients who undergo third line therapy show larger improvements in symptom score than those who do not. Conclusion: NDO is a common cause for LUTS in patients with MS. 40% of our MS patients with NDO progress to third line therapy with no UD factors predictive of progression. Symptom improvements are greater those patients who undergo third line therapies compared to those who remain on medical therapy.

Urology

Raffee S, **Griffin M**, **Massie L**, **Basheer A**, **Tundo K**, **Brown A**, **Air E**, and **Atiemo H**. Lower urinary tract symptoms in women with spinal pathologies: a prospective prevalence study. *Neurourology and Urodynamics* 2020; 39:S198-S199.

Introduction: The relationship between spinal pathologies and lower urinary tract symptoms (LUTS) is largely unknown. The incidence of LUTS in patients with lumbar disk disease has been estimated to be between 27% and 92%. Further, the effect of spine surgery on lower urinary tract symptoms has not been definitively established. The objective of this study was to determine the prevalence of urinary dysfunction among female patients with spinal pathologies and to evaluate the effects of spinal surgery on these symptoms using validated questionnaires. Methods: After IRB approval, women with lower spine complaints were identified in the neurosurgery clinic. Patients were asked to fill out the Pelvic Floor Distress Inventory (PFDI-20) and Pelvic Floor Impact Questionnaire (PFIQ-7) at their initial visit. Exclusion criteria included primary spinal pathology in the cervical spine. If the patient elected to undergo spine surgery after their initial evaluation, questionnaires were obtained at 6 weeks and 6 months postoperatively. Patient demographics, medical and surgical history were obtained through a review of the electronic medical record. Results: A total of 169 patients were recruited between April 2017 and July 2019. See Table 1. At baseline, 72.7% answered “yes” to at least one question on the Urinary Distress Inventory (UDI-6). The average score was 23.5/100. Those with higher UDI-6 scores were strongly correlated to higher Urinary Impact Questionnaire (UIQ-7) score (Pearson correlation coefficient= 0.69). Colorectal-Anal Distress Inventory (CRADI-8) was also evaluated with 64.3% presenting with some level of bowel complaints. The average score was only 14.4/100. Higher baseline UDI-6 and CRADI-8 scores were observed for patients with a history of a prior hysterectomy, use of stool softeners, and a spinal pathology including L3 ($P < 0.05$). Postoperative questionnaires were obtained from 22 women at 6 weeks and 8 women at 6 months, with the average UDI-6 scores being 19.9/100 and 31.2/100, respectively. Conclusion: Though the majority of women presented with some level of urinary bother, quality of life impact appeared low. More significant bother was seen in patients that had L3 spinal involvement at their initial assessment. At this point, there was no demonstrable influence of surgery on urinary symptoms, though the number of patients followed postoperatively was small.