

OAKLAND UNIVERSITY WILLIAM BEAUMONT SCHOOL OF MEDICINE

PUBLICATION LIST

October - December 2019

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Abbas A, Mando R, **Hanzel G**, **Gallagher M**, **Safian R**, Kassas S and **Shannon F** (2019). "Invasive versus echocardiographic evaluation of suboptimal valve hemodynamics and procedural futility following valve-in-valve transcatheter aortic valve replacement." Journal of the American College of Cardiology 74(13): B745-B745.

[Full Text](#)

Department of Internal Medicine

Department of Surgery

Abdel-Magiud EM, Taha EA, Bakr RM, Ismail SA, Sayed SK, Makboul M, **Kamel-ElSayed S** and Abdel Motaleb AA (2019). "Effects of different therapeutic modalities for postacne scars on circulating collagen III." Journal of Cosmetic Dermatology. ePub Ahead of Print.

[Full Text](#)

Department of Foundational Medical Studies

Background: Therapies for postacne scarring act through modulation of elastin and collagen, and collagen III might therefore represent a biomarker of treatment effectiveness. Patients and Methods: Patients (n = 70) with postacne scars and individuals without scars (n = 56) were included in this case-control study. Patients were treated with Dermaroller microneedling, trichloroacetic acid chemical reconstruction, punch excision, or scar subcision. Scar severity was graded immediately before and after treatment with a photographic quartile scale and the ECCA scale. Serum levels of collagen III were measured in control individuals and in patients, before treatment, 1 month after the first treatment session, and 4 months after the final session. Results: Circulating levels of collagen III were significantly higher in patients with postacne scarring (24.1 +/- 12.5) before treatment than in control individuals (2.6 +/- 0.8). Circulating levels of collagen in patients were significantly lower 4 months posttreatment (14.3 +/- 8.1) than at baseline. The mean percentage change in serum collagen III was positively correlated with both the mean percentage improvement by photographic evaluation (r = .530, P < .000) and the mean percentage change in the ECCA scale (r = .632, P < .000). Conclusion: Circulating collagen III is a biomarker for improvement of postacne scarring following different therapies.

Amen A, Karabon P, Bartram C, Irwin K, Dunne R, Wolff M, Daya MR, Vellano K, McNally B, Jacobsen RC and **Swor R** (2019). "Disparity in receipt and utilization of telecommunicator CPR instruction." [Prehospital Emergency Care : Official Journal of the National Association of EMS Physicians and the National Association of State EMS Directors](#). pp. 1-9.
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OUWB Medical Student Author

Department of Emergency Medicine

Introduction: Telecommunicator Assisted Cardiopulmonary Resuscitation (T-CPR) is independently associated with improved survival and improved functional outcome after adult Out of Hospital Cardiac Arrest (OHCA). The objective of this study was to evaluate whether there are racial and socioeconomic disparities in the provision of T-CPR instruction and subsequent CPR performance. Methods: We performed a retrospective review of a convenience sample of EMS agencies throughout the United States that utilized the Cardiac Arrest Registry to Enhance Survival (CARES) dispatch registry during the period 1/2014-12/2017. Data were collected by dispatch agencies after review of 9-1-1 OHCA audio recordings. Elements related to dispatcher CPR instruction, barriers to bystander CPR (BCPR) performance, patient race (White, Black, Hispanic-Latino, or other) and Utstein data were captured from the CARES database. These data were merged with census tract data from incident locations. The effects of race and income (Socioeconomic status, SES) on outcome were analyzed using multilevel logistic regression. Results: A total of 3,807 cases were identified from 37 dispatch agencies in 6 states. The sample was predominantly White (57.5%) and male (64.9%) with an average age of 60.3 +/-19.9. In the adjusted analysis, there were no differences in the odds of receiving CPR instruction by race (black vs white), OR= 0.96 (95% CI. 0.70, 1.32) or for increased income, (OR= 1.00, 95% CI 0.99, 1.02). There was a significant difference in receipt of T-CPR instruction by patient age, OR =0.99 (95% CI, 0.98, 0.99). Subsequent utilization of T-CPR instruction to perform BCPR was less likely for patients that had a lower income, OR =1.03 (95% CI 1.01, 1.05). There was also a decreased rate of BCPR provision by patient age OR =0.99 (95% CI, 0.99, 1.00), but there was no difference in rate of BCPR provision by race, OR =0.86 (95% CI 0.61, 1.23). Conclusion: We identified differences in age but not race or SES in the provision of T-CPR instruction by dispatch centers. We also identified decreased CPR provision by age and income after receipt of T-CPR instructions. In this sample, we found no evidence of racial disparities in the provision of T-CPR instruction or subsequent provision of BCPR.

Anderson DR, Morgano GP, Bennett C, Dentali F, Francis CW, Garcia DA, Kahn SR, Rahman M, Rajasekhar A, Rogers FB, **Smythe MA**, Tikkinen KAO, Yates AJ, Baldeh T, Balduzzi S, Brozek JL, Etxeandia-Ikobaltzeta I, Johal H, Neumann I, Wiercioch W, Yepes-Nunez JJ, Schunemann HJ and Dahm P (2019). "American Society of Hematology 2019 guidelines for management of venous thromboembolism: Prevention of venous thromboembolism in surgical hospitalized patients." [Blood Advances](#) 3(23): 3898-3944.

[Full Text](#)

Department of Foundational Medical Studies (BH)

Background: Venous thromboembolism (VTE) is a common source of perioperative morbidity and mortality. Objective: These evidence-based guidelines from the American Society of Hematology (ASH) intend to support decision making about preventing VTE in patients undergoing surgery. Methods: ASH formed a multidisciplinary guideline panel balanced to minimize bias from conflicts of interest. The McMaster University GRADE Centre supported the guideline-development process, including performing systematic reviews. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach was used to assess evidence and make recommendations, which were subject to public comment. Results: The panel agreed on 30 recommendations, including for major surgery in general (n = 8), orthopedic surgery (n = 7), major general surgery (n = 3), major neurosurgical procedures (n = 2), urological surgery (n = 4), cardiac surgery and major vascular surgery (n = 2), major trauma (n = 2), and major gynecological surgery (n = 2). Conclusions: For patients undergoing major surgery in general, the panel made conditional recommendations for mechanical prophylaxis over no prophylaxis, for pneumatic compression prophylaxis over graduated compression stockings, and against inferior vena cava filters. In patients undergoing total hip or total knee arthroplasty, conditional recommendations included using either aspirin or anticoagulants, as well as for a direct oral anticoagulant over low-molecular-weight heparin (LMWH). For major general surgery, the panel suggested pharmacological prophylaxis over no prophylaxis, using LMWH or unfractionated heparin. For major neurosurgery, transurethral resection of the prostate, or radical prostatectomy, the panel suggested against pharmacological prophylaxis. For major trauma surgery or major

gynecological surgery, the panel suggested pharmacological prophylaxis over no prophylaxis.

Anusim N, Ionescu F and **Jaiyesimi I** (2019). "Demographics and survival in malignant pleural mesothelioma: Analysis of seer data." Journal of Thoracic Oncology 14(11): S1145-S1145.

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Department of Internal Medicine

Anusim N, Khoury J, Ionescu F, Thapa S and **Jaiyesimi I** (2019). "Demographics and survival in plasma cell leukemia (SEER data analysis)." American Journal of Hematology 94: S11-S11.

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Department of Internal Medicine

Bahado-Singh RO, Syngelaki A, Mandal R, Han B, Li L, Bjorndahl TC, Wang N, Maulik D, Dong E, Turkoglu O, Tseng CL, Zeb A, **Redman M**, Wishart DS and Nicolaides KH (2019). "First-trimester metabolomic prediction of stillbirth." Journal of Maternal-Fetal and Neonatal Medicine 32(20): 3435-3441.

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Department of Obstetrics & Gynecology

Background: Stillbirth remains a major problem in both developing and developed countries. Omics evaluation of stillbirth has been highlighted as a top research priority. Objective: To identify new putative first-trimester biomarkers in maternal serum for stillbirth prediction using metabolomics-based approach. Methods: Targeted, nuclear magnetic resonance (NMR) and mass spectrometry (MS), and untargeted liquid chromatography-MS (LC-MS) metabolomic analyses were performed on first-trimester maternal serum obtained from 60 cases that subsequently had a stillbirth and 120 matched controls. Metabolites by themselves or in combination with clinical factors were used to develop logistic regression models for stillbirth prediction. Prediction of stillbirths overall, early (<28 weeks and <32 weeks), those related to growth restriction/placental disorder, and unexplained stillbirths were evaluated. Results: Targeted metabolites including glycine, acetic acid, L-carnitine, creatine, lysoPCaC18:1, PCaeC34:3, and PCaeC44:4 predicted stillbirth overall with an area under the curve [AUC, 95% confidence interval (CI)] = 0.707 (0.628-0.785). When combined with clinical predictors the AUC value increased to 0.740 (0.667-0.812). First-trimester targeted metabolites also significantly predicted early, unexplained, and placental-related stillbirths. Untargeted LC-MS features combined with other clinical predictors achieved an AUC (95%CI) = 0.860 (0.793-0.927) for the prediction of stillbirths overall. We found novel preliminary evidence that, verruculotoxin, a toxin produced by common household molds, might be linked to stillbirth. Conclusions: We have identified novel biomarkers for stillbirth using metabolomics and demonstrated the feasibility of first-trimester prediction.

Bahado-Singh RO, Vishweswaraiah S, Aydas B, Mishra NK, Yilmaz A, Guda C and **Radhakrishna U** (2019). "Artificial intelligence analysis of newborn leucocyte epigenomic markers for the prediction of autism." Brain Research 1724: 146457.

[Full Text](#)

Department of Obstetrics & Gynecology

A great diversity of factors contribute to the pathogenesis of autism and autism spectrum disorder (ASD). Early detection is known to correlate with improved long term outcomes. There is therefore intense scientific interest in the pathogenesis of and early prediction of autism. Recent reports suggest that epigenetic alterations may play a vital role in disease pathophysiology. We conducted an epigenome-wide analysis of newborn leucocyte (blood spot) DNA in autism as defined at the time of sample collection. Our goal was to investigate the epigenetic basis of autism and identification of early biomarkers for disease prediction. Infinium HumanMethylation450 BeadChip assay was performed to measure DNA methylation level in 14 autism cases and 10 controls. The accuracy of cytosine methylation for autism detection using six different Machine Learning/Artificial Intelligence (AI) approaches including Deep-Learning (DL) was determined. Ingenuity Pathway Analysis (IPA) was further used to interrogate autism pathogenesis by identifying over-represented biological pathways. We found highly significant dysregulation of CpG methylation in 230 loci (249 genes). DL yielded an AUC (95% CI)=1.00 (0.80-1.00) with 97.5% sensitivity and 100.0% specificity for autism detection. Epigenetic dysregulation was identified in several important candidate genes including some previously linked to autism development e.g.: EIF4E, FYN, SHANK1, VIM, LMX1B, GABRB1, SDHAP3 and

PACS2. We observed significant enrichment of molecular pathways involved in neuroinflammation signaling, synaptic long term potentiation, serotonin degradation, mTOR signaling and signaling by Rho-Family GTPases. Our findings suggest significant epigenetic role in autism development and epigenetic markers appeared highly accurate for newborn prediction.

Bahado-Singh RO, Vishweswaraiah S, Er A, Aydas B, Turkoglu O, Taskin BD, Duman M, Yilmaz D and **Radhakrishna U** (2019). "Artificial Intelligence and the detection of pediatric concussion using epigenomic analysis." Brain Research 1726: 146510.

[Full Text](#)

Department of Obstetrics & Gynecology

Concussion, also referred to as mild traumatic brain injury (mTBI) is the most common type of traumatic brain injury. Currently concussion is an area of intense scientific interest to better understand the biological mechanisms and for biomarker development. We evaluated whole genome-wide blood DNA cytosine ('CpG') methylation in 17 pediatric concussion isolated cases and 18 unaffected controls using Illumina Infinium MethylationEPIC assay. Pathway analysis was performed using Ingenuity Pathway Analysis to help elucidate the epigenetic and molecular mechanisms of the disorder. Area under the receiver operating characteristics (AUC) curves and FDR p-values were calculated for mTBI detection based on CpG methylation levels. Multiple Artificial Intelligence (AI) platforms including Deep Learning (DL), the newest form of AI, were used to predict concussion based on i) CpG methylation markers alone, and ii) combined epigenetic, clinical and demographic predictors. We found 449 CpG sites (473 genes), those were statistically significantly methylated in mTBI compared to controls. There were four CpGs with excellent individual accuracy (AUC \geq 0.90-1.00) while 119 displayed good accuracy (AUC \geq 0.80-0.89) for the prediction of mTBI. The CpG methylation changes \geq 10% were observed in many CpG loci after concussion suggesting biological significance. Pathway analysis identified several biologically important neurological pathways that were perturbed including those associated with: impaired brain function, cognition, memory, neurotransmission, intellectual disability and behavioral change and associated disorders. The combination of epigenomic and clinical predictors were highly accurate for the detection of concussion using AI techniques. Using DL/AI, a combination of epigenomic and clinical markers had sensitivity and specificity \geq 95% for prediction of mTBI. In this novel study, we identified significant methylation changes in multiple genes in response to mTBI. Gene pathways that were epigenetically dysregulated included several known to be involved in neurological function, thus giving biological plausibility to our findings.

Baker EA, Vara AD, Salisbury MR, Fleischer MM, **Baker KC**, **Fortin PT**, Roberts RV and Friedrich CR (2019). "Titania nanotube morphologies for osseointegration via models of in vitro osseointegrative potential and in vivo intramedullary fixation." Journal of Biomedical Materials Research Part B-Applied Biomaterials. ePub Ahead of Print.

[Full Text](#)

Department of Orthopaedic Surgery

As total joint replacements increase annually, new strategies to attain solid bone-implant fixation are needed to increase implant survivorship. This study evaluated two morphologies of titania nanotubes (TiNT) in in vitro experiments and an in vivo rodent model of intramedullary fixation, to simulate joint arthroplasty conditions. TiNT surfaces were prepared via an electrochemical etching process, resulting in two different TiNT morphologies, an aligned structure with nanotubes in parallel and a trabecular bone-like structure. In vitro data showed bone marrow cell differentiation into osteoblasts as well as osteoblastic phenotypic behavior through 21 days. In vivo, both TiNT morphologies generated greater bone formation and bone-implant contact than control at 12 weeks, as indicated by μ CT analyses and histology, respectively. TiNT groups also exhibited greater strength of fixation compared to controls, when subjected to wire pull-out testing. TiNT may be a promising surface modification for promoting osseointegration.

Balinski AM and Preuss CV (2019). "Cilostazol," In Preuss C (ed). StatPearls. Treasure Island (FL): StatPearls Publishing.

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OUIWB Medical Student Author

Cilostazol is a quinolone derivative primarily used in the treatment of intermittent claudication associated with early-stage peripheral vascular disease.[1] Intermittent claudication is a condition caused by the narrowing of arteries that supply the legs with oxygenated blood. Patients with intermittent claudication

develop pain when walking due to a lack of oxygen-containing blood reaching the operating leg muscles. Cilostazol decreases the pain of intermittent claudication by dilating these arteries, which improves blood flow and oxygen to the legs. Cilostazol is an effective therapy for improving walking distances in patients with intermittent claudication, and the artery disease guidelines of the American College of Cardiology/American Heart Association reference a therapeutic trial of cilostazol.[2] [Level I] Cilostazol has also been shown to be significantly more effective than clopidogrel and aspirin alone for long-term prevention of severe vascular events in patients with a history of transient ischemic attack or non-cardioembolic ischemic stroke.[3]

Balogh EP, Bindman AB, Eckhardt SG, Halabi S, **Harvey RD, Jaiyesimi I**, Miksad R, Moses HL, Nass SJ, Schilsky RL, Sun S, Torrente JM and Warren KE (2019). "Challenges and opportunities to updating prescribing information for longstanding oncology drugs." *Oncologist*. ePub Ahead of Print.

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OUWB Medical Student Author

Department of Internal Medicine

A number of important drugs used to treat cancer-many of which serve as the backbone of modern chemotherapy regimens-have outdated prescribing information in their drug labeling. The Food and Drug Administration is undertaking a pilot project to develop a process and criteria for updating prescribing information for longstanding oncology drugs, based on the breadth of knowledge the cancer community has accumulated with the use of these drugs over time. This article highlights a number of considerations for labeling updates, including selecting priorities for updating; data sources and evidentiary criteria; as well as the risks, challenges, and opportunities for iterative review to ensure prescribing information for oncology drugs remains relevant to current clinical practice.

Bangma JT, Kwiatkowski E, Psioda M, Santos HP, Hooper SR, Douglass L, Joseph RM, Frazier JA, Kuban KCK, O'Shea TM, Fry RC, Shah B, Singh R, Van Marter L, Martin C, Ware J, Cole C, Perrin E, Bednarek F, Frazier J, Ehrenkranz R, Benjamin J, O'Shea TM, Bose C, Warner D, Engelke S, Poortenga M, Pastyrnak S, Karna P, Paneth N, Lenski M, Schreiber M, Hunter S, Msall M, Batton D, **Klarr J**, Christianson K, Klein D, Pimental M, Hallisey C, Coster T, Nylen E, Neger E, Mattern K, Venuti L, Powers B, Foley A, Williams J, Romano E, Hiatt D, Peters N, Brown P, Anusinha E, Bose G, Wereszczak J, Bernhardt J, Adams J, Wilson D, Darden-Saad N, Sutton D, Rathbun J, Miras K, Weiland D, Yoon G, Ramoskaite R, Wiggins S, Washington K, Martin R, Prendergast B, Kring B, Smith A, McQuiston S, Butler S, Wilson R, McGhee K, Lee P, Asgarian A, Sadhwani A, Henson B, Keller C, Walkowiak J, Barron S, Miller A, Dessureau B, Wood M, Damon-Minow J, Mayes L, Tsatsanis K, Chawarska K, Kim S, Dieterich S, Bears K, Waldrep E, Friedman J, Hounshell G, Allred D, Helms R, Whitley L, Stainback G, Bostic L, Jacobson A, McKeeman J, Meyer E, Price J, Lloyd M, Plesha-Troyke S, Scott M, Solomon KM, Brooklier K, Vogt K and Investigators E (2019). "Early life antecedents of positive child health among 10-year-old children born extremely preterm." *Pediatric Research* 86(6): 758-765.

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Department of Pediatrics

Background: To identify modifiable antecedents during pre-pregnancy and pregnancy windows associated with a positive child health at 10 years of age. Methods: Data on 889 children enrolled in the Extremely Low Gestational Age Newborn (ELGAN) study in 2002-2004 were analyzed for associations between potentially modifiable maternal antecedents during pre-pregnancy and pregnancy time windows and a previously described positive child health index (PCHI) score at 10 years of age. Stratification by race was also investigated for associations with investigated antecedents. Results: Factors associated with higher PCHI (more positive health) included greater gestational age, birth weight, multiple gestation, and medical interventions, including assisted reproduction and cervical cerclage. Factors associated with lower PCHI included correlates of lower socioeconomic status, pre-pregnancy chronic medical disorders in the mother such as pre-pregnancy body mass index (BMI), and maternal asthma. When stratified by race, variation in significant results was observed. Conclusions: Among children born extremely preterm, medical interventions and higher socioeconomic status were associated with improved PCHI, while chronic illness and high BMI in the mother is associated with lower PCHI at 10 years of age. Knowledge of such antecedent factors could inform efforts to develop interventions that promote positive child health outcomes in future pregnancies.

Bangma JT, Kwiatkowski E, Psioda M, Santos HP, Hooper SR, Douglass L, Joseph RM, Frazier JA, Kuban KCK, O'Shea

TM, Fry RC, Singh R, Van Marter L, Martin C, Ware J, Cole C, Perrin E, Bednarek F, Frazier JA, Ehrenkranz R, Smith A, O'Shea M, Bose C, Warner D, Engelke S, Poortenga M, Pastyrnak S, Karna P, Paneth N, Lenski M, Schreiber M, Hunter S, Msall M, Batton D, **Klarr J**, Christianson K, Klein D, Pimental M, Hallisey C, Coster T, Nysten E, Neger E, Mattern K, Venuti L, Powers B, Foley A, Williams J, Romano E, Hiatt D, Peters N, Brown P, Anusinha E, Bose G, Wereszczak J, Bernhardt J, Adams J, Smith A, Darden-Saad N, Sutton D, Sutton D, Rathbun J, Miras K, Weiland D, Yoon G, Ramoskaite R, Wiggins S, Washington K, Martin R, Prendergast B, Smith A, McQuiston S, Butler S, Wilson R, McGhee K, Lee P, Asgarian A, Sadhwani A, Henson B, Keller C, Walkowiak J, Barron S, Miller A, Dessureau B, Wood M, Damon-Minow J, Romano E, Mayes L, Tsatsanis K, Chawarska K, Kim S, Dieterich S, Bearrs K, Waldrep E, Friedman J, Hounshell G, Allred D, Helms R, Whitley L, Stainback G, Bostic L, Jacobson A, McKeeman J, Meyer E, Pastyrnak S, Price J, Lloyd M, Plesha-Troyke S, Scott M, Solomon KM, Brooklier K, Vogt K and Investigators E (2019). "Understanding positive child health." [Pediatric Research](#) 86(6): 690-691.

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Department of Pediatrics

Bauer ME, Housey M, **Bauer ST**, Behrmann S, Chau A, Clancy C, Clark EAS, Einav S, Langen E, Leffert L, Lin S, Madapu M, Maile MD, McQuaid-Hanson E, Priessnitz K, Sela HY, Shah A, Sobolewski P, Toledo P, Tsen LC and Bateman BT (2019). "Risk Factors, etiologies, and screening tools for sepsis in pregnant women: A multicenter case-control study." [Anesthesia and Analgesia](#) 129(6): 1613-1620.

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Department of Obstetrics & Gynecology

Background: Given the significant morbidity and mortality of maternal sepsis, early identification is key to improve outcomes. This study aims to evaluate the performance characteristics of the systemic inflammatory response syndrome (SIRS), quick Sequential [Sepsis-related] Organ Failure Assessment (qSOFA), and maternal early warning (MEW) criteria for identifying cases of impending sepsis in parturients. The secondary objective of this study is to identify etiologies and risk factors for maternal sepsis and to assess timing of antibiotics in patients diagnosed with sepsis. Methods: Validated maternal sepsis cases during the delivery hospitalization from 1995 to 2012 were retrospectively identified at 7 academic medical centers in the United States and Israel. Control patients were matched by date of delivery in a 1:4 ratio. The sensitivity and specificity of SIRS, qSOFA, and MEW criteria for identifying sepsis were calculated. Data including potential risk factors, vital signs, laboratory values, and clinical management were collected for cases and controls. Results: Eighty-two sepsis cases during the delivery hospitalization were identified and matched to 328 controls. The most common causes of sepsis were the following: chorioamnionitis 20 (24.4%), endometritis 19 (23.2%), and pneumonia 9 (11.0%). Escherichia coli 12 (14.6%), other Gram-negative rods 8 (9.8%), and group A Streptococcus 6 (7.3%) were the most commonly found pathogens. The sensitivities and specificities for meeting criteria for screening tools were as follows: (1) SIRS (0.93, 0.63); (2) qSOFA (0.50, 0.95); and (3) MEW criteria for identifying sepsis (0.82, 0.87). Of 82 women with sepsis, 10 (12.2%) died. The mortality rate for those who received antibiotics within 1 hour of diagnosis was 8.3%. The mortality rate was 20% for the patients who received antibiotics after >1 hour. Conclusions: Chorioamnionitis and endometritis were the most common causes of sepsis, together accounting for about half of cases. Notable differences were observed in the sensitivity and specificity of sepsis screening tools with the highest to lowest sensitivity being SIRS, MEW, and qSOFA criteria, and the highest to lowest specificity being qSOFA, MEW, and SIRS. Mortality was doubled in the cohort of patients who received antibiotics after >1 hour. Clinicians need to be vigilant to identify cases of peripartum sepsis early in its course and prioritize timely antibiotic therapy.

Beigel JH, Aga E, Elie-Turenne MC, Cho J, Tebas P, **Clark CL**, Metcalf JP, Ozment C, Raviprakash K, Beeler J, Holley HP, Warner S, Chorley C, Lane HC, Hughes MD, Davey RT and Team IRCS (2019). "Anti-influenza immune plasma for the treatment of patients with severe influenza A: A randomised, double-blind, phase 3 trial." [Lancet Respiratory Medicine](#) 7(11): 941-950.

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Department of Emergency Medicine

Background: Infection with influenza virus causes substantial morbidity and mortality globally, although antiviral treatments are available. Previous studies have suggested that anti-influenza immune plasma could be beneficial as treatment, but they were not designed as randomised, blinded, placebo-controlled trials. Therefore, we aimed to prospectively evaluate the clinical efficacy of high-titre immune plasma compared

with standard low-titre plasma to improve outcomes in patients with severe influenza A infection. Methods: We did this randomised, double-blind, phase 3 trial at 41 US medical centres to assess the efficacy of high-titre anti-influenza plasma (haemagglutination inhibition antibody titre $\geq 1:80$) compared with low-titre plasma ($\leq 1:10$). Children and adults with PCR-confirmed influenza A infection, a National Early Warning score of 3 or greater, and onset of illness within 6 days before randomisation were eligible. Patients were randomly assigned (2:1) using an interactive web response system to receive either two units (or paediatric equivalent) of high-titre plasma (high-titre group) or low-titre plasma (low-titre group), and were followed up for 28 days from randomisation. High-titre and low-titre plasma had the same appearance. Randomisation was stratified by severity (in intensive care unit, not in intensive care but requiring supplemental oxygen, or not in intensive care and not requiring supplemental oxygen) and age (< 18 years and ≥ 18 years). All participants, site staff, and the study team were masked to treatment allocation until after the final database lock. The primary endpoint was clinical status assessed by a six-point ordinal scale on day 7 (death, in intensive care, hospitalised but requiring supplemental oxygen, hospitalised not requiring supplemental oxygen, discharged but unable to resume normal activities, and discharged with full resumption of normal activities) analysed in a proportional odds model (an odds ratio [OR] > 1 indicates improvement in clinical status across all categories for the high-titre vs the low-titre group). The primary analysis was done in the intention-to-treat population, excluding two participants who did not receive plasma. This trial is registered with ClinicalTrials.gov, NCT02572817. Findings: Participants were recruited between Jan 26, 2016, and April 19, 2018. Of 200 participants enrolled (177 adults and 23 children), 140 met the criteria for randomisation and were assigned to the high-titre group (n=92) or to the control low-titre group (n=48). One participant from each group did not receive plasma. At baseline, 60 (43%) of 138 participants were in intensive care and 55 (71%) of 78 participants who were not in intensive care required oxygen. 93% of planned plasma infusions were completed. The study was terminated in July, 2018, when independent efficacy analysis showed low conditional power to detect an effect of high-titre plasma even if full accrual (150 participants) was achieved. The proportional OR for improved clinical status on day 7 was 1.22 (95% CI 0.65-2.29, $p=0.54$). 47 (34%) of 138 participants experienced 88 serious adverse events: 32 (35%) with 60 events in the high-titre group and 15 (32%) with 28 events in the low-titre group. The most common serious adverse events were acute respiratory distress syndrome (ARDS; four [4%] vs two [4%]), allergic transfusion reactions (two [2%] vs two [4%]), and respiratory distress (three [3%] vs none). 65 (47%) participants experienced 183 adverse events: 42 (46%) with 126 events in the high-titre group and 23 (49%) with 57 events in the low-titre group. The most common adverse events were anaemia (four [3%] vs two [4%]) and ARDS (four [3%] vs three [5%]). Ten patients died during the study (six [7%] in the high-titre group vs four [9%] in the low-titre group, $p=0.73$). The most common cause of death was worsening of acute respiratory distress syndrome (two [2%] vs two [4%] patients). Interpretation High-titre anti-influenza plasma conferred no significant benefit over non-immune plasma. Although our study did not have the precision to rule out a small, clinically relevant effect, the benefit is insufficient to justify the use of immune plasma for treating patients with severe influenza A.

Bono MJ and **Reygaert WC** (2019). "Urinary Tract Infection." [StatPearls](#). Treasure Island (FL): StatPearls Publishing. [Full Text](#)

Department of Foundational Medical Studies (OU)

Uncomplicated urinary tract infection (UTI) is a bacterial infection of the bladder and associated structures. These are patients with no structural abnormality and no comorbidities, such as diabetes, immunocompromised, or pregnant. Uncomplicated UTI is also known as cystitis or lower UTI. Forty percent of women in the United States will develop a UTI during their lifetime, making it one of the most common infections in women. UTI is uncommon in circumcised males, and by definition, any male UTI is considered complicated. Many cases of uncomplicated UTI will resolve spontaneously, without treatment, but many patients seek treatment for symptoms. Treatment is aimed at preventing spread to the kidneys or developing into upper tract disease/pyelonephritis, which can cause the destruction of the delicate structures in the nephrons and lead to hypertension.[1][2][3] E.coli causes the majority of UTI but other organisms of importance include proteus, klebsiella, and enterococcus. The diagnosis of UTI is made from the clinical history and urinalysis, but the proper collection of the urine sample is important.

Brackney A, Berger D and Shook D (2019). "Can bedside cardiac ultrasound better predict the need for escalation of

care compared to computed tomography in patients with pulmonary embolisms?" Annals of Emergency Medicine 74(4): S145-S145.

[Full Text](#)

Department of Emergency Medicine

Brisson RJ, Kochanny S, Arshad S, Dekker A, DeSouza JA, Saloura V, Vokes EE and Seiwert TY (2019). "A pilot study of the pan-class I PI3K inhibitor buparlisib in combination with cetuximab in patients with recurrent or metastatic head and neck cancer." Head and Neck 41(11): 3842-3849.

[Full Text](#)

OUWB Medical Student Author

Background: This study assessed the maximum tolerated dose (MTD) of the PI3K inhibitor buparlisib given concurrently with cetuximab in recurrent and metastatic (R/M) head and neck squamous cell carcinoma (HNSCC). Methods: Twelve patients with R/M HNSCC were enrolled. Patients were given oral buparlisib starting day 7 and daily thereafter. The dose of buparlisib was escalated in a 3 + 3 design followed by a dose expansion cohort of 6 patients. The MTD of buparlisib per protocol was 100 mg daily with cetuximab given intravenously every 14 days starting day 0. Results: Ten patients had ≥ 2 previous treatment regimens (11 with prior cetuximab). There were no dose limiting toxicities observed during dose escalation. One patient achieved a partial response and 4 achieved stable disease. Conclusion: Based on this pilot study, buparlisib at 100 mg daily plus cetuximab proved to be well-tolerated. Patients previously treated with cetuximab monotherapy showed benefit from this combination.

Bulica B, Sidiropoulos C, Mahajan A, **Zillgitt A**, Kaminski P and Bowyer SM (2019). "Sensorimotor integration and GABA-ergic activity in embouchure dystonia: An assessment with magnetoencephalography." Tremor and Other Hyperkinetic Movement 2019: 9.

[Full Text](#)

Department of Neurology

Background: Embouchure dystonia (ED) is a task-specific dystonia affecting musicians thought to be related to alteration in sensorimotor processing and loss of cortical inhibition. Case Report: Magnetoencephalography-coherence source imaging (MEG-CSI) was used to map connectivity between brain regions by imaging neuronal oscillations that are coherent across the brain in patient with ED at rest and while using the index finger to evoke dystonia normally triggered by playing the flute. Discussion: During rest, there was increased coherence in the bilateral frontal and parietal regions that became more focal during dystonia. Diffuse hyperexcitability and increased coherence persisted in bilateral parietal regions as well as the bilateral frontal regions.

Burns WP, Hartman ND, Weygandt PL, **Jones SC**, Caretta-Weyer H and Moore KG (2019). "Critical electrocardiogram curriculum: Setting the standard for flipped-classroom EKG instruction." The Western Journal of Emergency Medicine 21(1): 52-57.

[Full Text](#)

Department of Emergency Medicine

Introduction: Electrocardiogram (EKG) interpretation is integral to emergency medicine (EM). In 2003 Ginde et al. found 48% of emergency medicine (EM) residency directors supported creating a national EKG curriculum. No formal national curriculum exists, and it is unknown whether residents gain sufficient skill from clinical exposure alone. Methods: The authors sought to assess the value of this EKG curriculum, which provides exposure to critical EKG patterns, a framework for EKG interpretation when the diagnosis is not obvious, and implementation guidelines and open access to any interested residency. The Foundations of Emergency Medicine (FoEM) EKG I course launched in January 2016, followed by EKG II in July 2017; they are benchmarked to post-graduate year 1 (PGY) and PGY2 level learners, respectively. Selected topics included 15 published critical EKG diagnoses and 33 selected by the authors. Cases included presenting symptoms, EKGs, and Free Open Access Medical Education (FOAM) links. Full EKG interpretations and question answers were provided. Results: Enrollment during 2017-2018 included 37 EM residencies with 663 learners in EKG I and 22 EM residencies with 438 learners in EKG II. Program leaders and learners were surveyed annually. Leaders indicated that content was appropriate for intended PGY levels. Leaders and learners indicated the curriculum improved the ability of learners to interpret EKGs while working in the emergency department

(ED). Conclusion: There is an unmet need for standardization and improvement of EM resident EKG training. Leaders and learners exposed to FoEM EKG courses report improved ability of learners to interpret EKGs in the ED.

Chen CJ, Lee CC, Ding D, Tzeng SW, Kearns KN, Kano H, Atik A, Ironside N, Joshi K, Huang PP, Kondziolka D, Mathieu D, Iorio-Morin C, **Grills IS**, Quinn TJ, Siddiqui Z, Marvin K, Feliciano C, Faramand A, Starke RM, Barnett G, Lunsford LD and Sheehan JP. (2019). "Stereotactic radiosurgery for unruptured versus ruptured pediatric brain arteriovenous malformations." *Stroke* 50(10): 2745-2751.

[Request Form](#)

Department of Radiation Oncology

Background and Purpose: The effects of prior hemorrhage on stereotactic radiosurgery (SRS) outcomes for pediatric arteriovenous malformations (AVMs) are not well defined. The aim of this multicenter, retrospective cohort study is to compare the SRS outcomes for unruptured versus ruptured pediatric AVMs. Methods: The International Radiosurgery Research Foundation pediatric AVM database from 1987 to 2018 was reviewed retrospectively. Favorable outcome was defined as AVM obliteration, no post-SRS hemorrhage, and no permanently symptomatic radiation-induced changes. Associations between prior hemorrhage and outcomes were adjusted for baseline differences, inverse probability weights, and competing risks. Results: The study cohort comprised 153 unruptured and 386 ruptured AVMs. Favorable outcome was achieved in 48.4% and 60.4% of unruptured and ruptured AVMs, respectively (adjusted odds ratio, 1.353; P=0.190). Cumulative AVM obliteration probabilities were 51.2%, 59.4%, 64.2%, and 70.0% for unruptured and 61.0%, 69.3%, 74.0%, and 79.3% for ruptured AVMs at 4, 6, 8, and 10 years, respectively (subhazard ratio, 1.311; P=0.020). Cumulative post-SRS hemorrhage probabilities were 4.5%, 5.6%, 5.6%, and 9.8% for unruptured and 4.7%, 6.1%, 6.1%, and 10.6% for ruptured AVMs at 4, 6, 8, and 10 years, respectively (subhazard ratio, 1.086; P=0.825). Probabilities of AVM obliteration (adjusted subhazard ratio, 0.968; P=0.850) and post-SRS hemorrhage (adjusted subhazard ratio, 1.663; P=0.251) were comparable between the 2 cohorts after inverse probability weight adjustments. Symptomatic (15.8% versus 8.1%; adjusted odds ratio, 0.400; P=0.008) and permanent (9.2% versus 5.0%; adjusted odds ratio, 0.441; P=0.045) radiation-induced change were more common in unruptured AVMs. Conclusions: The overall outcomes after SRS for unruptured versus ruptured pediatric AVMs are comparable. However, symptomatic and permanent radiation-induced change occur more frequently in pediatric patients with unruptured AVMs.

Chen S, David S, Khan Z, Patel N, Metzger DC, Wood F, Wasserman H, Lotfi A, **Hanson I, Dixon S**, Lalonde T, Genereux P, Ozan MO, Maehara A and Stone G (2019). "1-year outcomes of supersaturated oxygen therapy in acute anterior myocardial infarction: The IC-HOT study." *Journal of the American College of Cardiology* 74(13): B497-B497.

[Full Text](#)

Department of Internal Medicine

Chen Z, Chopp M, Zacharek A, **Li W**, Venkat P, Wang F, Landschoot-Ward J and Chen J (2019). "Brain-derived microparticles (BDMPs) contribute to neuroinflammation and lactadherin reduces BDMP induced neuroinflammation and improves outcome after stroke." *Frontiers in Immunology* 10: 2747.

[Full Text](#)

Department of Pathology

Microparticles (MPs, ~size between 0.1 and 1 μm) are lipid encased containers derived from intact cells which contain antigen from the parent cells. MPs are involved in intercellular communication and regulate inflammation. Stroke increases secretion of brain derived MP (BDMP) which activate macrophages/microglia and induce neuroinflammation. Lactadherin (Milk fat globule-EGF factor-8) binds to anionic phospholipids and extracellular matrices, promotes apoptotic cell clearance and limits pathogenic antigen cross presentation. In this study, we investigate whether BDMP affects stroke-induced neuroinflammation and whether Lactadherin treatment reduces stroke initiated BDMP-induced neuroinflammation, thereby improving functional outcome after stroke. Middle aged (8–9 months old) male C57BL/6J mice were subjected to distal middle cerebral artery occlusion (dMCAo) stroke, and BDMPs were extracted from ischemic brain 24 h after dMCAo by ultracentrifugation. Adult male C57BL/6J mice were subjected to dMCAo and treated via tail vein injection at 3 h after stroke with: (A) +PBS (n = 5/group); (B) +BDMPs (1.5 × 10⁸, n = 6/group); (C) +Lactadherin (400 μg/kg, n = 5/group); (D) +BDMP+Lactadherin (n = 6/group). A battery of

neurological function tests were performed and mice sacrificed for immunostaining at 14 days after stroke. Blood plasma was used for Western blot assay. Our data indicate: (1) treatment of Stroke with BDMP significantly increases lesion volume, neurological deficits, blood brain barrier (BBB) leakage, microglial activation, inflammatory cell infiltration (CD45, microglia/macrophages, and neutrophils) into brain, inflammatory factor (TNF α , IL6, and IL1 β) expression in brain, increases axon/white matter (WM) damage identified by decreased axon and myelin density, and increases inflammatory factor expression in the plasma when compared to PBS treated stroke mice; (2) when compared to PBS and BDMP treated stroke mice, Lactadherin and BDMP+Lactadherin treatment significantly improves neurological outcome, and decreases lesion volume, BBB leakage, axon/WM injury, inflammatory cell infiltration and inflammatory factor expression in the ischemic brain, respectively. Lactadherin treatment significantly increases anti-inflammatory factor (IL10) expression in ischemic brain and decreases IL1 β expression in plasma compared to PBS and BDMP treated stroke mice, respectively. BDMP increases neuroinflammation and aggravates ischemic brain damage after stroke. Thus, Lactadherin exerts anti-inflammatory effects and improves the clearance of MPs to reduce stroke and BDMP induced neurological deficits.

Chung KC, **Huynh KA** and Rohrich RJ (2019). "Common fallacies in designing a research project: Guidance principles." Plastic and Reconstructive Surgery 144(5): 1247-1253.

[Full Text](#)

OUWB Medical Student Author

Cordeiro D, Xu Z, Mehta GU, Ding D, Vance ML, Kano H, Sisterson N, Yang HC, Kondziolka D, Lunsford LD, Mathieu D, Barnett GH, Chiang V, Lee J, Sneed P, Su YH, Lee CC, Krsek M, Liscak R, Nabeel AM, El-Shehaby A, Karim KA, Reda WA, Martinez-Moreno N, Martinez-Alvarez R, Blas K, **Grills I, Lee KC**, Kosak M, Cifarelli CP, Katsevman GA and Sheehan JP (2019). "Hypopituitarism after Gamma Knife radiosurgery for pituitary adenomas: A multicenter, international study." Journal of Neurosurgery 131(4): 1188-1196.

[Full Text](#)

Department of Radiation Oncology

Objective: Recurrent or residual adenomas are frequently treated with Gamma Knife radiosurgery (GKRS). The most common complication after GKRS for pituitary adenomas is hypopituitarism. In the current study, the authors detail the timing and types of hypopituitarism in a multicenter, international cohort of pituitary adenoma patients treated with GKRS. Methods: Seventeen institutions pooled clinical data obtained from pituitary adenoma patients who were treated with GKRS from 1988 to 2016. Patients who had undergone prior radiotherapy were excluded. A total of 1023 patients met the study inclusion criteria. The treated lesions included 410 nonfunctioning pituitary adenomas (NFPAs), 262 cases of Cushing's disease (CD), and 251 cases of acromegaly. The median follow-up was 51 months (range 6–246 months). Statistical analysis was performed using a Cox proportional hazards model to evaluate factors associated with the development of new-onset hypopituitarism. Results: At last follow-up, 248 patients had developed new pituitary hormone deficiency (86 with NFPA, 66 with CD, and 96 with acromegaly). Among these patients, 150 (60.5%) had single and 98 (39.5%) had multiple hormone deficiencies. New hormonal changes included 82 cortisol (21.6%), 135 thyrotropin (35.6%), 92 gonadotropin (24.3%), 59 growth hormone (15.6%), and 11 vasopressin (2.9%) deficiencies. The actuarial 1-year, 3-year, 5-year, 7-year, and 10-year rates of hypopituitarism were 7.8%, 16.2%, 22.4%, 27.5%, and 31.3%, respectively. The median time to hypopituitarism onset was 39 months. In univariate analyses, an increased rate of new-onset hypopituitarism was significantly associated with a lower isodose line ($p = 0.006$, HR = 8.695), whole sellar targeting ($p = 0.033$, HR = 1.452), and treatment of a functional pituitary adenoma as compared with an NFPA ($p = 0.008$, HR = 1.510). In multivariate analyses, only a lower isodose line was found to be an independent predictor of new-onset hypopituitarism ($p = 0.001$, HR = 1.38). Conclusions: Hypopituitarism remains the most common unintended effect of GKRS for a pituitary adenoma. Treating the target volume at an isodose line of 50% or greater and avoiding whole-sellar radiosurgery, unless necessary, will likely mitigate the risk of post-GKRS hypopituitarism. Follow-up of these patients is required to detect and treat latent endocrinopathies.

Davis FM, Jerzal E, Albright J, Kazmers A, Monsour A, **Bove P** and Henke PK (2019). "Variation in the elective management of small abdominal aortic aneurysms and physician practice patterns." Journal of Vascular Surgery 70(4): 1089-1098.

[Request Form](#)

Department of Surgery

Objective: Recent vascular societal guidelines have recommended an abdominal aortic aneurysm (AAA) size threshold for elective intervention; however, limited data have documented how well these AAA diameter benchmarks are being met. The objective of this study was to analyze variation in management of AAAs based on diameter and to determine the physician's rationale for intervention on small AAAs in relation to recommended treatment guidelines. Methods: A retrospective review of a statewide vascular surgery registry of all elective endovascular or open surgical AAA repairs from January 2012 to January 2016 was performed. Patients were dichotomized on the basis of aortic diameter at time of intervention into either guideline size AAAs or small AAAs, which were defined as <5.5 cm in men, <5.0 cm in women, or with growth <1.0 cm/y. An internal review was conducted of all small AAAs to determine the physician's rationale for intervention. The primary outcomes were variation in adherence to recommended treatment guidelines and the physician's rationale for treatment of small AAAs. Risk-adjusted major complication and mortality rates were calculated at 30 days and 1 year using a propensity score matching analysis. Results: Among the 3932 patients who underwent an elective AAA repair, 485 (12.3%) were repaired at diameters smaller than recommended by guidelines. The median AAA size in the small AAA cohort was 5.1 cm (interquartile range, 4.7-5.3 cm) vs 5.6 cm (interquartile range, 5.2-6.1 cm) in the guideline-based group. Percentage of small AAA repairs varied widely between hospitals from 1.4% to 44.4%. The physician's rationale for the majority of early interventions included the patient's anxiety (12.0%), combined aortoiliac occlusive disease (14.8%), aneurysm anatomy (28.2%), and does not adhere to guidelines (30%). The small AAA cohort had no significant difference in the 30-day or 1-year risk-adjusted mortality in comparison to guideline size AAAs. Conclusions: Despite well-established aortic diameter threshold guidelines, marked variation exists both at the hospital level and in terms of the physician's rationale for the management of elective AAA repairs. These findings demonstrate the challenge of providing uniform care for patients with AAAs despite established guidelines.

Dokter J, Tennyson LE, Nguyen L, Han E and **Sirls LT** (2019). "The clinical rate of antibiotic change following empiric treatment for suspected urinary tract infections." [International Urology and Nephrology](#). ePub Ahead of Print.

[Full Text](#)

OUWB Medical Student Author

Department of Urology

Purpose: To determine the rate of antibiotic change in an outpatient setting following empiric treatment of culture proven UTI and to identify risk factors associated with change. Methods: Patients with suspected UTI and urine culture were reviewed (January 2016-June 2016). Those with a positive culture were categorized by whether or not they were treated empirically. Empiric treatment was evaluated for associations with clinical-demographic data, symptoms and urinalysis (UA). Antibiotic change was evaluated with clinical-demographic data, urine culture, and resistance patterns. Results: 916 urine cultures (636 patients) were included. 391 (43%) cultures were positive, and 164 (42%) were treated empirically. Clinical-demographic data did not differ between groups. Those treated empirically had more documented UTI symptoms (93 vs 58%, $P < 0.001$), and UA abnormalities including positive nitrites (51 vs 29%, $P < 0.001$), 3+ leukocyte esterase (27 vs 19%, $P = 0.002$) and 3+ blood (13 vs 4%, $P = 0.005$). Of those treated empirically, 42/164 (26%) required an antibiotic change, and this was associated with immunosuppression (12 vs 2%, $P = 0.027$) resistance to > 3 antibiotics (33 vs 20%, $P = 0.039$) and also resistance to fluoroquinolone (50 vs 30%, $P = 0.016$), monobactam (19 vs 7% $P = 0.042$) and TMP-SMX (52 vs 19%, $P < 0.001$). Conclusions: Almost one-quarter of patients treated empirically required antibiotic change. This was driven largely by bacterial resistance. New technologies allowing rapid bacterial identification and sensitivity may improve patient care.

Dombrowski D, **Long GW**, **Chan J** and **Brown OW** (2019). "Screening chest computed tomography is indicated in all patients with abdominal aortic aneurysm." [Annals of Vascular Surgery](#). ePub Ahead of Print.

[Request Form](#)

Department of Surgery

OUWB Medical Student Author

Background: This study quantifies the prevalence of thoracic aortic aneurysm (TAA) in patients with known abdominal aortic aneurysm (AAA). Methods: A retrospective review of patients with a diagnosis of AAA from

January 2007 to December 2017 within Beaumont Health was undertaken. Radiology reports of abdominal ultrasound, computed tomography (CT), and magnetic resonance imaging were reviewed to identify patients with AAA. Of these, patients with a chest CT scan performed within 180 days before or after abdominal imaging were reviewed for diagnosis of TAA. AAA was defined as aortic diameter ≥ 30 mm, and TAA was defined as aortic diameter ≥ 40 mm. Results: The cohort included 218 patients with a chest CT scan performed within 180 days of initial diagnosis of AAA. The mean age at diagnosis of AAA was 74 years; 82 (37.6%) were women. There were no differences between men and women in the prevalence of diabetes mellitus, hypertension, hyperlipidemia, chronic obstructive pulmonary disease, tobacco use, and family history of aortic aneurysm. Forty concomitant AAAs and TAAs were detected, for an overall prevalence of 18.3%, with no significant difference between men and women (15% vs. 24%, $P = 0.07$). Women were diagnosed with AAA at an older age than men (76 vs. 73 years, $P = 0.01$) and had lower body mass index (23 vs. 26, $P = 0.01$), smaller maximum AAA diameter (36.5 vs. 40 mm, $P = 0.03$), and larger TAA (47 vs. 41 mm, $P = 0.01$). TAAs were classified by location: 47.5% (19/40), ascending; 32.5% (13/40), descending; and 20% (8/40), ascending and descending. Six patients had thoracoabdominal aortic aneurysms: 2 patients with extent II, 2 with extent III, and 2 with extent V. These patients were included in the overall analysis; excluding them resulted in a rate of concomitant AAA/TAA of 16%. No significant differences were noted in comorbidities or AAA size between the TAA/AAA and AAA only groups. Conclusions: TAAs appear to occur concomitantly with AAAs with significant frequency. Women appear to have larger TAA diameter than men, despite smaller sized AAA at diagnosis. These data support creating guidelines for obtaining a screening chest CT scan in all patients diagnosed with an AAA.

Edwards CT, Alslaim HS, Alebbini MM, **Evuomwan MO**, **Chan JC**, Hamouri S and **Novotny NM** (2019). "Contrasting esophageal coin removal in countries with different sized coins in circulation." International Journal of Pediatric Otorhinolaryngology 129: 109775.

[Full Text](#)

Department of Surgery

OUIB Medical Student Author

Farshad S, **Kanaan C**, Savedchuk S, Karmo DS, **Halalau A** and **Swami A** (2019). "Systemic lupus erythematosus (SLE) with acute nephritis, antineutrophil cytoplasmic antibody- (ANCA-) associated vasculitis, and thrombotic thrombocytopenic purpura (TTP): A rare case report with literature review." Case Reports in Rheumatology 2019: 8750306.

[Full Text](#)

Department of Internal Medicine

OUIB Medical Student Author

Thrombotic thrombocytopenic purpura (TTP) is a potentially fatal disorder that requires urgent identification and treatment. The association of TTP with systemic lupus erythematosus (SLE) and vasculitis has been reported, however, never simultaneously. A 33-year-old woman with a history of SLE presented with acute abdominal pain, fever, arthralgias, and skin rash. She had acute severe hypertension, diffuse abdominal tenderness, and petechial rash. Diagnostic work-up revealed active urine sediment with proteinuria and hematuria and elevated creatinine, anemia, and thrombocytopenia. She was diagnosed with acute lupus nephritis and early microangiopathic hemolytic anemia in the setting of hypertensive urgency and started on intravenous methylprednisolone 500 mg once a day. Within 48 hours, she developed shock with multiorgan dysfunction and succumbed to her illness. Laboratory tests later showed ADAMTS13 activity less than 10% consistent with TTP and p-antineutrophil cytoplasmic antibody (ANCA) positivity. Autopsy revealed small-vessel vasculitis of the visceral organs. Kidney biopsy demonstrated diffuse proliferative glomerulonephritis. This case illustrates the occurrence of SLE nephritis, p-ANCA vasculitis, and severe TTP with rapidly fatal course, and the importance of having a low threshold for initiating plasma exchange therapy. Here, we discuss the case and provide a literature review on cases of TTP with SLE and vasculitis.

Feldmann KJ, **Goldstein JA**, Marinescu V, **Dixon SR** and **Raff GL** (2019). "Disparate impact of ischemic injury on regional wall dysfunction in acute anterior vs inferior myocardial infarction." Cardiovascular Revascularization Medicine 20(11): 965-972.

[Full Text](#)

Department of Internal Medicine

Background: Acute transmural ischemia should induce similar magnitude of wall motion abnormality (WMA) in both anterior myocardial infarction (AMI) and inferior (IMI). However, patients with AMI generally suffer more severe hemodynamic compromise. Methods: This retrospective study compared WMA's in ST segment elevation MI patients undergoing primary reperfusion and subsequent cardiac MRI. Regional systolic wall motion and thickening were assessed in all segments throughout the left ventricle (LV). Results: We analyzed 37 patients (AMI=24 vs IMI=13). Reperfusion success was achieved in all and there were no differences between groups in door-to-balloon time (AMI median 77 vs IMI 119min, $p=0.085$). Compared to IMI, in AMI LV ejection fraction was more depressed ($37 \pm 7.6\%$ vs $51 \pm 10.3\%$, $P=0.0006$) and regional WMA more severe (total regional WMA score= 2.63 ± 0.53 vs 2.1 ± 0.52 , $P=0.007$). Regional dyskinesia was commonly observed in AMI patients but was rare in IMI (79% vs 7% of cases). Similarly, AMI manifested systolic thinning, whereas thickening was depressed but still present in IMI patients. Strikingly, WMA severity differed downstream relative to the origin of the infarct artery: In all AMI cases, WMA worsened from proximal anterior toward the distal apical zone; in IMI the pattern was reverse, with WMA consistently most severe in the basal segment of the inferior-posterior wall with preservation toward the apical distribution of the infarct vessel. Conclusion: These results demonstrate a disparate impact of ischemic injury on mechanical performance of the anterior vs inferior-posterior walls. These findings may be attributable to differences between the walls in architecture, mechanics and coronary blood flow. These observations may have implications for myocardial salvage, remodeling and prognosis.

Fernandez C, **Grills IS**, Ye H, Hope AJ, Guckenberger M, Mantel F, Kestin LL, Belderbos J and Werner-Wasik M (2019). "Stereotactic image-guided lung radiotherapy (SBRT) for clinical early-stage NSCLC: A long-term report from a multi-institutional database of patients treated with or without a pathologic diagnosis." Practical Radiation Oncology. ePub Ahead of Print.

[Full Text](#)

Department of Radiation Oncology

Objective: Early stage lung cancer is treated with stereotactic body radiotherapy (SBRT) in patients unfit or unwilling to undergo surgical resection. Some patients' comorbidities are so severe that they are unable to even undergo biopsy. Clinical diagnosis without biopsy before SBRT has been utilized, but there are limited data on its efficacy. Methods: Data on patients treated with SBRT for non-small cell lung cancer (NSCLC), with and without tissue confirmation, were collected from multiple institutions across Europe, Canada, and the United States. Patients with a minimum of two years of comprehensive follow up were selected for analysis. Treatment and patient characteristics were compared. Overall survival (OS), disease-free survival (DFS), cause-specific survival (CSS), rates of local recurrence (LR), regional recurrence (RR), and distant metastasis (DM) were calculated and analyzed. Results: Seven hundred one patients were identified, of which 67% had tissue confirmation of their tumors. OS, CSS, and DFS three and five-year outcomes were 83.8%, 93.1%, 69%, and 60.6%, 86.7%, 45.5%, respectively. LR, RR, and DM rates at three and five-years were 6.4%, 9.3%, 14.3%, and 10.5%, 14.3%, 19.7%, respectively. There were no statistically significant differences in survival outcomes or recurrences between the biopsy and no biopsy cohorts. Conclusions: SBRT for clinically diagnosed lung cancers is efficacious in appropriately selected patients, with similar outcomes as those with pathologic diagnosis. Thorough clinical and radiographic evaluation in a multidisciplinary setting is critical to the management of these patients.

Fidler J, Soto J, Al-Hawary M, Allen B, Brook O, Gee M, Grand D, Guglielmo F, Gupta A, Gunn M, Khandelwal A, Ramalingam V, **Sokhandon F**, Wells M, Park SH, Huete A, Strate L and Bruining D (2019). "SAR GI bleeding DFP annual report." Abdominal Radiology 44(12): 3998-3999.

[Full Text](#)

Department of Diagnostic Radiology and Molecular Imaging

Flierl MA, Sobh AH, Culp BM, **Baker EA** and Sporer SM (2019). "Evaluation of the painful total knee arthroplasty." Journal of the American Academy of Orthopaedic Surgeons 27(20): 743-751.

[Request Form](#)

Department of Orthopaedic Surgery

Total knee arthroplasty (TKA) has been associated with notable improvements in health-related quality of life

of patients with end-stage knee arthritis. Although most patients experience substantial symptomatic relief after TKA, up to 19% of patients are unsatisfied with their outcome. With the dramatic, projected increase in the number of TKAs performed annually, it is crucial to appreciate the various modes of failure associated with this procedure. A comprehensive understanding of the symptomatology and thorough clinical examination aid in identifying the etiology of ongoing knee pain. Ancillary testing including conventional laboratory analyses, imaging studies, and diagnostic injections supplement a thorough history and physical examination. In addition, novel laboratory markers, RNA/DNA-based tests, and novel imaging modalities are emerging as beneficial tools in evaluating patients with a painful TKA. A well-structured, algorithmic approach in the management of these patients is essential in correctly diagnosing the patient and optimizing clinical outcomes.

Fritz CG, Bojrab DI, Lin KF, Schutt CA, Babu SC and Hong RS (2019). "Surgical explantation of bone-anchored hearing devices: A 10-year single institution review." Otolaryngology-Head and Neck Surgery 162(1): 95-101.

[Full Text](#)

OUWB Medical Student Author

Department of Surgery

Objective: To identify clinical variables associated with the decision to surgically discontinue bone-anchored hearing device function. Study Design Retrospective chart review. Setting Tertiary neurotology referral center. Subjects and Methods: This study examines surgical interventions performed on existing bone-anchored hearing devices at a single institution from 2008 to 2018. Patient characteristics, indications for implantation, and complications prompting surgical intervention were assessed. Results: Seventy-seven cases were included in this study. Among patients in the younger cohort (<37 years old), 100% (13 of 13) of those discontinuing their device had a contralateral normal-hearing ear. Conversely, 0% (0 of 14) of the younger patients with bilateral hearing loss surgically discontinued their devices. Within the older cohort (>= 37 years old), female patients (P = .002) and those with an increased body mass index (P = .035) were more likely to surgically discontinue their devices. Multivariate analysis revealed that a contralateral normal-hearing ear (P = .001) and infection without soft tissue overgrowth of the abutment (P = .026) were the strongest predictors of device discontinuation, after adjusting for potential confounders. Conclusion: Surgical discontinuation is associated with several clinical variables. Targeted interventions that are viable alternatives to removal, such as device relocation, should be presented to younger patients with a contralateral normal-hearing ear who experience persistent complications. Patients with persistent infection in the absence of soft tissue overgrowth would especially benefit from enhanced counseling on proper hygiene.

Gaines R, Mando R, Tucker C, **Hanzel G, Gallagher M, Shannon F and Abbas A** (2019). "Does energy loss index improve the comparison of echocardiographic-derived aortic valve area compared with invasively-derived aortic valve area pre-TAVR?" Journal of the American College of Cardiology 74(13): B147-B147.

[Full Text](#)

Department of Internal Medicine

Department of Surgery

Gajecka M, Vishweswaraiah S, Karolak JA, Mrugacz M, Ratnamala U, Mishra NK, Guda C, Chettiar SS, Johar KR, **Radhakrishna U** and Swierkowska J (2019). "Hypermethylated genes and pathways in Polish children with high myopia." European Journal of Human Genetics 27: 1228-1228.

[Request Form](#)

Department of Obstetrics & Gynecology

Ginsburg KB, Schwabe JR, Cochrane JA, Tapper A, **Burks F** and Rambhatla A (2019). "Low serum albumin correlates with adverse events following surgery for male urinary incontinence: Analysis of the American College of Surgeons National Surgical Quality Improvement Project." Urology. ePub Ahead of Print.

[Full Text](#)

Department of Urology

Objective: To investigate the incidence and risk factors associated with artificial urinary sphincter (AUS) and male urethral sling placement (MUS), revision, and removal. Methods: We identified CPT codes of patients undergoing AUS and sling placement, revision, and removal in the American College of Surgeons National

Surgery Quality Improvement Program database. Bivariate analysis was used to compare preoperative parameters against adverse events of interest (Length of stay (LOS) >1, readmission, reoperation, other postoperative complications, and death). Variables that were significant or neared significance ($P < .1$) in the univariate analysis were entered into multivariable logistic regression models. Multivariable models were used to estimate the probability of adverse events. Results: About 2792 patients underwent surgical treatment for stress urinary incontinence in the American College of Surgeons National Surgery Quality Improvement Program database from 2008 to 2016. Increased length of stay was the most common adverse event (12.7%), followed by other postoperative complications (4.9%), readmission (4%), reoperation (2.3%), and death (0.3%). We noted an association between perioperative adverse events and preoperative hypoalbuminemia. Patients with preoperative hypoalbuminemia compared with patients with normal preoperative serum albumin had an increase predicted probability of LOS >1 day (42% vs 10%), readmission (10% vs 4%), reoperation (6% vs 2%), other postoperative complications (18% vs 4%) after adjusting for other factors. Conclusion: Surgical treatment for stress urinary incontinence is well tolerated with acceptable levels of perioperative adverse events. Low serum albumin (<3.5 ng/dL) was associated with perioperative adverse events. These data may affect preoperative decision making and direct future quality improve efforts at the highest risk patients to help minimize perioperative morbidity and mortality.

Gisriel S, Haberichter K, Huang S and **Huang J** (2019). "Utility of flow cytometry in the diagnostic evaluation of recurrent or persistent nodular lymphocyte-predominant Hodgkin lymphoma." *American Journal of Clinical Pathology* 152: S108-S108.

[Request Form](#)

Department of Pathology

Gnanenthiran SR, Naoum C, Leipsic JA, Achenbach S, Al-Mallah MH, Andreini D, Bax JJ, Berman DS, Budoff MJ, Cademartiri F, Callister TQ, Chang HJ, **Chinnaiyan K**, Chow BJW, Cury RC, DeLago A, Feuchtner G, Hadamitzky M, Hausleiter J, Kaufman PA, Kim YJ, Maffei E, Marques H, Goncalves PD, Pontone G, **Raff GL**, Rubinshtein R, Shaw LJ, Villines TC, Gransar H, Lu Y, Jones EC, Pena JM, Lin FY, Kritharides L and Min JK (2019). "Long-term prognostic utility of computed tomography coronary angiography in older populations." *European Heart Journal-Cardiovascular Imaging* 20(11): 1279-1286.

[Full Text](#)

Department of Internal Medicine

Aims: The long-term prognostic value of coronary computed tomography angiography (CCTA)-identified coronary artery disease (CAD) has not been evaluated in elderly patients (≥ 70 years). We compared the ability of coronary CCTA to predict 5-year mortality in older vs. younger populations. **Methods and Results:** From the prospective CONFIRM (COronary CT Angiography Evaluation For Clinical Outcomes: An International Multicenter) registry, we analysed CCTA results according to age <70 years ($n = 7198$) vs. ≥ 70 years ($n = 1786$). The severity of CAD was classified according to: (i) maximal stenosis degree per vessel: none, non-obstructive (1-49%), or obstructive ($>50\%$); (ii) segment involvement score (SIS): number of segments with plaque. Cox-proportional hazard models assessed the relationship between CCTA findings and time to mortality. At a mean 5.6 \pm 1.1 year follow-up, CCTA-identified CAD predicted increased mortality compared with patients with a normal CCTA in both <70 years [non-obstructive hazard ratio (HR) confidence interval (CI): 1.70 (1.19-2.41); one-vessel: 1.65 (1.03-2.67); two-vessel: 2.24 (1.21-4.15); three-vessel/left main: 4.12 (2.27-7.46), $P < 0.001$] and ≥ 70 years [non-obstructive: 1.84 (1.15-2.95); one-vessel: HR (CI): 2.28 (1.37-3.81); two-vessel: 2.36 (1.33-4.19); three-vessel/left main: 2.41 (1.33-4.36), $P = 0.014$]. Similarly, SIS was predictive of mortality in both <70 years [SIS 1-3: 1.57 (1.10-2.24); SIS ≥ 4 : 2.42 (1.65-3.57), $P < 0.001$] and ≥ 70 years [SIS 1-3: 1.73 (1.07-2.79); SIS ≥ 4 : 2.45 (1.52-3.93), $P < 0.001$]. CCTA findings similarly predicted long-term major adverse cardiovascular outcomes (MACE) (all-cause mortality, myocardial infarction, and late revascularization) in both groups compared with patients with no CAD. **Conclusion:** The presence and extent of CAD is a meaningful stratifier of long-term mortality and MACE in patients aged <70 years and ≥ 70 years old. The presence of obstructive and non-obstructive disease and the burden of atherosclerosis determined by SIS remain important predictors of prognosis in older populations.

Goyal A and **Salman B** (2019). "Case 2: Chronic testicular torsion in a healthy neonate." *NeoReviews* 20(11): e667-

e669.

[Request Form](#)

Department of Pediatrics

Goyal A and **Salman B** (2019). "Index of suspicion in the nursery." *NeoReviews* 20(11): e667-e669.

[Request Form](#)

Department of Pediatrics

Gralow JR, Barlow WE, Paterson AHG, Miao JL, Lew DL, Stopeck AT, Hayes DF, Hershman DL, Schubert MM, Clemons M, Van Poznak CH, Dees EC, Ingle JN, Falkson CI, Elias AD, Messino MJ, **Margolis JH**, Dakhil SR, Chew HK, Dammann KZ, Abrams JS, Livingston RB and Hortobagyi GN (2019). "Phase III randomized trial of bisphosphonates as adjuvant therapy in breast cancer: S0307." *Journal of the National Cancer Institute*. ePub Ahead of Print.

[Full Text](#)

Department of Internal Medicine

Background: Adjuvant bisphosphonates, when given in a low estrogen environment, can decrease breast cancer recurrence and death. Treatment guidelines include recommendations for adjuvant bisphosphonates in postmenopausal patients. SWOG/Alliance/Canadian Cancer Trials Group/ECOG-ACRIN/NRG Oncology study S0307 compared the efficacy of three bisphosphonates in early stage breast cancer. Methods: Patients with stage I-III breast cancer were randomized to 3 years of intravenous zoledronic acid, oral clodronate, or oral ibandronate. The primary endpoint was disease-free survival (DFS) with overall survival (OS) a secondary outcome. All statistical tests were two-sided. Results: 6,097 patients enrolled. Median age was 52.7 years. Prior to randomization, 73.2% of patients indicated preference for oral versus intravenous formulation. DFS did not differ across arms in a log-rank test ($p = 0.49$). 5-year DFS was 88.3% (zoledronic acid, 95% CI 86.9%-89.6%), 87.6% (clodronate, 95% CI 86.1%-88.9%), and 87.4% (ibandronate, 95% CI 85.6%-88.9%). 5-year OS also did not differ between arms (log rank $p = 0.50$) and was 92.6% (zoledronic acid, 95% CI 91.4%-93.6%), 92.4% (clodronate 95% CI 91.2%-93.5%), and 92.9% (ibandronate 95% CI 91.5%-94.1%). Bone as first site of recurrence did not differ between arms ($P = 0.93$). Analyses based on age and tumor subtypes showed no treatment differences. Grade 3/4 toxicity was 8.8% (zoledronic acid), 8.3% (clodronate), and 10.5% (ibandronate). Osteonecrosis of the Jaw (ONJ) was highest for zoledronic acid (1.26%), compared to clodronate (0.36%) and ibandronate (0.77%). Conclusions: We found no evidence of differences in efficacy by type of bisphosphonate, either in overall analysis or subgroups. Despite an increased rate of ONJ with zoledronic acid, overall toxicity grade differed little across arms. Given that patients expressed preference for oral formulation, efforts to make oral agents available in the U.S. should be considered.

Grewal DS, Charles S, Parolini B, Kadonosono K and **Mahmoud TH** (2019). "Autologous retinal transplant for refractory macular holes: Multicenter international collaborative study group." *Ophthalmology* 126(10): 1399-1408.

[Full Text](#)

Department of Ophthalmology

Purpose: To report the structural and functional outcomes of autologous neurosensory retinal transplant for closure of refractory large macular holes (MHs). Design: Multicenter, retrospective, consecutive case series. Participants: A total of 41 eyes of 41 patients with a full-thickness MH refractory to prior vitrectomy with internal limiting membrane (ILM) peel and tamponade. Methods: All patients underwent pars plana vitrectomy, autologous neurosensory retinal transplant with gas, silicone oil tamponade, or short-term perfluoro-n-octane heavy-liquid tamponade. All patients had at least 6 months' follow-up. Main Outcome Measures: Anatomic closure of MH, change in ellipsoid zone (EZ) and external limiting membrane (ELM) defect on OCT, visual acuity (VA) recovery, and surgical complications were analyzed. Results: Mean number of prior surgeries was 1.5 +/- 0.94 (range, 1-3), and patients were followed for a mean of 11.1 +/- 7.7 months (range, 6-36 months). Complete anatomic closure of MH by OCT was achieved in 36 of 41 eyes (87.8%). Mean corrected VA (logarithm of the minimum angle of resolution [logMAR]) improved ($P = 0.03$) from 1.11 +/- 0.66 (range, 0.48-3) to 1.03 +/- 0.51 (range, 0.1-2) at the last postoperative visit. The VA improved (≥ 0.3 logMAR units) in 15 eyes (36.6%), was stable in 17 eyes (41.5%), and worsened in 9 eyes (21.9%). Among eyes with anatomic closure, VA improved in 52.3% and worsened in 13.8%, whereas in those without closure, VA worsened in 40% and improved in none. Mean preoperative largest basal diameter was 1468.1 +/- 656.4 μ m (range, 621-2600 μ m), and mean inner-opening diameter was 825 +/- 422.5 μ m (range, 336-1649 μ m).

mu m). Mean preoperative EZ defect was 1777.3 +/- 513.8 mu m (range, 963-2808 mu m), which decreased to 1370 +/- 556.9 mu m (range, 288-2000 mu m) at final follow-up (P = 0.007). Mean preoperative ELM was 1681.5 +/- 429 mu m (range, 1172-2606 mu m), which decreased to 1408.5 +/- 571.2 mu m (range, 200-2000 mu m) at final follow-up (P = 0.017). Major postoperative complications were retinal detachment (n = 1) and vitreous hemorrhage (n = 1). There were no cases of proliferative vitreoretinopathy, endophthalmitis, suprachoroidal hemorrhage, or choroidal neovascularization. Conclusions: The autologous retinal transplant technique offers a high degree of anatomic success and proved safe in this initial experience for closure of refractory MHs.

Grunberger G (2019). "Fred W. Whitehouse, MD, MACP (1926–2019)." [Diabetes Care](#) 42(12): 2167-2170.

[Full Text](#)

Department of Internal Medicine

Grunberger G, Rosenfeld CR, Bode BW, Abbott SD, Nikkel C, Shi L and Strange P (2019). "Effectiveness of V-Go((R)) for patients with type 2 diabetes in a real-world setting: A prospective observational study." [Drugs Real World Outcomes](#). ePub Ahead of Print.

[Full Text](#)

Department of Internal Medicine

Background: V-Go is a wearable, patch-like, 24-h insulin delivery device that delivers both a continuous preset basal rate and on-demand bolus dosing. The aim of this study was to observe glycemic control, insulin dosing, and hypoglycemia risk in patients switched to V-Go in a real-world setting. The primary objective was to compare change in mean hemoglobin A1c (HbA1c) from baseline to the end of V-Go use. Methods: This prospective, open-label, multicenter study recruited patients with type 2 diabetes (T2D) and suboptimal glycemic control (HbA1c \geq 7%) across 28 centers. Efficacy analyses were conducted for all patients with a post-baseline HbA1c and results stratified based on prior antihyperglycemic medication therapies. Insulin dosing was at the discretion of the health care provider and the protocol did not mandate glycemic targets. Treatment satisfaction surveys were utilized to gain patient feedback on the use of V-Go. Results: One hundred eighty-eight patients were enrolled in the study, among whom 140 patients had a valid post-baseline HbA1c and were included in the primary efficacy analysis. Use of V-Go resulted in a change of - 0.64%; (P = 0.003) in HbA1c from baseline, and in those prescribed insulin, the total daily dose of insulin was decreased by 12 units/day (P < 0.0001). Twenty-two patients (12%) reported hypoglycemic events (\leq 70 mg/dL), with an event rate of 1.51 events/patient/year. Conclusion: In a T2D population with suboptimal HbA1c, initiating V-Go therapy in a real-world setting significantly improved glycemic control and led to significant insulin dose reductions. ClinicalTrials.gov registry identifier: NCT01326598.

Gulati S and Boland MV (2019). "Association of surgical setting and deployment of a new electronic health record with ophthalmic operative times." [JAMA Ophthalmology](#) 137(9): 969-974.

[Full Text](#)

OUWB Medical Student Author

Importance: Determining the association of surgical setting and implementation of a new electronic health record (EHR) system with ophthalmic operative times is important for surgical planning and resource allocation. Objective: To assess the associations of surgical setting and EHR system replacement with operative times for ophthalmic surgery. Design, Setting, and Participants: This case series included ophthalmic surgeries from July 2015 to November 2016 in 2 ambulatory surgical centers and 1 hospital outpatient department in a single academic eye institute. Operative times from consecutive surgical cases performed by board-certified ophthalmologists were extracted from 2 EHR systems. Those performed after replacement EHR system implementation were divided into three 50-day time categories (immediate posttransition, intermediate posttransition, and late posttransition periods). Multivariable regression analyses assessed the associations of surgical setting (hospital outpatient department vs ambulatory surgical center) with total operating room times for comparable surgeons performing cataract surgery and deployment of a new EHR system in the OR on several operative time measures. Data were evaluated from November 2016 to March 2018. Main Outcomes and Measures: Room duration, procedure duration, turnaround time, and total OR time. Results: A total of 11064 cases performed by 76 surgeons were included in this analysis. The mean total OR time was 2.9 (95% CI, 0.5-5.4; P =.02) minutes longer in the immediate posttransition period and 1.2

(95% CI, 0.1-2.2; P = .04) minutes longer in the intermediate posttransition period relative to surgeries performed before EHR system replacement. No difference in the total OR time was found between the late posttransition and pretransition periods. Relative to ambulatory surgical centers, the mean total OR time was 15.9 (95% CI, 14.7-17.0) minutes longer, and the mean turnaround time was 5.1 (95% CI, 4.3-6.0) minutes longer at the hospital outpatient department for comparable surgeons performing cataract surgery (P < .001 for both). Conclusions and Relevance: The mean total OR time per case lengthened after the replacement of an EHR system in the OR, but this increase was small (shorter than 3 minutes) and limited to surgeries performed during the first 100 days after the EHR system transition. Modeling to assess surgical setting demonstrated all operative time measures were longer for cataract cases performed at the hospital outpatient department relative to those at ambulatory surgical centers. These data have implications for the fiscal and logistical management of ophthalmic surgery.

Gupta A, **Menoch M, Levasseur K and Gonzalez IE** (2019). "Screening pediatric patients in new-onset syncope (SPINS) study." Clinical Pediatrics 59(2): 127-133.

[Full Text](#)

Department of Pediatrics

Objectives: The primary objective is to determine the frequency of history findings associated with cardiac syncope. Second, to determine the frequency of abnormal electrocardiograms (EKG) in patients presenting with typical vasovagal syncope. Methods: Retrospective chart review from January 2006 to April 2017 of children aged 5 to 18 years presenting to the emergency department with a chief complaint of syncope. Target population was all patients with first episode of syncope and a documented EKG. Excluded patients were those with head trauma, drug intoxication, current pregnancy, seizure, and any endocrine problem. Patients with cardiac causes of syncope were identified by an abnormal EKG or echocardiogram. Specific history findings (past cardiac history, chest pain, palpitations, syncope with exercise, absence of prodrome with syncope) were compared with those with and without cardiac etiology of syncope. The possibility of missing a patient with cardiac cause of syncope based on specific history findings was identified. Results: Of the total 4115 visits of patients with chief complaints of syncope, 2293 patients (55.7%) met the inclusion criteria. Nine patients (0.39%) were identified with cardiac etiology of syncope. The remaining were determined to be of vasovagal origin. All patients with cardiac etiology of syncope were found to have one positive specific history findings. A total of 1972 patients were identified with absence of specific history findings; no patient had a cardiac etiology of syncope. Conclusions: This study identifies screening questions to identify cardiac syncope. Implementing these standard questions could potentially decrease resource utilization and time for evaluation as well as guide follow-up.

Hamstra DA, Pugh SL, Lepor H, Rosenthal SA, Pienta KJ, Gomella L, Peters C, D'Souza DP, Zeitzer KL, Jones CU, Hall WA, Horwitz E, Pisansky TM, Souhami L, Hartford AC, Dominello M, Feng F and Sandler HM (2019). "Gleason pattern 5 is associated with an increased risk for metastasis following androgen deprivation therapy and radiation: An analysis of RTOG 9202 and 9902." Radiotherapy and Oncology 141: 137-143.

[Full Text](#)

Department of Radiation Oncology

Background/Purpose: Stratification of Gleason score (GS) into three categories (2–6, 7, and 8–10) may not fully utilize its prognostic discrimination, with Gleason pattern 5 (GP5) previously identified as an independent adverse factor. Materials/Methods: Patients treated on RTOG 9202 (n = 1292) or RTOG 9902 (n = 378) were pooled and assessed for association of GS and GP5 on biochemical failure (BF), local failure (LF), distant metastasis (DM), and overall survival (OS). Fine and Gray's regression and cumulative incidence methods were used for univariate and multivariate analyses. Results: With median follow-up of 9.4 years, patients with GS 8–10 with GP5 had worse outcome than GS 4 + 4 for DM on both RTOG9202 (p = 0.038) and RTOG9902 (p < 0.001) with a trend toward worse OS (p = 0.059 and p = 0.089, respectively), but without differences in BF or LF. At 10-years DM was higher by 11% (RTOG 9202) and 18% (RTOG 9902) with GP5 compared to GS 4 + 4. On multivariate analysis restricted to long-term androgen deprivation therapy the presence of GP5 substantially increased distant metastasis (HR = 0.43, 95%CI: 0.24–0.76, p = 0.0039) with a trend toward worse OS (HR:0.74, 95% CI:0.54–1.0, p = 0.052) without association with LF (HR:0.55, 95%CI:0.28–1.09, p = 0.085) or BF (HR:1.15, 95%CI:0.84–1.59, p = 0.39). We did not observed substantial differences between Gleason 3 + 5, 5 + 3, or Gleason 9–10. Conclusions: These results validate GP5 as an

independent prognostic factor which is strongest for DM. As a result GP5 should be considered when stratifying patients with GS 8 and may be a patient population in which to evaluate newly approved systemic therapies or additional local treatments. © 2019 Elsevier B.V.

Han DH, Beecy A, Anchouche K, Gransar H, Dunham PC, Lee JH, Achenbach S, Al-Mallah MH, Andreini D, Berman DS, Bax JJ, Budoff MJ, Cademartiri F, Callister TQ, Chang HJ, **Chinnaiyan K**, Chow BJW, Cury RC, DeLago A, Feuchtner G, Hadamitzky M, Hausleiter J, Kaufmann PA, Kim YJ, Leipsic JA, Maffei E, Marques H, Goncalves PD, Pontone G, **Raff GL**, Rubinshtein R, Villines TC, Lu Y, Pena JM, Shaw LJ, Min JK and Lin FY (2019). "Risk reclassification with coronary computed tomography angiography-visualized nonobstructive coronary artery disease according to 2018 American College of Cardiology/American Heart Association Cholesterol Guidelines (from the Coronary Computed Tomography Angiography Evaluation for Clinical Outcomes : An International Multicenter Registry CONFIRM)." [American Journal of Cardiology](#) 124(9): 1397-1405.

[Full Text](#)

Department of Internal Medicine

The 2018 American College of Cardiology (ACC)/American Heart Association (AHA) cholesterol management guideline recommends risk enhancers in the borderline-risk and statin recommended/intermediate-risk groups. We determined the risk reclassification by the presence and severity of coronary computed tomography angiography (CCTA)-visualized coronary artery disease (CAD) according to statin eligibility groups. Of 35,281 individuals who underwent CCTA, 1,303 asymptomatic patients (age 59, 65% male) were identified. Patients were categorized as low risk, borderline risk, statin recommended/intermediate risk or statin recommended/high risk according to the guideline. CCTA-visualized CAD was categorized as no CAD, nonobstructive, or obstructive. Major adverse cardiovascular events (MACE) were defined as a composite outcome of all-cause mortality, nonfatal myocardial infarction, and late coronary revascularization (>90 days). We tested a reclassification wherein no CAD reclassifies downward, and the presence of any CAD reclassifies upward. During a median follow-up of 2.9 years, 93 MACE events (7.1%) were observed. Among the borderline-risk and statin-recommended/intermediate-risk groups eligible for risk enhancers, the presence or absence of any CCTA-visualized CAD led to a net increase of 2.3% of cases and 22.4% of controls correctly classified (net reclassification index [NRI] 0.27, 95% CI 0.13 to 0.41, $p = 0.0002$). The NRI was not significant among low- or statin-recommended/high-risk patients (all $p > 0.05$). The presence or absence of CCTA-visualized CAD, including both obstructive and nonobstructive CAD, significantly improves reclassification in patients eligible for risk enhancers in 2018 ACC/AHA guidelines. Patients in low- and high-risk groups derive no significant improvement in risk reclassification from CCTA.

Hawryluk GWJ, Aguilera S, Buki A, Bulger E, Citerio G, Cooper DJ, Arrastia RD, Diringer M, Figaji A, Gao GY, Geocadin R, Ghajar J, Harris O, Hoffer A, Hutchinson P, Joseph M, Kitagawa R, Manley G, Mayer S, Menon DK, Meyfroidt G, **Michael DB**, Oddo M, Okonkwo D, Patel M, Robertson C, Rosenfeld JV, Rubiano AM, Sahuquillo J, Servadei F, Shutter L, Stein D, Stocchetti N, Taccone FS, Timmons S, Tsai E, Ullman JS, Vespa P, Videtta W, Wright DW, Zammit C and Chesnut RM (2019). "A management algorithm for patients with intracranial pressure monitoring: the Seattle International Severe Traumatic Brain Injury Consensus Conference (SIBICC)." [Intensive Care Medicine](#) 45(12).

[Full Text](#)

Department of Neurosurgery

Background: Management algorithms for adult severe traumatic brain injury (sTBI) were omitted in later editions of the Brain Trauma Foundation's sTBI Management Guidelines, as they were not evidence-based. Methods: We used a Delphi-method-based consensus approach to address management of sTBI patients undergoing intracranial pressure (ICP) monitoring. Forty-two experienced, clinically active sTBI specialists from six continents comprised the panel. Eight surveys iterated queries and comments. An in-person meeting included whole- and small-group discussions and blinded voting. Consensus required 80% agreement. We developed heatmaps based on a traffic-light model where panelists' decision tendencies were the focus of recommendations. Results: We provide comprehensive algorithms for ICP-monitor-based adult sTBI management. Consensus established 18 interventions as fundamental and ten treatments not to be used. We provide a three-tier algorithm for treating elevated ICP. Treatments within a tier are considered empirically equivalent. Higher tiers involve higher risk therapies. Tiers 1, 2, and 3 include 10, 4, and 3 interventions, respectively. We include inter-tier considerations, and recommendations for critical neuroworsening to assist the recognition and treatment of declining patients. Novel elements include

guidance for autoregulation-based ICP treatment based on MAP Challenge results, and two heatmaps to guide (1) ICP-monitor removal and (2) consideration of sedation holidays for neurological examination. Conclusions: Our modern and comprehensive sTBI-management protocol is designed to assist clinicians managing sTBI patients monitored with ICP-monitors alone. Consensus-based (class III evidence), it provides management recommendations based on combined expert opinion. It reflects neither a standard-of-care nor a substitute for thoughtful individualized management.

Healy C, Coughlan H, Williams J, Clarke M, Kelleher I and **Cannon M** (2019). "Changes in self-concept and risk of psychotic experiences in adolescence: A longitudinal population-based cohort study." Journal of Child Psychology and Psychiatry 60(11): 1164-1173.

[Full Text](#)

Department of Internal Medicine

Background: Psychotic experiences (PEs) are commonly reported in adolescence and are associated with a range of negative outcomes. Few targets for intervention for PEs have been identified. One potential target is self-concept: an individual's beliefs about his/her personal attributes. Improvements in self-concept have been shown to reduce psychotic symptoms in patients with schizophrenia but no study has investigated the relationship between changes in self-concept and risk of PEs in the general population. We aimed to investigate: (a) the relationship between child and adolescent self-concept and adolescent PEs; and (b) whether changes in self-concept between childhood and adolescence were associated with risk of adolescent PEs. Method: Using data from age 9 and age 13 (n = 7,423) of the child cohort (Cohort'98) from the Growing Up in Ireland study we investigated the relationship between self-concept at age 9 and age 13 and PEs at age 13. PEs were measured using the Adolescent Psychotic Symptoms Screener and self-concept was measured using the Piers Harris-II. Using a stratified analysis, we investigated the relationship between change in self-concept between age 9 and age 13 and the risk of PEs at age 13. Additionally we investigated changes across the six self-concept subscales. Results: Psychotic experiences were reported by 13% of participants at age 13. 'Very low' self-concept at age 9 was associated with an increased risk of PEs at age 13 (Adjusted-OR: 2.74, CI: 1.80-4.19), and 'High' self-concept at age 9 was associated with a decreased risk of PEs at age 13 (Adjusted-OR: 0.77, CI: 0.60-0.97). The stratified analysis indicated that improvements in self-concept reduced the odds of adolescent PEs and decline in self-concept increased the odds of adolescent PEs. This effect was noted across the majority of the self-concept subscales. Conclusions: There is a strong relationship between self-concept and PEs. The antecedents of low self-concept may be a useful target for preventative psychiatry. Broad-spectrum interventions targeting self-concept in childhood may help to reduce the incidence of PEs in adolescence.

Healy C, Gordon AA, Coughlan H, Clarke M, Kelleher I and **Cannon M** (2019). "Do childhood psychotic experiences improve the prediction of adolescent psychopathology? A longitudinal population-based study." Early Intervention in Psychiatry 13(5): 1245-1251.

[Full Text](#)

Department of Internal Medicine

Aims: (a) To investigate the utility of childhood PE as a predictor of adolescent psychopathology while accounting for three known risk factors: childhood mental disorder; traumatic experiences and poor childhood functioning, and (b) to investigate the additive effects of including childhood PE in predictive clinical model of adolescent psychopathology. Method: The study sample comprised of 86 Irish youths who completed two waves of the "Adolescent Brain Development" study (baseline age: 11.7 and follow-up age: 15.7). At baseline, participants completed a clinical interview assessing for PE, mental disorders, traumatic experiences and global functioning in childhood. The internalizing and externalizing problems sub-scales from the Youth Self Report questionnaire were used as follow-up outcomes variables in adolescence. Results: Logistic regression analyses revealed that childhood PE was the only predictor significantly associated with both internalizing (univariate OR: 7.58, CI: 2.59-22.15; multivariate OR: 5.43, CI: 1.53-19.29) and externalizing (univariate OR: 11.76, CI: 3.70-37.41; multivariate OR: 30.39, CI: 5.28-174.80) problems in adolescence. All predictive models with PE significantly predicted adolescent outcomes (area under the curve range: 0.70-0.81; all P < 0.05) and adding PE to the models improved the predictive value for externalizing problems (P = 0.02). Conclusion: Childhood PE is a powerful predictor of adolescent psychopathology, particularly for externalizing problems. Routine assessment of PE and targeted support for children who report PE may

reduce the incidence of mental disorder in adolescence.

Imam Z and **Cappell MS** (2019). "Correction to: Increased average number of medical publications per interviewee from 2009 to 2018: A study of 100 interviewees to an academic gastroenterology fellowship program." [BMC Medical Education](#) 19(1): 440.

[Full Text](#)

Department of Internal Medicine

Following publication of the original article [1], due to miscommunication during proofing, the author notified us the bellow corrections. In this Correction, correct and incorrect versions are shown.

Imam Z and **Cappell MS** (2019). "Increased average number of medical publications per interviewee from 2009 to 2018: A study of 100 interviewees to an academic gastroenterology fellowship program." [BMC Medical Education](#) 19(1): 402.

[Full Text](#)

Department of Internal Medicine

Background: Gastroenterology fellowship candidates may strive to improve their qualifications for this extremely competitive fellowship. Objective: To analyze whether extreme competitiveness of gastroenterology fellowship positions has affected fellowship interview selection by statistically analyzing 13 parameters of interviewees to identify statistically significant time changes during last 10 years. Methods: Retrospective time-trend-analyses (performed 2018) on thirteen prospectively-obtained-parameters of 47 interviewees (2009-2011) vs. 53 interviewees (2016-2018) for gastroenterology fellowship. SETTING: William-Beaumont-Hospital, Royal-Oak: academic fully-accredited gastroenterology fellowship, teaching hospital of Oakland-University-William-Beaumont-School-of-Medicine, tertiary-care hospital, GI fellowship since 1973. Results: Statistically significant increases occurred from 2009 to 2011 vs. 2016-2018 in number of publications, including mean number of: abstracts (1.69 ± 0.37 vs. 7.54 ± 1.16 , $p < 0.0001$); peer-reviewed articles (1.48 ± 0.30 vs. 6.13 ± 1.29 , $p < 0.0001$); and total publications (3.17 ± 0.48 vs. 12.76 ± 1.99 , $p < 0.0001$). Increased publications were associated with graduating from foreign medical schools (correlation coefficient = 0.26, $p = .03$), and were, surprisingly, correlated with lower letters-of-recommendation-scores (Kruskal-Wallis-statistic = 5.82, $p = .002$). USMLE-Step-1 scores significantly increased from 2009 to 2011 to 2016-2018 (235 ± 14.1 vs. 244.9 ± 13.5 , $p = 0.001$) (previously reported finding). Nine other parameters did not significantly change with time. Conclusions: Current report of >four-fold-increase in publications by gastroenterology fellowship interviewees at one academic-medical-center is novel. Increased focus on scholarship by applicants may be explained by their having only three parameters to improve their credentials during residency: publications, letters-of-recommendation, and honors awarded during residency (other parameters determined before residency and immutable). Current findings may benefit medical residents/medical-residency-program-directors by focusing more on publications for applications. Association between research productivity and medical promotions likely strongly motivates medical research of residents and may motivate academic faculty. Increased exposure to research/publications may improve the clinical acumen of GI fellowship applicants by enhancing their skills in critically reading the medical literature.

Imam Z, Khasawneh M, **Jomaa D**, Iftikhar H and Sayedahmad Z (2019). "Drug induced liver injury attributed to a curcumin supplement." [Case Reports in Gastrointestinal Medicine](#) 2019: 6029403.

[Full Text](#)

OUIWB Medical Student Author

More severe reactions, higher acute liver failure rates, and higher recurrence rates on re-challenge occur with supplement-related Drug Induced Liver Injury (DILI) (Medina-Caliz et al., 2018). We report a case of curcumin-induced hepatocellular DILI in a 78-year old female admitted with jaundice, with a one-month latency. Extensive evaluation for alternative etiologies of hepatotoxicity was unremarkable. The Roussel Uclaf Causality Assessment Method (RUCAM) score of 6 for the supplement indicated a probable association (score >8: highly probable association). Peak levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were >20 times upper limit of normal. A 48% decrease in AST and ALT levels was observed 7 days after discontinuation of the supplement, and resolution of transaminitis was observed in 42 days. No re-challenge was performed. In conclusion, this case emphasizes the importance of recognizing

curcumin supplements as DILI triggers. Furthermore, it reiterates the need for careful evaluation of herbal and dietary supplements (HDS) consumed by patients to identify potential DILI culprits, and to ultimately prevent DILI reactions with significant morbidity and mortality.

Ionescu F, Anusim N, Khoury J, **Gaikazian S, Stender M** and **Jaiyesimi I** (2019). "Demographics and survival in B-cell prolymphocytic leukemia: An analysis of SEER data." American Journal of Hematology 94: S27-S28.

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Department of Internal Medicine

Jae SY, Kurl S, Kunutsor SK, **Franklin BA** and Laukkanen JA (2019). "Relation of maximal systolic blood pressure during exercise testing to the risk of sudden cardiac death in men with and without cardiovascular disease." European Journal of Preventive Cardiology. ePub Ahead of Print.

[Full Text](#)

Department of Internal Medicine

Jinna S and **Khandhar PB** (2019). "Hydroxyurea Toxicity." StatPearls. Treasure Island (FL): StatPearls Publishing.

[Full Text](#)

OUIWB Medical Student Author

Hydroxyurea is an antineoplastic agent used alone or in combination with other chemotherapeutic drugs or radiation in the treatment of resistant leukemias and carcinomas of the head and neck. It is also used to increase fetal hemoglobin concentration, thus reducing the frequency of severe crisis and reducing the necessity for blood transfusions in patients with sickle cell anemia. They also use hydroxyurea off-label in the treatment of polycythemia vera,[1] essential thrombocythemia,[2] psoriasis, acute myeloid leukemia, meningioma, melanoma, and ovarian cancer.

Jinna S and **Khandhar PB** (2019). "Thrombocytopenia." StatPearls. Treasure Island (FL): StatPearls Publishing.

[Full Text](#)

OUIWB Medical Student Author

A platelet count that falls below the lower limit of normal, i.e., 150000/microliter (for adults) is defined as thrombocytopenia. Platelets are blood cells that help in blood clotting and wound healing - risks associated with thrombocytopenia range from no risk at all to bleeding risks and thrombosis. The correlation of severity of thrombocytopenia and bleeding risk is uncertain. Spontaneous bleeding can occur with a platelet count under 10000/microliter and surgical bleeding with counts below 50000/microL. Thrombocytopenia is associated with risk of thrombosis in conditions like heparin-induced thrombocytopenia (HIT), antiphospholipid antibody syndrome (APS), disseminated intravascular coagulation (DIC), thrombotic microangiopathy (TMA), paroxysmal nocturnal hemoglobinuria (PNH).

Kadri AN, Alkhawam H, **Hader I**, Chahine J, Gad M, Gajulapalli RD, Ali A, Hernandez AV, Werns S and Kapadia S (2019). "The impact of HIV on coronary artery procedure in patients of coronary artery disease." Journal of the American College of Cardiology 74(13): B824-B824.

[Full Text](#)

Department of Internal Medicine

Karnib S and **Chinnaiyan KM** (2019). "Coronary computed tomography angiography: Enhancing risk stratification and diagnosis of cardiovascular disease in women." Current Treatment Options in Cardiovascular Medicine 21(10): 62.

[Full Text](#)

Department of Internal Medicine

Purpose of Review: There are numerous gender- and sex-based differences that contribute to the increased morbidity and mortality related to atherosclerotic cardiovascular disease (ASCVD) in women. Early detection of risk and targeted management of atherosclerotic disease is fundamental to reduce ASCVD risk and improve outcomes in women. In this review, we examine the utility of cardiac computed tomography (CT) and coronary CT angiography (CTA) in three ASCVD scenarios including coronary artery calcium scoring for risk stratification in asymptomatic women, and coronary CTA for diagnosis and prognosis of stable ischemic heart disease and acute chest pain. The risks of radiation exposure and the potential applications of novel

technologies in women are explored. Recent Findings: CTA provides the capabilities of early recognition and management of nonobstructive coronary artery disease (CAD). Recent advancements in plaque composition and morphology further enhance the prognostic yield from coronary CTA. Innovations in stress perfusion and computational fluid dynamics allow for evaluation of physiological measures of ischemia. In addition, developments in artificial intelligence (AI) may also help unlock a deeper understanding of atherosclerosis and risk in women. Coronary CTA is an accurate and useful modality for early detection and management of ASCVD in women. Novel technologies hold great promise for furthering our understanding of sex-specific pathophysiology and potential improvement in clinical management and outcomes.

Keihani S, Rogers DM, Putbrese BE, Anderson RE, Stoddard GJ, Nirula R, Luo-Owen X, Mukherjee K, Morris BJ, Majercik S, Piotrowski J, Dodgion CM, Schwartz I, Elliott SP, DeSoucy ES, Zakaluzny S, Sherwood BG, Erickson BA, Baradaran N, Breyer BN, Fick CN, Smith BP, Okafor BU, Askari R, Miller BD, Santucci RA, Carrick MM, Allen L, Norwood S, **Hewitt T, Burks FN**, Heilbrun ME, Gross JA and Myers JB (2019). "The American Association for the Surgery of Trauma (AAST) Renal Injury Grading Scale: Implications of the 2018 revisions for injury reclassification and predicting bleeding interventions." Journal of Trauma and Acute Care Surgery. ePub Ahead of Print.

[Full Text](#)

Department of Urology

OUWB Medical Student Author

Background: In 2018, the AAST published revisions to the renal injury grading system to reflect the increased reliance on CT scans and non-operative management of high-grade renal trauma (HGRT). We aimed to evaluate how these revisions will change the grading of HGRT and if it outperforms the original 1989 grading in predicting bleeding control interventions. Methods: Data on HGRT were collected from 14 Level-1 trauma centers from 2014-2017. Patients with initial CT scans were included. Two radiologists reviewed the scans to re-grade the injuries according to the 1989- and 2018-AAST grading systems. Descriptive statistics were used to assess grade reclassifications. Mixed-effect multivariable logistic regression was used to measure the predictive ability of each grading system. The areas under the curves (AUC) were compared. Results: Of the 322 injuries included, 27.0% were upgraded, 3.4% were downgraded, and 69.5% remained unchanged. Of the injuries graded as III or lower using the 1989-AAST, 33.5% were upgraded to grade IV using the 2018-AAST. Of grade V injuries, 58.8% were downgraded using the 2018-AAST. There was no statistically significant difference in the overall AUCs between the 2018-AAST and 1989-AAST grading for predicting bleeding interventions (0.72 vs. 0.68, P=0.34). Conclusion: About one-third of the injuries previously classified as grade III will be upgraded to grade IV using the 2018-AAST, which adds to the heterogeneity of grade IV injuries. Although the 2018-AAST grading provides more anatomic details on injury patterns and includes important radiologic findings, it did not outperform the 1989-AAST grading in predicting bleeding interventions.

Kentor R, Hoodin F, Byrd M, Kullgren AK, LaLonde L, Ostarello L, **Smith P**, Carson D, MacDonald K, Inoue S, **Kitchen B** and Yanik AG (2019). "Caregiver disclosure of oncofertility risks among adolescent cancer patients." Pediatric Blood & Cancer 66: S116-S116.

[Request Form](#)

Department of Pediatrics

OUWB Medical Student Author

Khalil JG, Smuck M, Koreckij T, Keel J, Beall D, Goodman B, Kalapos P, Nguyen D, Garfin S and Investigators IT (2019). "A prospective, randomized, multicenter study of intraosseous basivertebral nerve ablation for the treatment of chronic low back pain." Spine Journal 19(10): 1620-1632.

[Full Text](#)

Department of Orthopaedic Surgery

Background Context: Current literature suggests that degenerated or damaged vertebral endplates are a significant cause of chronic low back pain (LBP) that is not adequately addressed by standard care. Prior 2-year data from the treatment arm of a sham-controlled randomized controlled trial (RCT) showed maintenance of clinical improvements at 2 years following radiofrequency (RF) ablation of the basivertebral nerve (BVN). Purpose: The purpose of this RCT was to compare the effectiveness of intraosseous RF ablation of the BVN to standard care for the treatment of chronic LBP in a specific subgroup of patients suspected to

have vertebroprogenic related symptomatology. Study Design/Setting: A prospective, parallel, open label RCT was conducted at 20 U.S. sites. Patient Sample: A total of 140 patients with chronic LBP of at least 6 months duration, with Modic Type 1 or 2 vertebral endplate changes between L3 and S1, were randomized 1:1 to undergo either RF ablation of the BVN or continue standard care. Outcome Measures: Oswestry Disability Index (ODI) was collected at baseline, 3, 6, 9, and 12-months postprocedure. Secondary outcome measures included a 10-point Visual Analog Scale (VAS) for LBP, ODI and VAS responder rates, SF-36, and EQ-5D-5L. The primary endpoint was a between-arm comparison of the mean change in ODI from baseline to 3 months post-treatment. Methods: Patients were randomized 1:1 to receive RF ablation or to continue standard care. Self-reported patient outcomes were collected using validated questionnaires at each study visit. An interim analysis to assess for superiority was prespecified and overseen by an independent data management committee when a minimum of 60% of patients had completed their 3-month primary endpoint visit. Results: The interim analysis showed clear statistical superiority ($p < .001$) for all primary and secondary patient-reported outcome measures in the RF ablation arm compared with the standard care arm. This resulted in a data management committee recommendation to halt enrollment in the study and offer early cross-over to the control arm. These results are comprised of the outcomes of the 104 patients included in the intent-to-treat analysis of the 3-month primary endpoint, which included 51 patients in the RF ablation arm and 53 patients in the standard care arm. Baseline ODI was 46.1, VAS was 6.67, and mean age was 50 years. The percentage of patients with LBP symptoms ≥ 5 years was 67.3%. Comparing the RF ablation arm to the standard care arm, the mean changes in ODI at 3 months were -25.3 points versus -4.4 points, respectively, resulting in an adjusted difference of 20.9 points ($p < .001$). Mean changes in VAS were -3.46 versus -1.02 , respectively, an adjusted difference of 2.44 cm ($p < .001$). In the RF ablation arm, 74.5% of patients achieved a ≥ 10 -point improvement in ODI, compared with 32.7% in the standard care arm ($p < 0.001$). Conclusions: Minimally invasive RF ablation of the BVN led to significant improvement of pain and function at 3-months in patients with chronic vertebroprogenic related LBP.

Killinger KA, **Henrichsen JL**, Han E, **Dai YL**, Nguyen L, **Gilleran J**, Odabachian L, Boura JA, **Peters KM** and **Sirls LT** (2019). "Symptom and quality of life improvements after pelvic floor physical therapy in a clinical population of women with pelvic pain and other symptoms." *Female Pelvic Medicine & Reconstructive Surgery*. ePub Ahead of Print. [Request Form](#)

OUWB Medical Student Author

Department of Urology

Objectives: This study aimed to evaluate changes in validated symptom scores at intake and discharge in women undergoing pelvic floor physical therapy (PFPT) for pain and other pelvic floor symptoms. Methods: Consecutive women starting PFPT during 1 year were reviewed. History, demographics, and Pelvic Floor Distress Inventory Questionnaire - Short Form 20 (PFDI) total and domain scores (Pelvic Organ Prolapse Distress Inventory-6, Urogenital Distress Inventory-6, Colorectal-Anal Distress Inventory-8), Pelvic Floor Impact Questionnaire (PFIQ-7), and pain levels on a numeric rating scale (NRS) were collected at intake and discharge. Data were analyzed with descriptive statistics and sign tests. Results: Of 474 women, mean age was 50.3 ± 16.7 years (range, 18-87 years) and the most common indication for PFPT was pelvic pain (208/474; 43.9%). In women with complete data, pretreatment to posttreatment median scores improved on the PFDI (77.3 vs 41.8; $P < 0.0001$), Urogenital Distress Inventory (37.5 vs 16.0; $P < 0.0001$), and PFIQ (58.0 vs 19.0; $P < 0.0001$), and the minimal clinically important difference was met for the PFDI, PFIQ, and Colorectal-Anal Distress Inventory. Women with primarily pelvic pain ($n = 208$) achieved significant improvements in PFDI, PFIQ, and NRS scores ($P < 0.0001$ for all) as well as the minimal clinically important difference for these measures. Pain patients with a history of pelvic surgery ($n = 50$) also had significant improvements in PFIQ and NRS but not PFDI scores. Conclusions: Most women referred to PFPT demonstrated symptom improvements as measured by validated instruments.

Kim DH, Hwang RW, Lee GH, Joshi R, **Baker KC**, Arnold P, Sasso R, **Park D** and **Fischgrund J** (2019). "Potential significance of facet joint fusion or posteromedial fusion observed on CT imaging following attempted posterolateral or posterior interbody fusion." *Spine Journal*. ePub Ahead of Print.

[Full Text](#)

Department of Orthopaedic Surgery

Background Context: Radiologic evidence of successful lumbar fusion has traditionally been based on

bridging bone spanning the intertransverse processes (posterolateral fusion or PLF) or disc space (interbody fusion, or IBF). Often, postoperative computed tomography (CT) of unsuccessful PLF and IBF demonstrates bridging bone across the facet joints or connecting the medial transverse process to the ipsilateral superior articular facet of the caudal vertebra. The significance of this finding in terms of implant stability and clinical outcomes has not previously been reported. Purpose: To determine rates of facet joint fusion (FJF)/posteromedial fusion (PMF) following single-level PLF surgery, with or without interbody. A secondary goal was to determine comparative outcomes associated with isolated FJF/PMF versus PLF and IBF. Study Design: Retrospective CT-based review. Patient Sample: Two hundred-three patients underwent single-level PLF surgery with local autograft bone or PLF+IBF with local autograft bone. Outcome Measures: Fusion was assessed at 6-months and 12-months postoperatively using strict CT criteria. Patient reported outcome measures included visual analogue scale (VAS) scores for back pain and leg pain, Oswestry Disability Index (ODI), and SF-36. Methods: Thin-cut CTs were examined to determine whether successful fusion had occurred in seven different anatomic locations. One-way analysis of variance was used to determine significant differences in mean outcome scores and other continuous measures between groups at baseline and follow-up. Chi-square test of independence or Fisher's exact test was used to compare proportions between groups on categorical measures. Results: Two hundred-three patients and 157 patients completed 6- and 12 month follow-up, respectively. At 12 months, 35.1% of PLF patients demonstrated successful unilateral/bilateral PLF. Including unilateral or bilateral FJF/PMF, the fusion rate was 73.4%. Among PLF+IBF patients, 38.1% demonstrated successful IBF/PLF. Including unilateral or bilateral FJF/PMF, the fusion rate was 55.6%. All fusion groups demonstrated significant improvement in back pain and leg pain scores as well as ODI and SF-36 PF at 6- and 12 months compared with pre-op. No significant difference in any outcome measure, rates of implant loosening or reoperation was observed between successful PLF/IBF and FJF/PMF groups. Conclusions: FJF/PMF is often observed on postoperative CT evaluation following surgery originally performed to achieve PLF or IBF. Short-term follow-up suggests no significant difference in implant loosening rates or patient reported outcomes when FJF/PMF is observed versus PLF or IBF in such patients. Long-term clinical outcomes of FJF/PMF versus PLF or IBF remain unknown. These findings apply solely to single-level instrumented spinal fusion surgery utilizing pedicle screws with or without IBF.

Kim HJ, Jae SY, Choo J, Yoon JK, Kim SH, Königstein K, Schmidt-Trucksäss A and **Franklin BA** (2019). "Mediating effects of exercise capacity on the association between physical activity and health-related quality of life among adolescents with complex congenital heart disease." [American Journal of Human Biology](#) 31(6).

[Full Text](#)

Department of Internal Medicine

Objectives: There is little evidence on interrelationships between physical activity, sedentary behaviors, and health-related quality of life (HRQOL) among adolescents with congenital heart disease (CHD). We hypothesized that exercise capacity would have a mediating effect on the associations of either physical activity or sedentary behavior with HRQOL. Methods: Adolescents with complex CHD (n = 111) were consecutively recruited from an outpatient clinic in a general hospital in South Korea. Physical activity and sedentary behavior were assessed using the global physical activity questionnaire. Exercise capacity was directly measured by peak oxygen uptake using a symptom-limited maximal treadmill exercise test. HRQOL was evaluated by both adolescents and their parents using the Pediatric Quality of Life Inventory questionnaire. Results: The self-reported and parent proxy-reported HRQOL were positively associated with physical activity ($\beta = 0.16, P = .003$; $\beta = 0.12, P = .049$) and exercise capacity ($\beta = 0.63, P < .001$; $\beta = 0.66, P < .001$), but not with sedentary behavior in adjusted regression models. When both variables were entered in the same regression models, only exercise capacity remained significantly associated with the self-reported ($\beta = 0.50, P = .008$) and parent proxy-reported HRQOL ($\beta = 0.62, P = .003$). Exercise capacity acted as a full mediator variable on the relationship between physical activity and HRQOL ($P < .05$ for both). Conclusions: The present findings suggest that exercise capacity mediates the association between physical activity and HRQOL, highlighting the importance of improving exercise capacity to potentially enhance HRQOL in adolescents with complex CHD.

Kobeissi S, Majdalany BS, Goswami AK, **Kanaan CN**, Kokabi N and Khaja MS (2019). "Varicoceles." [Journal of Radiology Nursing](#) 38(4): 227-230.

[Full Text](#)

OUWB Medical Student Author

Kopin D, Seth M, Sukul D, **Dixon S**, Aronow HD, Lee D, Tucciarone M, Pielsticker E and Gurm HS (2019). "Primary and secondary vascular access site complications associated with percutaneous coronary intervention insights from the BMC2 registry." *Jacc-Cardiovascular Interventions* 12(22): 2247-2256.

[Full Text](#)

Department of Internal Medicine

Objectives: This study sought to describe the association between trends in primary and secondary vascular access sites and vascular access site complications (VASCs) among patients who underwent percutaneous coronary intervention (PCI) in Michigan. Background: The frequency of transradial PCI has increased. As a result, there is concern that operators may lose femoral-access proficiency resulting in a paradoxical increase in PCI complications. Anecdotally, an increase in secondary access use during PCI has also been observed. Methods: Data from the BMC2 (Blue Cross Blue Shield of Michigan Cardiovascular Consortium) registry was queried to evaluate the use of transradial and transfemoral PCI and their associated VASCs. Results: From 2013 to 2017, transradial PCI increased from 25.9% to 45.2% and the overall use of secondary vascular access increased from 4.9% to 8.7% with minimal change in overall VASCs (1.2% to 1.4%). The use of secondary vascular access was associated with increased VASCs (odds ratio [OR]: 5.82; 95% confidence interval [CI]: 5.26 to 6.43). Although, patients treated by operators in the highest tertile of radial use were more likely to experience femoral VASCs (adjusted OR: 1.51; 95% CI: 1.08 to 2.13), treatment by these operators was associated with an overall reduction in all VASCs (adjusted OR: 0.62; 95% CI: 0.46 to 0.83). Conclusions: Despite increased use of transradial PCI, there has been no significant decrease in VASCs. This is in part attributable to an increased incidence of femoral VASCs and increasing use of secondary vascular access. An overall reduction in VASCs was observed in the highest radial use operators. Further strategies are needed to reduce VASCs in the transradial era.

Kountanis J, Vahabzadeh C, **Bauer S**, Muzik M, Cassidy R, Aman C, MacEachern M and Bauer M (2019). "Labor epidural analgesia and the risk of postpartum depression: A meta-analysis of observational studies." *Journal of Clinical Anesthesia* 61: 109658.

[Full Text](#)

Department of Obstetrics & Gynecology

Study Objective: This study aims to systematically review the literature to evaluate the association between labor epidural analgesia (LEA) and postpartum depression (PPD). Design: Meta-analysis. Setting: Obstetric patients delivering vaginally with or without LEA in a hospital. Interventions: This study aimed to investigate the effects of providing LEA on developing PPD. Measurements: Pooled odds ratios (OR) and 95% confidence intervals (CI) were calculated using the random effects model. Results: A total of 356 full text articles were reviewed. Eleven articles studying 85,928 patients met inclusion criteria. The pooled unadjusted OR 1.03 and 95% CI (0.77, 1.37) suggest that LEA is not associated with a decreased risk of developing PPD. Conclusions: Labor epidural analgesia was not shown to confer protection against developing PPD according to this meta-analysis. Future studies are needed to explore whether other aspects of LEA, beyond its presence or absence, influence the onset of PPD.

Kuang SY (2019). "A broader outlook to reduce pre-exam stress." *Medical Teacher* 41(10): 1200-1201.

[Full Text](#)

Department of Foundational Medical Studies (OU)

Stress, depression, and job burnout are plaguing the medical field. These issues have many causes, one of which is a stigma or the fear of being stigmatized that leads the sufferer to deny the problem or delay seeking help. In this article, I will share a recent story of how a mind adjustment from a negative view of the past failure to a broader outlook quickly and effectively reduced the pre-exam stress of a student in a class I am teaching.

Kuang SY (2019). "Formative assessment: Question style matters." *Advances in Physiology Education* 43(4): 567-570.

[Full Text](#)

Department of Foundational Medical Studies (OU)

Kuang SY, Kamel-ElSayed S and Pitts D (2019). "How to receive criticism: Theory and practice from cognitive and cultural approaches." Medical Science Educator 29(4): 1109-1115.

[Full Text](#)

Department of Foundational Medical Studies (OU)

Mistakes in clinical practice may have life-or-death consequences for patients. Training in how to give and receive feedback has been emphasized in medical education for decades, yet medical practitioners continue to struggle with these practices. Giving feedback is difficult because it is not easy for a receiver to receive feedback. Current training programs lack an in-depth understanding of the causes of why receiving feedback is not easy. The purposes of this article are to (1) fill this gap by identifying the shared weaknesses in human nature as the causes underlying the difficulty in receiving feedback, especially criticism, using a cognitive approach; (2) develop logical principles to treat the identified causes; (3) show the shared common wisdom of how to receive criticism through a multicultural approach; and finally, (4) address how these cognitive and multicultural approaches may facilitate receiving criticism in the field of medical education.

Lau W, Shannon F, Hanzel G, Safian R, Abbas A, Sakwa M, Almany S, Hanson I, Chen NW and Fayne R (2019). "Transfemoral transcatheter aortic valve replacement using Fascia iliaca block as an alternative approach to conscious sedation as compare to general anesthesia: Findings from a single center." Journal of the American College of Cardiology 74(13): B792-B792.

[Full Text](#)

Department of Anesthesiology

Department of Surgery

Department of Internal Medicine

Laucis AMB, Jagsi R, Griffith KA, Dominello MM, Walker EM, Abu-Isa EI, **Dilworth JT**, Vicini F, Kocheril PG, Browne CH, Mietzel MA, Moran JM, Hayman J and Pierce LJ (2019). "The role of facility variation on racial disparities in use of hypofractionated whole breast radiotherapy." Journal of Clinical Oncology 37.

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Department of Radiation Oncology

Background: Concerns about racial disparities in the adoption of medical advances motivate investigation of the use of hypofractionated radiotherapy, a less burdensome and less costly approach that is efficacious for most patients with early-stage breast cancer. Methods: A prospectively collected statewide quality consortium database from 25 institutions was queried for breast cancer patients who completed hypofractionated (HF) or conventionally fractionated whole breast radiotherapy (RT) from 1/2012-12/2018. We used patient-level multivariable modeling to evaluate associations between HF use and race, controlling for patient and facility factors, and multilevel modeling to account for patient clustering within facilities. Results: Of 10,318 patients analyzed, 80% self-reported their race as White, 18% as Black, and 2% as Asian, similar to statewide and national distributions. 31% of Whites were treated at academic centers compared to 65% of Blacks and 65% of Asians. In 2018, HF was utilized in 75% of Whites versus 60% of Blacks and 68% of Asians. On patient-level multivariable analysis (see Table), Black and Asian race were significantly associated with a lower likelihood of HF receipt, despite accounting for treatment year, age, laterality, BMI, breast volume, comorbidities, stage, triple-negative status, IMRT use, academic center treatment, and 2011 ASTRO Hypofractionation Guideline eligibility. On multilevel analysis, race was no longer significantly associated with HF receipt. Conclusions: We observed that Black and Asian patients receive hypofractionated RT less often, despite more frequent treatment at academic centers. Multilevel modeling eliminated this disparity, suggesting that differences in facility-specific HF use may contribute. Further inquiry is needed to determine if reduction of facility-level variation may reduce disparities in accessing HF treatment.

Lee SE, Sung JM, Andreini D, Budoff MJ, Cademartiri F, **Chinnaiyan K**, Choi JH, Chun EJ, Conte E, Gottlieb I, Hadamitzky M, Kim YJ, Kumar A, Lee BK, Leipsic JA, Maffei E, Marques H, Pontone G, **Raff G**, Shin S, Stone PH, Samady H, Virmani R, Narula J, Berman DS, Shaw LJ, Bax JJ, Lin FY, Min JK and Chang HJ (2019). "Differential association between the progression of coronary artery calcium score and coronary plaque volume progression according to statins: The Progression of Atherosclerotic Plaque Determined by Computed Tomographic Angiography Imaging (PARADIGM) study." European Heart Journal Cardiovascular Imaging 20(11): 1307-1314.

[Full Text](#)

Department of Internal Medicine

Aims: Coronary artery calcium score (CACS) is a strong predictor of major adverse cardiac events (MACE). Conversely, statins, which markedly reduce MACE risk, increase CACS. We explored whether CACS progression represents compositional plaque volume (PV) progression differently according to statin use. Methods and Results: From a prospective multinational registry of consecutive patients (n = 2252) who underwent serial coronary computed tomography angiography (CCTA) at a ≥ 2 -year interval, 654 patients (61 \pm 10 years, 56% men, inter-scan interval 3.9 \pm 1.5 years) with information regarding the use of statins and having a serial CACS were included. Patients were divided into non-statin (n = 246) and statin-taking (n = 408) groups. Coronary PVs (total, calcified, and non-calcified; sum of fibrous, fibro-fatty, and lipid-rich) were quantitatively analysed, and CACS was measured from both CCTAs. Multivariate linear regression models were constructed for both statin-taking and non-statin group to assess the association between compositional PV change and change in CACS. In multivariate linear regression analysis, in the non-statin group, CACS increase was positively associated with both non-calcified ($\beta = 0.369$, $P = 0.004$) and calcified PV increase ($\beta = 1.579$, $P < 0.001$). However, in the statin-taking group, CACS increase was positively associated with calcified PV change ($\beta = 0.756$, $P < 0.001$) but was negatively associated with non-calcified PV change ($\beta = -0.194$, $P = 0.026$). Conclusion: In the non-statin group, CACS progression indicates the progression of both non-calcified and calcified PV progression. However, under the effect of statins, CACS progression indicates only calcified PV progression, but not non-calcified PV progression. Thus, the result of serial CACS should be differently interpreted according to the use of statins.

Lee Y, **Banooni A**, Yuki K, Staffa SJ, DiNardo JA and Brown ML (2019). "Incidence and predictors of postoperative nausea and vomiting in children undergoing electrophysiology ablation procedures." Paediatric Anaesthesia. ePub Ahead of Print.

[Full Text](#)

Department of Anesthesiology

Background: Postoperative nausea and vomiting remains a significant concern for patients undergoing general anesthesia for percutaneous radiofrequency catheter ablation and cryoablation for tachyarrhythmias. Aim: Our objective was to examine the incidence and risk factors for nausea and vomiting in the recovery room. Methods: Children aged > 2 and ≤ 18 years who underwent general anesthesia for a percutaneous radiofrequency catheter ablation or cryoablation for a tachyarrhythmia between January 1, 2013, and January 1, 2016, were retrospectively reviewed. Outcomes included postoperative nausea, vomiting, and a composite of postoperative nausea and vomiting in the recovery room. Results: We identified 611 patients with a mean age of 13.3 \pm 3.9 years, 54.5% male, and a mean length of anesthesia was 3.9 \pm 1.0 hours. Vomiting or retching in the postanesthesia care unit occurred in 7.4% of patients and nausea in an additional 12.4%. A composite of nausea and vomiting occurred in 95 patients (15.5%). On multivariable analysis, a subhypnotic propofol infusion (OR 0.45, 95% CI 0.23-0.88, $P = .019$) and shorter anesthetic duration (OR 0.81 per 30 minutes, 95% CI 0.70-0.94, $P = .006$) were independently associated with less vomiting in the recovery room. A history of PONV (OR 2.24, 95% CI 1.24-4.05, $P = .007$) was independently associated with a composite of nausea and vomiting in the recovery room. Conclusions: A shorter anesthetic time and a subhypnotic propofol infusion were predictive of a lower rate of postoperative vomiting in patients undergoing general anesthesia for electrophysiologic ablation procedures.

Lemor A, Basir M, Patel K, Salam M, Schreiber T, Kaki A, Jain T, **Hanson I, Almany S, Timmis S, Dixon S**, Kolski B, Todd J, Senter S, Marso S, Lasorda D, Wilkins C, Lalonde T, Attallah A, Larkin T, Dupont A, Marshall J, Patel N, Green M, Tehrani B, Truesdell A, Sharma R, Akhtar Y, O'Neill B, Finley J, Rahman A, Foster M, Askari R, Goldsweig A, Martin S, Bharadwaj A, Khuddus M, Caputo C, Korpas D, Cawich I, Kapur N, McAllister D, Blank N, Alraies MC, Fisher R, Khandelwal A, Alaswad K, Johnson T, Hacala M and O'Neill W (2019). "Culprit-vessel versus multivessel percutaneous coronary intervention in cardiogenic shock: Insights from the National Cardiogenic Shock Initiative." Journal of the American College of Cardiology 74(13): B796-B796.

[Full Text](#)

Department of Internal Medicine

Lerchenfeldt S and Eng M (2019). "A survey of health sciences faculty practices and attitudes regarding the peer feedback component of team-based learning." Medical Science Educator 29(4): 1211-1219.

[Full Text](#)

Department of Foundational Medical Studies (OU)

Background: Peer feedback, an essential component of team-based learning (TBL), fosters accountability among team members. Effective utilization can be advantageous for both students and faculty, although there may be many implementation challenges. Our study objectives were to (1) identify current practices of peer feedback in TBL, (2) identify curricular assessment related to peer feedback, and (3) identify challenges with peer feedback in TBL. Methods: A survey link was sent via medical and TBL web boards. The survey asked for both quantitative and qualitative information regarding the peer feedback process. Quantitative results were analyzed using SPSS®. NVivo® was used to identify and code themes in open-ended responses. Both investigators reviewed and agreed upon themes. Results: Sixty-one TBL users in health professions completed the survey. Multiple health professions were represented with medicine and pharmacy being the most common. Information on current practices showed a wide variety of implementation. Curricular alignment was common. Time and training were the most common challenges and difficulties. Conclusions: Meaningful feedback should be considered an important curricular outcome. Specific learning objectives and appropriate assessment strategies should be developed to meet the mission of the program. Students must receive guidance from faculty members on how to improve their skills in providing effective feedback. Overall, faculty saw peer evaluation as valuable. However, the time commitment, lack of student training, and student attitudes make implementation difficult. Future research should focus on best practices to streamline the TBL feedback process and on student training regarding how to provide effective feedback.

Liang J, Lack D, Zhou J, Liu Q, **Grills I** and **Yan D** (2019). "Intrafraction 4D-cone beam CT acquired during volumetric arc radiotherapy delivery: kV parameter optimization and 4D motion accuracy for lung stereotactic body radiotherapy (SBRT) patients." *Journal of Applied Clinical Medical Physics* 20(12): 10-24.

[Request Form](#)

Department of Radiation Oncology

Purpose: Elekta XVI 5.0 allows for four-dimensional cone beam computed tomography (4D CBCT) image acquisition during treatment delivery to monitor intrafraction motion. These images can have poorer image quality due to undersampling of kV projections and treatment beam MV scatter effects. We determine if a universal intrafraction preset can be used for stereotactic body radiotherapy (SBRT) lung patients and validate the accuracy of target motion characterized by XVI intrafraction 4D CBCT. Methods: The most critical parameter within the intrafraction preset is the nominal AcquisitionInterval, which controls kV imaging acquisition frequency. An optimal value was determined by maximizing the kV frame number acquired up to 1000 frames, typical of pretreatment 4D CBCT. CIRS motion phantom intrafraction phase images for 16 SBRT beams were obtained. Mean target position, time-weighted standard deviation, and amplitude for these images as well as target motion for three SBRT lung patients were compared to respective pretreatment 4D CBCTs. Evaluation of intrafraction 4D CBCT reconstruction revealed inclusion of MV only images acquired to remove MV scatter effects. A workaround to remove these images was developed. Results: AcquisitionInterval of 0.1°/frame was optimal. The number of kV frames acquired was 567–1116 and showed strong linear correlation with beam monitor unit (MUs). Phantom target motion accuracy was excellent with average differences in target position, standard deviation and amplitude range of ≤ 0.5 mm. Target tracking for SBRT patients also showed good agreement. Evaluation of phase sorting wave forms showed that inclusion of MV only images significantly impacts intrafraction image reconstruction for patients and use of workaround is necessary. Conclusions: A universal intrafraction imaging preset can be used safely for SBRT lung patients. The number of kV projections with MV delivery parameters varies; however images with fewer kV projections still provided accurate target position information. Impact of the reconstruction workaround was significant and is mandated for all 4D CBCT intrafraction imaging performed at our institution.

Liu G, Yang J, Nie X, Zhu X, **Li X**, Zhou J, **Kabolizadeh P**, Li Q, Quan H and **Ding X** (2019). "A patients-based statistical model of radiotherapy dose distribution in nasopharyngeal cancer." *Dose Response* 17(4): 1559325819892359.

[Full Text](#)

Department of Radiation Oncology

Purpose: To develop a patients-based statistical model of dose distribution among patients with nasopharyngeal cancer (NPC). Methods and Materials: The dose distributions of 75 patients with NPC were

acquired and preprocessed to generate a dose-template library. Subsequently, the dominant modes of dose distribution were extracted using principal component analysis (PCA). Leave-one-out cross-validation (LOOCV) was performed for evaluation. Residual reconstruction errors between the doses reconstructed using different dominating eigenvectors and the planned dose distribution were calculated to investigate the convergence characteristics. Three-dimensional Gamma analysis was performed to investigate the accuracy of dose reconstruction. Results: The first 29 components contained 90% of the variance in dose distribution, and 45 components accounted for more than 95% of the variance on average. The residual error of the LOOCV model for the cumulative sum of components over all patients decreased from 8.16 to 4.79 Gy when 1 to 74 components were included in the LOOCV model. The 3-dimensional Gamma analysis results implied that the PCA model was capable of dose distribution reconstruction, and the accuracy was especially satisfactory in the high-dose area. Conclusions: A PCA-based model of dose distribution variations in patients with NPC was developed, and its accuracy was determined. This model could serve as a predictor of 3-dimensional dose distribution.

Lloyd V, Morse M, Purakal B, Parker J, Benard P, Crone M, Pfiffner S, **Szmyd M** and Dinda S (2019). "Hormone-like effects of bisphenol A on p53 and estrogen receptor alpha in breast cancer cells." *BioResearch Open Access* 8(1): 169-184.

[Full Text](#)

OUWB Medical Student Author

Bisphenol A (BPA) is a polymerizing agent commonly found in plastics that has been linked to xenoestrogenic activity. In this study, we analyzed the estrogen-like effects of BPA on the expression of estrogen receptor (ER) α and p53 with hormonal and antihormonal treatments in T-47D and MCF-7 cells. Cells were cultured in medium containing 5% charcoal-stripped fetal bovine serum for 6 days to deplete any endogenous steroids or effectors. The cells were then treated for 24 h with 600 nM BPA, which was determined to be the optimal value by a concentration study of BPA from 1 nM to 2 μ M. Extracted cellular proteins were quantified and subjected to sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE)/Western blot analysis. The cell proliferation assays were quantified upon exposure to BPA. Laser confocal microscopy was performed to determine the cytolocalization of p53 and ER α upon treatment with BPA. Western blot analysis revealed that BPA caused an increase in the cellular protein p53 in a concentration-dependent manner. While treatment with BPA did not affect the cytolocalization of p53, an increase in cell proliferation was observed. Our studies provide interesting leads to delineate the possible mechanistic relationship among BPA, ER, and tumor suppressor proteins in breast cancer cells.

Lombardo DJ, Siljander MP, Sobh A, **Moore DD** and **Karadsheh MS** (2019). "Periprosthetic fractures about total knee arthroplasty." *Musculoskeletal Surgery*. ePub Ahead of Print.

[Full Text](#)

Department of Orthopaedic Surgery

Periprosthetic fracture after total knee arthroplasty presents a difficult complication for many orthopaedic surgeons. These fractures occur most frequently around the distal femur followed by the patella and then tibia. These fractures are frequently complicated by poor bone quality or compromised bone due to the presence of the implants. Surgical treatment is typically necessary and requires varied techniques of open fixation, intramedullary fixation, or revision arthroplasty. Outcomes of these injuries vary widely. This review aims to describe the epidemiology, classification, treatment options and outcomes for periprosthetic fractures following total knee arthroplasty.

Macari D, Kawak S, **Raofi V**, **Wasvary H** and **Jaiyesimi I** (2019). "Recurrence pattern and outcomes in T4 colon cancer: A single institution analysis." *Journal of Surgical Oncology* 121(2): 337-341.

[Full Text](#)

Department of Surgery

Department of Internal Medicine

Background and Objectives: Patients with T4 colon adenocarcinoma have an increased risk of locoregional and distant recurrence. This study defines the metastatic pattern, predictors of recurrence, and efficacy of adjuvant treatment in T4 colon cancer. Methods: A retrospective review was performed of patients with T4 colon adenocarcinoma from May 2005 to November 2015 at a tertiary care hospital. Baseline factors, follow-

up, recurrence, and survival were collected and analyzed. Results: Locoregional recurrence (LR) rates for N0, N1, and N2 were 21/85 (24.7%), 14/50 (28%), and 21/46 (45.7%), respectively (P = .014). Multivariate analysis for distant recurrence was significant for positive nodes (hazard ratio [HR], 3.3; 95% confidence interval [CI], 1.1-9.9). Multivariate analysis for LR was significant for the following variables: perforation (HR, 2.7; 95% CI, 1.2-6.2), lymphovascular invasion (HR, 2.7; 95% CI, 1.1-6.7), positive nodes (HR, 2.8; 95% CI, 1.2-6.9), and positive margins (HR, 5.0; 95% CI, 2.1-12.1). Multivariate analysis for overall survival was significant for: signet ring histology (HR, 2.5; 95% CI, 1.2-5.8), positive nodes (HR, 2.3; 95% CI, 1.2-4.4), and positive margin (HR, 2.8; 95% CI, 1.4-5.8). Conclusion: T4 colon adenocarcinoma has a high risk of LR and mortality. Clinical trials utilizing the aforementioned high-risk features may increase the ability to demonstrate beneficial intervention.

Macias S, Kirma J, Yilmaz A, Moore SE, McKinley MC, McKeown PP, Woodside JV, **Graham SF** and Green BD (2019). "Application of 1H-NMR metabolomics for the discovery of blood plasma biomarkers of a Mediterranean diet." *Metabolites* 9(10).

[Full Text](#)

Department of Obstetrics & Gynecology

The Mediterranean diet (MD) is a dietary pattern well-known for its benefits in disease prevention. Monitoring adherence to the MD could be improved by discovery of novel dietary biomarkers. The MEDiterranean Diet in Northern Ireland (MEDDINI) intervention study monitored the adherence of participants to the MD for up to 12 months. This investigation aimed to profile plasma metabolites, correlating each against the MD score of participants (n = 58). Based on an established 14-point scale MD score, subjects were classified into two groups ("low" and "high"). 1H-Nuclear Magnetic Resonance (1H-NMR) metabolomic analysis found that citric acid was the most significant metabolite (p = 5.99 x 10⁻⁴; q = 0.03), differing between 'low' and 'high'. Furthermore, five additional metabolites significantly differed (p < 0.05; q < 0.35) between the two groups. Discriminatory metabolites included: citric acid, pyruvic acid, betaine, mannose, acetic acid and myo-inositol. Additionally, the top five most influential metabolites in multivariate models were also citric acid, pyruvic acid, betaine, mannose and myo-inositol. Metabolites significantly correlated with the consumption of certain food types. For example, citric acid positively correlated fruit, fruit juice and vegetable constituents of the diet, and negatively correlated with sweet foods alone or when combined with carbonated drinks. Citric acid was the best performing biomarker and this was enhanced by paired ratio with pyruvic acid. The present study demonstrates the utility of metabolomic profiling for effectively assessing adherence to MD and the discovery of novel dietary biomarkers.

Maisels MJ (2019). "A rebound hyperbilirubinemia prediction rule." *Journal of Pediatrics* 214: 238-241.

[Full Text](#)

Department of Pediatrics

Maloy JD, Chen NW, **Qu L**, Merwine SJ, **Ziadeh J** and **Berger DA** (2019). "Opioid prescribing habits in the acute emergency department visit: Before and after implementation of departmental prescribing guidelines." *Annals of Emergency Medicine* 74(4): S75-S75.

[Full Text](#)

Department of Emergency Medicine

Department of Foundational Medical Studies (BH)

Mando R, **Hanzel G**, **Gallagher M**, **Safian R**, Kassas S, **Shannon F** and **Abbas A** (2019). "Incidence of patient prosthesis mismatch following native and valve-in-valve transcatheter aortic valve replacement based on indexed aortic valve area compared to energy loss index." *Journal of the American College of Cardiology* 74(13): B742-B742.

[Full Text](#)

Department of Internal Medicine

Department of Surgery

Mando R, **Hanzel G**, **Gallagher M**, **Shannon F**, **Safian R** and **Abbas A** (2019). "Invasive corroboration of echocardiographic low stroke volume index in aortic stenosis and its impact on transaortic gradient and aortic valve area." *Journal of the American College of Cardiology* 74(13): B144-B144.

[Full Text](#)

Department of Internal Medicine

Department of Surgery

Mankuzhy NP, Walling E, Anderson B and Mody R (2019). "Cryptic ETV6-ABL1 fusion and MLL2 truncation revealed by integrative clinical sequencing in multiply relapsed acute lymphoblastic leukemia." Journal of Pediatric Hematology/Oncology 41(8): 653-656.

[Request Form](#)

OUWB Medical Student Author

The ETV6-ABL1 fusion is a rare genetic aberration classified as Philadelphia chromosome-like high-risk B-cell precursor acute lymphoblastic leukemia. We present the case of a child with multiply relapsed B-cell precursor acute lymphoblastic leukemia in which next-generation sequencing identified this cryptic fusion, undetected by standard testing, resulting in sustained clinical response to targeted therapy with imatinib. Upon subsequent relapse, repeat next-generation sequencing identified an additional aberration, MLL2-ADCY9, as a possible molecular driver conferring resistance to therapy. This report demonstrates the exciting potential of integrative clinical sequencing in identifying previously undetected actionable findings leading to improved outcomes in pediatric oncology patients.

Mankuzhy NP, Anderson B, Heider A, Michniacki TE, Kumar-Sinha C and Mody R (2019). "KRAS mutant tenosynovial giant cell tumor in a pediatric patient: A case report." Translational Pediatrics 8(5): 449-454.

[Full Text](#)

OUWB Medical Student Author

Tenosynovial giant cell tumors (TSGCT) are a group of rare, benign soft tissue tumors with common histologic and cytogenetic features, with a median age of diagnosis being 47 years. Generally divided into localized and diffuse subtypes, TSGCTs are typically driven by overexpression of macrophage colony stimulating factor receptor-1 (CSF1R). Treatment of TSGCT is tumor resection, followed by radiation therapy in cases of incomplete resection. Even when the tumor is completely removed, recurrence rates can be as high as 30% in some anatomical locations. Here we report the identification of a previously undescribed KRAS p.G12D activating mutation within a pediatric TSGCT patient, who clinically presented with an enlarging right lower extremity mass pathologically consistent with TSGCT. The patient continues to be in remission three years after complete surgical removal. KRAS mutations are usually found in adult cancers, such as lung and pancreatic, as well as giant cell lesion of the jaw. This case demonstrates the utility of integrative clinical sequencing in identifying lesions with aggressive potential and aiding in complex diagnoses.

Martin S, Han E and **Peters KM** (2019). "A novel approach to managing post retropubic vaginal sling pain." Urology. ePub Ahead of Print.

[Full Text](#)

Department of Urology

Objective: To describe a novel technique of using peripheral nerve neuromodulation (PNNM) for the treatment of refractory, mesh-induced chronic pelvic pain. Chronic pelvic pain associated with mesh can be a debilitating complication and there is currently no consensus on treatment. PNNM has been shown to be successful in the treatment of post-traumatic neuralgias but has yet to be studied in mesh complications. **Materials and Methods:** We present a case of a 50-year-old woman who had unrelenting pelvic pain after retropubic sling placement. She failed multiple therapies including medications, mesh removal, pelvic floor physical therapy, pudendal neuromodulation, and pelvic floor onabotulinumtoxinA trigger point injections. **Results:** The only treatment that provided temporary relief of this patient's pain was transvaginal trigger point injections along with a right pudendal nerve block using 40 mg triamcinolone and 0.5% ropivacaine. To help define if treatment at the site of her pain would provide relief, a series of blocks were done by advancing a needle retropubically to her area of pain and injecting triamcinolone and 0.5% ropivacaine. This injection, which corresponded to the previous tract of her retropubic sling, provided temporary, but profound, relief. PNNM was then done with placement of the electrode in the retropubic space at the site of her pain. This provided instantaneous relief of almost all of her pain symptoms. Twelve months postoperatively, the patient continued to have >90% improvement in her pain. **Conclusion:** Focused PNNM

is a simple procedure and can provide symptomatic relief for refractory postvaginal mesh pain.

McDermott PN (2019). "Surface dose and acute skin reactions in external beam breast radiotherapy." [Medical Dosimetry](#). ePub Ahead of Print.

[Request Form](#)

Department of Radiation Oncology

The biologically relevant depth for acute skin reactions in radiotherapy is 70 microm. The dose at this depth is difficult to measure or calculate and can be quite different than the dose at a depth of as little as 1 mm. For breast radiotherapy with medial and lateral tangential beams, the skin dose depends on both the contribution from the entrance beam and the exit beam. The skin dose has been estimated in a breast model hemi-ellipse accounting for field size, beam energy, obliquity, lack of backscatter, fractionation, size and shape of the hemi-ellipse. The dose has been held constant along the axis of symmetry of the hemi-ellipse by introducing modulation as in clinical IMRT practice. Dose distributions have been computed as a function of the polar angle from the center of the hemi-ellipse. The exit dose always dominates the entrance dose for all realistic parameters. As a result, the surface dose is higher for 18 MV than 6 MV over the entire surface for all reasonable sizes and shapes of the hemi-ellipse. The results of these calculations suggest that substituting an 18 MV beam for a 6 MV beam to achieve greater skin sparing may have just the opposite effect. The ratio of the surface dose to the mid-depth dose ranges from about 35% at polar angle 0(o) to up to 70% at polar angle 80(o). The dose rises sharply at angles above 30(o). The surface dose rises moderately at all angles as the size of the hemi-ellipse increases. The effect of shape is somewhat complex: as the breast becomes flatter, doses at intermediate angles increase, but doses at small and large angles decrease. The biologically effective dose for erythema and moist desquamation is about 2 to 3 Gy higher at all polar angles for conventional fractionation (2.00 Gyx25 fractions) than for hypofractionation (2.66 Gyx16).

McLean SA, Ressler K, Koenen KC, Neylan T, Germine L, Jovanovic T, Clifford GD, Zeng D, An X, Linnstaedt S, Beaudoin F, House S, Bollen KA, Musey P, Hendry P, Jones CW, Lewandowski C, **Swor R**, Datner E, Mohiuddin K, Stevens JS, Storrow A, Kurz MC, McGrath ME, Fermann GJ, Hudak LA, Gentile N, Chang AM, Peak DA, Pascual JL, Seamon MJ, Sergot P, Peacock WF, Diercks D, Sanchez LD, Rathlev N, Domeier R, Haran JP, Pearson C, Murty VP, Insel TR, Dagum P, Onnela JP, Bruce SE, Gaynes BN, Joormann J, Miller MW, Pietrzak RH, Buysse DJ, Pizzagalli DA, Rauch SL, Harte SE, Young LJ, Barch DM, Lebois LAM, van Rooij SJH, Luna B, Smoller JW, Dougherty RF, Pace TWW, Binder E, Sheridan JF, Elliott JM, Basu A, Fromer M, Parlikar T, Zaslavsky AM and Kessler R (2019). "The AURORA Study: A longitudinal, multimodal library of brain biology and function after traumatic stress exposure." [Molecular Psychiatry](#) 25(2): 283-296.

[Request Form](#)

Department of Emergency Medicine

Adverse posttraumatic neuropsychiatric sequelae (APNS) are common among civilian trauma survivors and military veterans. These APNS, as traditionally classified, include posttraumatic stress, postconcussion syndrome, depression, and regional or widespread pain. Traditional classifications have come to hamper scientific progress because they artificially fragment APNS into siloed, syndromic diagnoses unmoored to discrete components of brain functioning and studied in isolation. These limitations in classification and ontology slow the discovery of pathophysiologic mechanisms, biobehavioral markers, risk prediction tools, and preventive/treatment interventions. Progress in overcoming these limitations has been challenging because such progress would require studies that both evaluate a broad spectrum of posttraumatic sequelae (to overcome fragmentation) and also perform in-depth biobehavioral evaluation (to index sequelae to domains of brain function). This article summarizes the methods of the Advancing Understanding of Recovery after trauma (AURORA) Study. AURORA conducts a large-scale (n = 5000 target sample) in-depth assessment of APNS development using a state-of-the-art battery of self-report, neurocognitive, physiologic, digital phenotyping, psychophysical, neuroimaging, and genomic assessments, beginning in the early aftermath of trauma and continuing for 1 year. The goals of AURORA are to achieve improved phenotypes, prediction tools, and understanding of molecular mechanisms to inform the future development and testing of preventive and treatment interventions.

McQuivey KS, Christopher ZK, Chung AS, Makovicka J, **Guettler J** and **Levasseur K** (2019). "Implementing the lever sign in the emergency department: Does it assist in acute anterior cruciate ligament rupture diagnosis? A pilot study." [Journal of Emergency Medicine](#) 57(6): 805-811.

[Full Text](#)

Department of Orthopaedic Surgery

Department of Emergency Medicine

Background: Within the emergency department (ED) setting, anterior cruciate ligament (ACL) rupture is commonly misdiagnosed, leading to improper treatment and potential meniscal injury and total joint replacement. Utilizing traditional clinical tests to diagnosis ACL rupture leads to the correct diagnosis in about 30% of cases. The lever sign is a new and effective clinical test used to diagnose ACL rupture with 100% sensitivity. Objective: We aim to study if the lever sign used in the ED setting is more sensitive to diagnose ACL rupture than traditional tests. Methods: Patients between 12 and 55 years of age were examined utilizing either traditional methods or the lever sign. Diagnostic findings in the ED were compared with those of a sports medicine specialist using magnetic resonance imaging as the diagnostic standard. A survey was given to ED providers to collect data on diagnosis and physician confidence in diagnosis. Results: The sensitivity of the lever sign was 100% (94.7% accuracy, 93.75% specificity), whereas the sensitivity of the anterior drawer/Lachman test was 40% (87.5% accuracy, 100% specificity). Physician confidence in diagnosis was higher utilizing the lever sign vs. the anterior drawer/Lachman test at 8.45 (± 1.82) compared with 7.72 (± 1.82) out of 10, respectively. There was no statistically significant association between diagnostic accuracy with either test and level of training of the ED provider. Conclusion: Implementation of the lever sign in the ED setting resulted in a higher sensitivity, higher physician confidence in screening test diagnosis, and a decrease in the number of undiagnosed ACL ruptures.

Menkes DL and **Pierce R** (2019). "Needle EMG muscle identification: A systematic approach to needle EMG examination." *Clinical Neurophysiology Practice* 4: 199-211.

[Full Text](#)

Department of Neurology

The proper performance of needle electromyography (EMG) requires that the examiner obtain a brief but comprehensive history, perform a directed examination and generate a short differential diagnosis as part of the initial patient encounter. Equally as important is to set reasonable expectations for this study's performance as electronic media do not necessarily portray all of the nuances of an electrodiagnostic study. In addition to these preliminary steps, this minimonograph discusses equipment used in EMG evaluations, EMG examination techniques, muscles commonly sampled, pain reduction techniques, and special considerations that may require study modification such as anticoagulation, lymphedema, obesity and supervening infection. Clinicians performing these studies will maximize useful data collection while minimizing patient discomfort if all of these recommendations are followed.

Metpally RP, Krishnamurthy S, Moran KM, Weller AE, Crist RC, Reiner BC, Doyle GA, Ferraro TN, **Radhakrishna U**, **Bahado-Singh R**, Troiani V and Berrettini WH (2019). "The imperative of clinical and molecular research on neonatal opioid withdrawal syndrome." *Molecular Psychiatry* 24(11): 1568-1571.

[Request Form](#)

Department of Obstetrics & Gynecology

Moore AB, Su E, Weiss RE, Yagapen AN, Malveau SE, Adler DH, **Bastani A**, Baugh CW, Caterino JM, **Clark CL**, Diercks DB, Hollander JE, Nicks BA, Nishijima DK, Shah MN, Stiffler KA, Storrow AB, Wilber ST and Sun BC (2019). "Frequency of abnormal and critical laboratory results in older patients presenting to the emergency department with syncope." *Academic Emergency Medicine*. ePub Ahead of Print.

[Full Text](#)

Department of Emergency Medicine

Mroue KM, **Adamson J**, Chen NW and **Rae RW** (2019). "Which patients presenting to the emergency department in atrial fibrillation with rapid ventricular response require a chest x-ray?" *Annals of Emergency Medicine* 74(4): S39-S40.

[Full Text](#)

Department of Emergency Medicine

OUIWB Medical Student Author

Nair GB and Castillo E (2019). "Longitudinal lung compliance imaging in idiopathic pulmonary fibrosis." *Radiology*

293(2): 272.

[Request Form](#)

Department of Internal Medicine

Navin MC, **Wasserman JA** and Haimann MH (2019). "Treatment over objection—Moral reasons for reluctance." Mayo Clinic Proceedings 94(10): 1936-1938.

[Request Form](#)

Department of Foundational Medical Studies (OU)

Noorulla F, **Dedon R** and **Maisels MJ** (2019). "Association of early direct bilirubin levels and biliary atresia among neonates." JAMA Network Open 2(10): e1913321-e1913321.

[Full Text](#)

OUWB Medical Student Author

Department of Pediatrics

Nyalakonda R and **Berman B** (2019). "A teenage female with transient dysarthria, pallor, and petechiae." Clinical Pediatrics 58(13): 1458-1461.

[Full Text](#)

OUWB Medical Student Author

Department of Pediatrics

Nygren M, Alafyouni M, Abbott R, **Jones S**, **Anderson W**, **Bastani A** and **Jaroszewski K** (2019). "The incidence and downstream effect of guideline non-adherence: The HEART Score in the community hospital emergency department setting." Annals of Emergency Medicine 74(4): S25.

[Full Text](#)

OUWB Medical Student Author

Department of Emergency Medicine

Study Objectives: Overutilization of hospital resources in low risk chest pain patients (LOWCPs) is a serious issue that has been addressed in multiple previous studies. It has been found that the implementation of accelerated diagnostic protocols for chest pain have shown substantial improvement in the utilization of health care resources. The development and subsequent validation of the history, electrocardiogram, age, risk factors, and troponin (HEART) score to identify ED chest pain patients who can safely be discharged without emergent provocative testing represents a potential breakthrough in the management of LOWCPs. Unfortunately, the gap between guideline development in academic centers and guideline adherence in community hospitals remains difficult to bridge. At our institution, multiple educational efforts to "get with the guidelines," including incorporating the HEART score into our electronic medical record, were attempted to assist in guideline adherence. Our study objective was to describe both the incidence and downstream effect of guideline non-adherence for LOWCPs placed in our community hospital observation unit with a HEART score < 4. Methods: Between January 1, 2017 and March 31, 2017, we performed a retrospective observational study of all patients who were placed in the ED observation unit of our 100,000 visit/year community ED for evaluation of possible acute coronary syndrome. LOWCPs were included in the study after an initial negative ED work-up, including a normal or nonspecific electrocardiogram and negative initial cardiac biomarkers. Trained research associates utilizing a structured data extraction template collected patient information in order to calculate a HEART score for all patients who did not have one documented. Patients were stratified into two cohorts: 1) HEART score < 4 (LOW) and 2) HEART score ≥ 4 (HIGH). Our primary outcome measure was the incidence of guideline non-adherence, defined by LOWCPs in LOW transferred to the ED observation unit to undergo urgent provocative testing. Our secondary outcomes include the difference between HIGH and LOW for the following adverse events: 1) The incidence of "abnormal" provocative testing defined by the presence of at least "moderate" coronary stenosis, 2) The incidence of NSTEMI, and 3) 30-day ED return rate. Data were analyzed using descriptive statistics and the chi-square test for significance of categorical variables. Results: A total of 149 patients (mean age 52.4 years, 56.4% female) met the inclusion criteria. 75 (50.34%) patients were in the LOW cohort, while 74 (49.66%) patients were in the HIGH cohort. Overall, 144 (96.64%) had stress testing and/or CT coronary angiography ordered during their observation stay. Of the patients with this additional testing, nine (6.12%) had

"abnormal" results. One patient in the LOW cohort and eight patients in the HIGH cohort had "abnormal" results ($p = 0.0151$). There was no difference in NSTEMI or 30-day ED return rates between the LOW and HIGH groups. Conclusion: In our community hospital setting, guideline non-adherence with the HEART score resulted in twice the number of patients undergoing urgent provocative testing with a significantly lower proportion of those patients having "abnormal" findings.

Ogawa T, Tyagi P, Ishizuka O, Ueda T, **Chancellor MB**, Chermansky CJ and Yoshimura N (2019). "Recent developments in imaging in BPS/IC." Current Bladder Dysfunction Reports 14(4): 301-307.

[Full Text](#)

Department of Urology

Purpose of Review: In this review, the current literature of imaging of bladder pain syndrome and interstitial cystitis (BPS/IC) will be addressed. Topics include BPS/IC, cystoscopy, computed tomography, and magnetic resonance image (MRI). Recent Findings: There are no randomized clinical trials on imaging of BPS/IC. Recently, contrast-enhanced MRI could detect the brain alterations and the changes in bladder permeability, and detection of the latter is enhanced by intravesical injection of contrast agents. Summary: MRI could advance the understanding of pathological changes in the brain and the bladder of BPS/IC patients. Especially, contrast-enhanced MRI has a potential to become a diagnostic tool although more evidences are necessary for clarifying the efficacy.

Omari A and **Mahmoud TH** (2019). "Vitreotomy." StatPearls. Treasure Island (FL): StatPearls Publishing.

[Full Text](#)

Department of Ophthalmology

Pars plana vitrectomy (PPV) is a surgical technique originally introduced by Robert Machemer.[1] The pars plana approach to the vitreous cavity allows access to the posterior segment to treat many vitreoretinal diseases. This procedure requires a great deal of technical skill and knowledge to ensure good outcomes. A successful vitrectomy can restore vision and improve the quality of life in patients suffering from many vitreoretinal diseases. However, the procedure can also be associated with complications. Although the chances are low when performed correctly, these complications can cause severe patient morbidity and blindness. Therefore, it is essential that clinicians have thorough knowledge regarding the topic, understand the procedure, when to use it, how to perform it, and post-operative management.

Omari A and **Shaheen KW** (2019). "Upper eyelid reconstruction." StatPearls. Treasure Island (FL): StatPearls Publishing.

[Full Text](#)

Department of Surgery

Upper eyelid reconstruction is a surgical procedure used to correct lid defects of the upper eyelid that occur from surgical resection of tumors, trauma, or congenital anomalies like a coloboma.[1] Reconstruction of upper eyelids due to surgical resections of neoplasms, such as skin cancers excised by Mohs micrographic surgery, requires additional consideration.[2] Restoration of the upper eyelid is much more complicated than the lower eyelid. Careful deliberation is necessary for the approach to reconstruction since the repair is highly dependent on the location and the extent of the defect. The eyelids serve essential functions to the face. In addition to providing cosmetic appearance, the eyelid mechanically protects the cornea and the globe. Furthermore, meibomian glands in the tarsus produce lipids that, upon contraction of the tarsal orbicularis oculi, stabilize the tear film to prevent dry eye. To serve this function, the upper eyelid must descend to cover the cornea during blinking but must be mobile enough to clear the visual axis upon elevation.[3] Ptosis can significantly impact the visual fields and the cosmetic appearance of the face. An ideal upper eyelid reconstruction should, therefore, address any of these potential functional or aesthetic deficits that can occur from eyelid defects.

Orelaru F, Bolanle G, Tolulope I and Ishmael J (2019). "Assessing knowledge of sickle cell trait/disease Inheritance in metropolitan Detroit." Journal of the National Medical Association 111(6): 656-664.

[Request Form](#)

OUWB Medical Student Author

Sickle cell disease (SCD) is an autosomal recessive disease not specific to one race. This study aims to assess knowledge about the inheritance pattern of sickle cell disease among college students in the Metropolitan

Detroit area. An electronic survey was administered to undergraduate students at Oakland University, and first through fourth year medical students at Oakland University William Beaumont School of Medicine (OUWB). The primary analysis compared knowledge of sickle cell disease inheritance pattern between different demographic categories. A total of 146 Oakland University (27.4%) and OUWB (72.6%) students responded to the survey. The average age of the respondents was 24.27 ± 4.09 . The majority of respondents were female (61%) and white (72.6%). In total, three (3) respondents - 1 white, 1 Asian and 1 African American, reported knowing that they have sickle cell disease/trait. In addition, one (1) white female respondent reported having an infant carrying the sickle cell trait. Most respondents (95.9%) knew that sickle cell disease/trait is genetically inherited, but a majority believed that it is associated only with African-Americans (67.8%). Respondents who were college graduates were more likely to correctly identify SCD inheritance patterns (98% compared to 85% of undergraduates; $p = 0.002$) and less likely to correctly answer the question "Who gets the disease?" (24% compared to 63%; $p < 0.001$). Most respondents (75%) think people should know if they have sickle cell trait/disease before marriage. The result shows that most respondents believe sickle cell disease is specific to African-Americans. However, because it is equally possible for all races to inherit this disease, knowing one's status could help prevent sickle cell-related deaths during rigorous exercises and enable individuals of reproductive age to make informed reproductive decisions in order to decrease sickle cell disease prevalence, and its associated financial and psychosocial burdens.

Pang YF, **Dalal B**, Ran RZ and Schrader S (2019). "Acute respiratory failure as an initial sign of zonisamide-induced Stevens-Johnson Syndrome." Chest 156(4): 1432A-1432A.

[Request Form](#)

Department of Internal Medicine

Park DK, Roberts R, Arnold P, Kim DH, Sasso R, **Baker KC** and **Fischgrund JS** (2019). "Lumbar spine fusion rates with local bone in posterolateral and combined posterolateral and interbody approaches." Journal of the American Academy of Orthopaedic Surgeons. Global Research & Reviews 3(11): e018.

[Full Text](#)

Department of Orthopaedic Surgery

Posterolateral lumbar fusion (PLF) used to treat degenerative lumbar conditions still faces pseudarthrosis. Bone graft choice is a key factor; a traditional choice has been autologous iliac crest bone graft (ICBG), but complication rates are quoted up to 39%. Local bone from laminectomy eliminates ICBG harvesting complications. Methods: Two hundred forty-one patients underwent either PLF or PLF with interbody at a single lumbar level with a prospective, multicenter, randomized controlled trial only using local bone graft. Fusion was assessed with radiographs and CT. Results: PLF fused bilaterally in 18% and unilaterally in 28.8% at 6 months and 35.7% and 50.3% at 12 months, respectively. At 6-month PLF + interbody, 1.1% fused bilaterally and 11.7% unilaterally; at 12 months, 5.4% fused all three areas, and 50.8% fused at least one area. Discussion: Local bone fused substantially less than the "benchmark" ICBG.

Partiali B, **Oska SR**, **Touriel R**, **Delise A**, **Barbat A** and **Folbe A** (2019). "Sex disparity in speaking opportunities at a major academic emergency medicine conference: Are women stuck under the glass ceiling?" Annals of Emergency Medicine 74(4): S32.

[Full Text](#)

OUWB Medical Student Author

Department of Surgery

Study Objectives: This study investigates trends in the representation of female speakers at the American College of Emergency Physicians (ACEP) scientific assembly - the largest academic emergency medicine conference in the world. Methods: Data was collected from the American College of Emergency Physicians (ACEP) Scientific Assembly's online database from 2016-2018. We collected information regarding each presentation given at the national conference, including the title of the presentation, speaker names, duration of the presentation, and specialty category. Speaker sex was recorded using Google searches and department Web sites. Using the Elsevier SCOPUS database, we identified h-index, number of publications, and number of times cited. Exclusion criteria were speakers who did not hold an MD or DO degree. We used SPSS software to obtain descriptive statistics and perform independent-tests. Results: From the three years

of conference data, there were a total of 939 invited speakers included in the analysis. Of the 939 invited speakers, 34.3% were women and 65.7% were men. In 2016, there were a total of 340 speakers, of whom 27.1% were female and 72.9% were male. In 2017, there were a total of 296 speakers, with women comprising 34.5% of speakers, and men making up the remaining 65.5%. In 2018, women made up 42.2% of the speakers presenting at the conference, and men made up the remaining 57.8%. Presentations given by women were shorter, on average, than presentations given by male speakers during all three years of conference data. In 2016, male presenters, on average, had statistically higher h-indices and were cited more times, on average, than their female counterparts (p-value<0.05). The average number of publications, however, did not significantly differ between men and women (p-value>0.05). In 2017 and 2018, male speakers, on average, had significantly higher h-indices, number of publications, and citations (p-value<0.05). Conclusion: These results demonstrate an upward trend in the representation of women speakers at the largest academic emergency medicine conference in the world. From 2016 to 2018, there was a steady increase in the proportion of female speakers, with women comprising 42.2% of all speakers at the 2018 conference. Women's presentations also increased in length, on average, from 2016 to 2018. Despite these advancements in representation, male speakers still speak for longer, on average, and make up the majority of presenters. Although women account for a significant portion of the workforce in emergency medicine, efforts to improve female representation in academic emergency medicine are necessary. Women currently only make up 28% of the workforce in academic emergency medicine. It can be argued that improving women's representation at scientific conferences may result in more opportunities for female engagement in academic emergency medicine.

Pattisapu AK and **Bozyk P** (2019). "Persistent hypoxemia with increased airway pressure: A case of intracardiac shunt." *Chest* 156(4): A1200.

[Full Text](#)

Department of Internal Medicine

Introduction: Persistent hypoxemia is a significant concern amongst the hospitalized population. Acute respiratory failure with hypoxia is one of the most common reasons for admission and deriving the exact etiology is often unclear and multifactorial. Atrial Septal Defect (ASD) and Patent foramen ovale (PFO) normally result in a left to right shunt or no significant shunting. With persistent hypoxemia, any trigger resulting in increasing pulmonary vascular resistance and right atrial pressure often results in exposure of the right to left shunt. Another infrequent and often overlooked cause is an increase in intra-thoracic pressure from mechanical ventilation. Case Presentation: 93 year old male with history of multiple myeloma, moderate mitral regurgitation and atrial tachycardia on sotalol and warfarin presented with syncope episode due to acute kidney injury. He had history of pulmonary embolism one year prior and is currently on warfarin. Echocardiogram at that time showed right ventricular systolic pressure (RVSP) of 26 mmHg with left ventricular ejection fraction of 60%. During this hospitalization, he subsequently found to be hypoxic, noted oxygen saturation (SaO₂) at 80% on room air. Patient's INR is therapeutic in the hospital. BNP was 296. Aspiration pneumonia and pulmonary edema was ruled out with negative chest radiograph. A-a gradient on arterial blood gas was 612. Patient was subsequently intubated and placed on mechanical ventilation with persistent hypoxemia despite increasing the positive end expiratory pressure (PEEP) to 10 cmH₂O and fraction of inspired oxygen (FiO₂) of 100%. Peak airway pressure was 23 cmH₂O with mean airway pressure of 12 cmH₂O. CT chest angiogram did not reveal pulmonary embolism. There were no other symptoms except for peripheral cyanosis. Transthoracic echocardiogram with bubble study detected right to left intracardiac shunt (not present in prior echo) with large Atrial Septal defect and residual pulmonary hypertension with an increase in RVSP of 35-40 mmHg. There was suspicion of chronic thromboembolic related pulmonary hypertension. Cardiology and cardiac surgery determined that due to patient's age, significant co-morbidities that he was not a surgical candidate for operative closure of Atrial Septal defect. Discussion: With mechanical ventilation, hypoxemia can usually improve with increasing PEEP. PEEP helps to recruit alveoli resulting in increase in functional residual capacity (FRC) and thus increased oxygenation. This in turn results in increased airway pressure. There should be high index of suspicion for intracardiac shunt when hypoxemia worsens with increasing airway pressures and pulmonary vascular resistance. Conclusions: Point of attack should be focused on decreasing pulmonary vascular resistance, improving ventilation and perfusion mismatch and minimizing intra-thoracic pressures in the case of right to left shunting with hypoxemia. Reference #1: Granati, G. T., & Teressa, G. (2016). Worsening hypoxemia in the face of increasing

PEEP: a case of large pulmonary embolism in the setting of intracardiac shunt. The American journal of case reports, 17, 454. Reference #2: De Picciotto, C., Duménil, C., Auzel, O., Giraud, V., & Bonay, M. (2017). Paradoxical worsening of hypoxemia in a patient treated by noninvasive positive pressure ventilation for obesity hypoventilation syndrome with concomitant obstructive sleep apnea: a case report. Journal of medical case reports, 11(1), 234. Disclosures: No relevant relationships by Paul Bozyk, source=Admin input
No relevant relationships by Anil Kumar Pattisapu, source=Web Response

Peter IM, Deraney RN, Orango O, Philip T, **Rosen B** and Cu-Uvin S (2019). "Radical hysterectomy for operable early cervical cancer in HIV-positive and HIV-negative women in western Kenya." International Journal of Gynecology & Obstetrics. ePub Ahead of Print.

[Full Text](#)

Department of Obstetrics & Gynecology

Radical hysterectomy is well tolerated with no increase in complications in HIV-infected women and is an appropriate form of treatment for early-stage cervical cancer in HIV-infected women.

Pratt RL (2019). "Educational avenues for promoting dialog on fascia." Clinical Anatomy 32(7): 871-876.

[Full Text](#)

Department of Foundational Medical Studies (OU)

If your healthcare professional students have not heard about the importance of fascia they definitely should, and if your residents have not heard about the manifestations of fascia health they definitely will from their patients. While fascia may not be the sexiest of organ systems, it is one of the most influential. Fascia is gaining interest from researchers, physicians, and many subdivisions of manual medicine including massage therapists. The fascial system is now being recognized with roles in pathology, fluid movement, and proprioception. It is also important in skeletal muscle movement, perception of pain, protein regulation and expression, cell signaling, neoplastic growth, and hormone distribution in our body. It can be the reason why we feel chronic pain or why we feel tightness after physical activity. The primary responsibility of fascia is to connect systems so that the body works as a whole, which is what permits this topic to be easily embedded anywhere in our health curricula. Whether you teach students in schools of medical, veterinary, dental, physical therapy, physician assistant studies, or occupational therapy, fascia matters. Whether you teach in an integrated curriculum or a curriculum that is designed for problem-based learning or a classical discipline-based curriculum, connective tissue has a place in academia. So, in our cramped curriculum how do we make sure that our current undergraduate and graduate students understand the complexity of fascia without adding additional time to coursework? To answer this question, this article demonstrates how fascia can fit anywhere in the curriculum because it is found everywhere. Clin. Anat. 32:871–876, 2019.

Price J, Hijazi M, Clavette-Lachapelle L and **Bahl A** (2019). "Ultra long versus standard long peripheral intravenous catheters: A randomized controlled trial of ultrasound-guided catheter survival." Annals of Emergency Medicine 74(4): S136.

[Full Text](#)

Department of Emergency Medicine

Study Objectives: Ultrasound-guided intravenous (IV) catheters have dismal dwell time with most IVs failing prior to completion of therapy. Catheter length in vein is a variable directly related to catheter survival. We investigate the survival of an ultra long peripheral IV compared to standard long peripheral IV placed under ultrasound (US)-guidance. Methods: We conducted a single site, 2-arm, nonblinded, randomized controlled trial of catheter survival. Adult patients presenting to the emergency department (ED) with a history of difficult vascular access were recruited to participate. Patients were randomized to receive either a standard long 4.78 cm length 20 gauge US-guided IV catheter or the intervention ultra long 6.35 cm length 20 gauge US-guided IV catheter. The primary outcome was catheter survival. All functional catheters removed with less than 24 hours dwell time were excluded from the survival analysis. Any catheter failure regardless of dwell time was included in the survival analysis. Secondary outcomes included evaluation of insertion parameters including first-stick success and time to insertion as well as complications including thrombosis and infection. Results: 270 patients were enrolled. 194 patients were included in the survival analysis with 99 in the standard long IV group and 95 in the ultra long IV group. Kaplan-Meier estimate of catheter median survival time was 135.88 hours (5.66 days) [95% CI 115-310] for the ultra long IV catheters compared to

77.67 hours (3.23 days) [95% CI 63-102] for the standard long IV catheters (Log-rank Test: $p = 0.008$). IVs with greater than 3.1 cm of the catheter residing in vein had a median survival of 128.90 hours (5.37 days) [95% CI 96-504] compared to 76.55 hours (3.18 days) [95% CI 63-115] for IVs with less than 3.1 cm in the vein ($p=0.04$). Conclusion: This study supports the use of ultra long IV catheters over the standard length options for upper arm insertions as these catheters have a favorable survival profile for difficult access ED patients. The improved survival is related to the amount of catheter residing in the vein with greater than 3.1 cm catheter in vein yielding the best longevity. Further, as ultra long catheters have similar insertion characteristics and no additional education/training is needed for insertion competency, adoption of these catheters can occur seamlessly at any ED.

Probst MA, Gibson T, Weiss RE, Yagapen AN, Malveau SE, Adler DH, **Bastani A**, Baugh CW, Caterino JM, **Clark CL**, Diercks DB, Hollander JE, Nicks BA, Nishijima DK, Shah MN, Stiffler KA, Storrow AB, Wilber ST and Sun BC (2019). "Risk stratification of older adults who present to the emergency department with syncope: The FAINT Score." Annals of Emergency Medicine 75(2): 147-158.

[Full Text](#)

Department of Emergency Medicine

Study Objective: Older adults with syncope are commonly treated in the emergency department (ED). We seek to derive a novel risk-stratification tool to predict 30-day serious cardiac outcomes. Methods: We performed a prospective, observational study of older adults (≥ 60 years) with unexplained syncope or near syncope who presented to 11 EDs in the United States. Patients with a serious diagnosis identified in the ED were excluded. We collected clinical and laboratory data on all patients. Our primary outcome was 30-day all-cause mortality or serious cardiac outcome. Results: We enrolled 3,177 older adults with unexplained syncope or near syncope between April 2013 and September 2016. Mean age was 73 years (SD 9.0 years). The incidence of the primary outcome was 5.7% (95% confidence interval [CI] 4.9% to 6.5%). Using Bayesian logistic regression, we derived the FAINT score: history of heart failure, history of cardiac arrhythmia, initial abnormal ECG result, elevated pro B-type natriuretic peptide, and elevated high-sensitivity troponin T. A FAINT score of 0 versus greater than or equal to 1 had sensitivity of 96.7% (95% CI 92.9% to 98.8%) and specificity 22.2% (95% CI 20.7% to 23.8%), respectively. The FAINT score tended to be more accurate than unstructured physician judgment: area under the curve 0.704 (95% CI 0.669 to 0.739) versus 0.630 (95% CI 0.589 to 0.670). Conclusion: Among older adults with syncope or near syncope of potential cardiac cause, a FAINT score of zero had a reasonably high sensitivity for excluding death and serious cardiac outcomes at 30 days. If externally validated, this tool could improve resource use for this common condition.

Quinn TJ, **Ding X**, **Li X**, **Wilson GD**, Buelow K, Sivananthan A, Thermoziar S, Henderson A, Epperly MW, Franicola D, Wipf P, Greenberger JS, **Stevens CW** and **Kabolizadeh P** (2019). "Amelioration of mucositis in proton therapy of Fanconi Anemia Fanca(-/-) Mice by JP4-039." In Vivo 33(6): 1757-1766.

[Full Text](#)

Department of Radiation Oncology

Background/Aim: We tested JP4-039, a GS-nitroxide radiation damage mitigator in proton therapy of Fanconi anemia (FA) mice. Materials and Methods: Fanca(-/-) and Fanca(+/-) bone marrow stromal cells were pre-treated with JP4-039 and irradiated with either protons or photons (0-10 GyRBE) followed by clonogenic survival and beta-Galactosidase senescence analysis. Fanca(-/-) and Fanca(+/-) mice were pretreated with JP4-039 for 10 min prior to oropharyngeal irradiation with either protons or photons (0 or 30 GyRBE) followed by sacrifice and measurement of oral cavity ulceration, distant hematopoietic suppression, and real-time polymerase chain reaction analysis. Results: JP4-039 reduced oral cavity ulceration in Fanca(-/-) mice, transcripts Nfkb, Ap1, Sp1, and Nrf2, and proton therapy induced distant marrow suppression. Conclusion: JP4-039 protected Fanca(-/-) and Fanca(+/-) cells and mouse oral cavity from both proton and photon radiation.

Quinn TJ and **Hamstra D** (2019). "Hypofractionation in prostate cancer using proton beam." International Journal of Radiation Oncology Biology Physics 105(4): 723-726.

[Full Text](#)

Department of Radiation Oncology

Ramsey T, Hojjat H, **Yuhan B**, Svider PF, Eloy JA, **Folbe AJ**, Raza SN and Fribley AM (2019). "Disparities in impact of nasopharyngeal cancer: An analysis of global health burden." [Laryngoscope](#) 129(11): 2482-2486.

[Full Text](#)

OUWB Medical Student Author

Department of Surgery

Objectives: Nasopharyngeal carcinoma has a unique worldwide racial and geographic distribution. Our objective was to evaluate socioeconomic disparities in the burden of nasopharyngeal cancer (NPC) between endemic and nonendemic regions. Methods: To demonstrate trends regarding societal burden of NPC and socioeconomic development, national disability-adjusted life year (DALY) rates and human development indices (HDI) between 1990 and 2015 were evaluated. Countries were divided based on the endemic versus nonendemic presence of NPC and further analyzed by HDI status as specified by the United Nations Development Program. Gini coefficients and concentration index were used to evaluate global equality in NPC burden over this period. Results: Age-standardized DALYs dropped from 36.1 in 1990 to 26.5 in 2015 (26.6% decline) ($r = -0.991$, $P < 0.001$). Lower socioeconomic countries harbored greater NPC burden upon controlling by endemic and nonendemic regions, as demonstrated by progressively negative concentration indexes. Health inequality was greater in nonendemic countries than in endemic countries ($P < 0.01$). Conclusion: To our knowledge, this is the first study to investigate socioeconomic-related changes in NPC burden using statistical tools such as the Gini coefficient and concentration index. Although the burden of NPC has steadily decreased, there remain persistent inequalities associated with socioeconomic disparities. Nasopharyngeal cancer burden is more pronounced in countries with lower HDI. Our results reinforce the importance of increasing resources for developing countries and continuing inquiry into the screening, diagnosis, and management of NPC. Level of Evidence: NA [Laryngoscope](#), 129:2482–2486, 2019.

Rao P, **Knapp AN**, Todorich B, **Drenser KA**, **Trese MT** and **Capone A, Jr.** (2019). "Anatomical surgical outcomes of patients with advanced Coats Disease and Coats-like detachments: Review of literature, novel surgical technique, and subset Analysis in patients with facioscapulohumeral muscular dystrophy." [Retina](#) 39: S182-S190.

[Full Text](#)

OUWB Medical Student Author

Department of Ophthalmology

Renard BM, Cami E, **Jiddou-Patros MR**, Said A, **Kado H**, **Trivax J**, **Berman A**, Gulati A, **Rabah M**, **Timmis S**, **Shoukfeh M**, **Abbas AE**, **Hanzel G**, **Hanson I**, **Dixon S** and **Safian RD** (2019). "Optimizing the technique for invasive fractional flow reserve to assess lesion-specific ischemia." [Circulation. Cardiovascular Interventions](#) 12(10): e007939.

[Full Text](#)

Department of Internal Medicine

Background: Invasive fractional flow reserve (FFRINV) is the standard technique for assessing myocardial ischemia. Pressure distortions and measurement location may influence FFRINV interpretation. We report a technique for performing invasive fractional flow reserve (FFRINV) by minimizing pressure distortions and identifying the proper location to measure FFRINV. Methods: FFRINV recordings were obtained prospectively during manual hyperemic pullback in 100 normal and diseased coronary arteries with single stenosis, using 4 measurements from the terminal vessel, distal-to-the-lesion, proximal vessel, and guiding catheter. FFRINV profiles were developed by plotting FFRINV values (y-axis) and site of measurement (x-axis), stratified by stenosis severity. $FFRINV \leq 0.8$ was considered positive for lesion-specific ischemia. Results: Erroneous FFRINV values were observed in 10% of vessels because of aortic pressure distortion and in 21% because of distal pressure drift; these were corrected by disengagement of the guiding catheter and re-equalization of distal pressure/aortic pressure, respectively. There were significant declines in FFRINV from the proximal to the terminal vessel in normal and stenotic coronary arteries ($P < 0.001$). The rate of positive FFRINV was 41% when measured from the terminal vessel and 20% when measured distal-to-the-lesion ($P < 0.001$); 41.5% of positive terminal measurements were reclassified to negative when measured distal-to-the-lesion. Measuring FFRINV 20 to 30 mm distal-to-the-lesion (rather than from the terminal vessel) can reduce errors in measurement and optimize the assessment of lesion-specific ischemia. Conclusions: Meticulous technique (disengagement of the guiding catheter, FFRINV pullback) is required to avoid erroneous FFRINV, which occur in 31% of vessels. Even with optimal technique, FFRINV values are influenced by stenosis severity and the site of pressure measurement. FFRINV values from the terminal vessel may overestimate lesion-specific

ischemia, leading to unnecessary revascularization.

Rizik DG, **Burke RF** and **Goldstein JA** (2019). "Urgent mechanical circulatory support and transcatheter mitral valve repair for refractory hemodynamic compromise." *Catheterization and Cardiovascular Interventions* 94(6): 886-892.

[Full Text](#)

Department of Internal Medicine

Patients presenting with hemodynamic instability attributable to left ventricular systolic dysfunction and concomitant severe mitral regurgitation (MR) are increasingly recognized and pose complex management challenges. Surgical therapy is typically precluded owing to prohibitive mortality. The role of percutaneous mechanical circulatory support in such cases is well established; however, such interventions may be neither sufficient to achieve optimal stability nor prove definitive. The advent of novel catheter-based mitral repair modalities now offers primary decisive therapeutic intervention. Three cases of cardiogenic shock with severe MR illustrate the salutary hemodynamic and clinical responses to percutaneous mechanical support and valve repair by mitral clip.

Sandrone S, Berthaud JV, Carlson C, Cios J, Dixit N, Farheen A, Kraker J, Owens JWM, **Patino G**, Sarva H, Weber D and Schneider LD (2019). "Strategic considerations for applying the flipped classroom to neurology education." *Annals of Neurology* 87(1): 4-9.

[Full Text](#)

Department of Foundational Medical Studies (OU)

Nowadays, the "flipped classroom" approach is taking the center stage within medical education. However, very few reports on the implementation of the flipped classroom in neurology have been published to date, and this educational model still represents a challenge for students and educators alike. In this article, neurology educators from the American Academy of Neurology's A. B. Baker Section on Neurological Education analyze reports of flipped classroom in other medical/surgical subspecialties, review the current implementation in neurology, and discuss future strategies to flip the neurology curriculum through contextualization of the benefits and the consequences. ANN NEUROL 2020;87:4-9.

Sangal RB and Sudan N (2019). "Baseline lighter sleep and lower saturation are associated with improved sleepiness and adherence on continuous rather than autotitrating positive airway pressure." *Clinical EEG Neuroscience*: 1550059419892759.

[Full Text](#)

Department of Family Medicine and Community Health

The objective was to test whether there were better outcomes on switching from autotitrating positive airway pressure (APAP) to continuous positive airway pressure (CPAP) in a clinic sample of patients with obstructive sleep apnea (OSA). Patients prescribed APAP in 2015-2016 and belonging to a subset characterized by side effects, or suboptimal response or adherence, were advised a switch to CPAP following a CPAP titration polysomnography. The main analysis was for improvement (after switch from APAP to CPAP) in (1) sleepiness, wakefulness inability, and fatigue, using change from baseline in the Sleepiness-Wakefulness Inability and Fatigue Test (delta SWIFT), and Epworth Sleepiness Scale (delta ESS), and (2) adherence using percentage of days with ≥ 4 -hour use and whether there was ≥ 4 -hour use on $\geq 70\%$ days. To determine possible predictors for switching, additional analysis was performed for differences at baseline between patients switching and those staying on APAP. A total of 148 patients were switched from APAP to CPAP and had greater improvement in delta SWIFT (5.2 vs 4.1, $P = .004$), greater improvement in delta ESS (3.6 vs 2.9, $P = .011$), and better adherence (79.4% vs 74.3%, $P = .006$) on CPAP than on APAP. More patients were adherent on CPAP than on APAP (83.1% vs 68.9%, $P = .006$). Patients switching had higher baseline arousal index and stage N1 sleep, and lower nadir oxygen saturation, than 96 patients not switching. Thus, there is a subset of patients with better outcomes after switching to CPAP than on APAP. Patients with baseline lighter sleep (indicated by more arousals and stage N1), or greater desaturation, may be more likely to do better on CPAP than on APAP. CPAP may be the preferable treatment in a significant subset of patients. If APAP is used first anyway, side effects, or suboptimal response or adherence, should lead to consideration of switching to CPAP based on a CPAP titration polysomnography.

Sawarynski KE and **Baxa DM** (2019). "Utilization of an online module bank for a research training curriculum:

Development, implementation, evolution, evaluation, and lessons learned." [Medical Education Online](#) 24(1): 1611297.

[Full Text](#)

Department of Foundational Medical Studies (OU)

Background: Students enter Oakland University William Beaumont School of Medicine's required research program, Embark, with variable levels of experience. Recognizing this, Embark allows for progression through the individual research project with flexibility. Since 2014, student self-directed curriculum personalization is promoted through a menu of online modules. Objective: This evaluation sought to understand student usage of the modules, identified strengths of the modules and preferred attributes of the modules. Gaining this evidence will provide information on how to best meet students' needs in a just-in-time format. Methods: A retrospective mixed methods analysis of the module library was conducted. The library was constructed using best practices as an educational tool. The retrospective evaluation included analysis of students' viewing patterns and answers to required course evaluations during the fall semesters of 2014 to 2017. Students' preference for modules was determined by viewing records and conjoint analysis. Results: Students' milestone preparation was not negatively impacted by relocation of curricular content from lecture to modules. Changes in module implementation within the course (2016) resulted in an increase of students viewing modules beyond only the minimum course requirements (71% (2016) from 10% (2014)). Data from both quantitative and qualitative evaluation questions show an increase in students' identifying the modules as a strength to individualize the course. The identified module strengths include content individualization, just-in-time access, while identified needs included a desire for additional modules. Students preferred modules that were animated, shorter in duration and curated from an external source. Conclusions: Online modules provide students with a rich set of resources allowing for individualized learning. Lessons learned in the implementation of the online modules may be transferable to many educational topics. When implementing similar technology projects, usage rates, learner feedback, and effect on appreciation of the content are important to frequently monitor.

Schutt CA, Sargent E, Kabolizadeh P, Grills IS and Jacob J (2019). "Proton beam radiation-induced glioblastoma multiforme." [Journal of Neurosurgical Sciences](#) 63(5): 609-610.

[Request Form](#)

Department of Radiation Oncology

Department of Surgery

Department of Neurosurgery

Segura-Hernandez M, Valadez-Jimenez VM, **Ysunza PA**, Sanchez-Valerio AP, Arch-Tirado E, Lino-Gonzalez AL and Hernandez-Lopez X (2019). "Acoustic analysis of voice in children with cleft lip and palate following vocal rehabilitation. Preliminary report." [International Journal of Pediatric Otorhinolaryngology](#) 126: 109618.

[Full Text](#)

Department of Physical Medicine & Rehabilitation

Background: Cleft lip and palate (CLP) is the most common craniofacial anomaly. CLP affects resonance, voice and speech. Besides the most frequently reported resonance and speech disorders, several reports have addressed acoustic abnormalities in the voice of patients with CLP. However, there are just a few reports focusing on vocal treatment in this population. Objective: To study whether a Speech and Language Pathology (SLP) intervention including vocal rehabilitation for children with CLP and velopharyngeal insufficiency (VPI) provides significant improvement of abnormal acoustic parameters of voice. Material and Methods: Fifteen children with cleft lip and palate (CLP) and velopharyngeal insufficiency (VPI) were studied. Age ranged 4-5 years. A matched control group of children without craniofacial anomalies and adequate speech, resonance and voice was assembled. All children underwent acoustic analysis of voice at the onset and at the end of SLP intervention including vocal rehabilitation. Results: Hypemasality persisted unchanged following SLP intervention. Mean Fundamental Frequency (FO) did not demonstrate a significant difference between the control and the active groups. At the onset of the intervention mean shimmer and jitter were significantly higher in all patients with CLP as compared to controls. At the end of the intervention shimmer and jitter significantly decreased in patients with CLP showing no differences as compared to controls. Conclusion: SLP intervention including vocal rehabilitation improves abnormal acoustic parameters of voice. Besides surgical treatment for VPI the SLP intervention in children with CLP should also address vocal rehabilitation.

Sheehan JP, **Grills I**, Chiang VL, Dong HM, Berg A, Warnick RE, Kondziolka D and Kavanagh B (2019). "Quality of life outcomes for brain metastasis patients treated with stereotactic radiosurgery: pre-procedural predictive factors from a prospective national registry." Journal of Neurosurgery 131(6): 1848-1854.

[Request Form](#)

Department of Radiation Oncology

Objective: Stereotactic radiosurgery (SRS) is increasingly used for the treatment of brain metastasis. To date, most studies have focused on survival, radiological response, or surrogate quality endpoints such as Karnofsky Performance Scale status or neurocognitive indices. The current study prospectively evaluated pre-procedural factors impacting quality of life in brain metastasis patients undergoing SRS. Methods: Using a national, cloud-based platform, patients undergoing SRS for brain metastasis were accrued to the registry. Quality of life prior to SRS was assessed using the 5-level EQ-5D (EQ5D-L) validated tool; additionally, patient and treatment attributes were collected. Patient quality of life was assessed as part of routine follow-up after SRS. Factors predicting a difference in the aggregate EQ5D-L score or the subscores were evaluated. Pre-SRS covariates impacting changes in EQ5D-L were statistically evaluated. Statistical analyses were conducted using multivariate linear regression models. Results: EQ5D-L results were available for 116 patients. EQ5D-L improvement (average of 0.387) was noted in patients treated with earlier SRS ($p = 0.000175$). Worsening overall EQ5D-L (average of 0.052 per lesion) was associated with an increased number of brain metastases at the time of initial presentation ($p = 0.0399$). Male sex predicted a risk of worsening (average of 0.347) of the pain and discomfort subscore at last follow-up ($p = 0.004205$). Baseline subscores of pain/discomfort were not correlated with pain/discomfort subscores at follow-up ($p = 0.604$), whereas baseline subscores of anxiety/depression were strongly positively correlated with the anxiety/depression follow-up subscores ($p = 0.0039$). Conclusions: After SRS, quality of life was likely to improve in patients treated early with SRS and worsen in those with a greater number of brain metastases. Sex differences appear to exist regarding pain and discomfort worsening after SRS. Those with high levels of anxiety and depression at SRS may benefit from medical treatment as this particular quality of life factor generally remains unchanged after SRS.

Shenouda K, Yuhan BT, Mir A, Gonik N, Eloy JA, **Liu JK, Folbe AJ** and Svider PF (2019). "Endoscopic resection of pediatric skull base tumors: An evidence-based review." Journal of Neurological Surgery Part B-Skull Base 80(5): 527-539.

[Request Form](#)

OUWB Medical Student Author

Department of Pathology

Department of Surgery

Objectives: To perform a systematic review examining experiences with endoscopic resection of skull base lesions in the pediatric population, with a focus on outcomes, recurrence, and surgical morbidities. Methods: PubMed/MEDLINE, Cochrane Library, Embase, and Web of Science databases were evaluated. Studies were assessed for level of evidence. Bias risk was evaluated using the Cochrane Bias tool, Grades of Recommendation, Assessment, Development and Evaluation (GRADE), and Methodological Index for Non-Randomized Studies (MINORS) criteria. Patient characteristics, pathology, site of primary disease, presenting symptoms, stage, procedure specific details, and complications were evaluated. Results were reported using the Preferred Reporting Systems for Systematic Reviews and Meta-Analysis guidelines. Results: Ninety-three studies met criteria for inclusion, encompassing 574 patients with skull base tumors. The GRADE and MINORS criteria determined the overall evidence to be moderate quality. The most common benign and malignant pathologies included juvenile nasopharyngeal angiofibromas ($n = 239$) and chondrosarcomas ($n = 11$) at 41.6 and 1.9%, respectively. Of all juvenile nasopharyngeal angiofibroma tumors, most presented at stage IIIa and IIIb (25.8 and 27.3%, respectively). Nasal obstruction (16.5%) and headache (16.0%) were common symptoms at initial presentation. Surgical approaches included endoscopic endonasal ($n = 193$, 41.2%) and endoscopic extended transsphenoidal ($n = 155$, 33.1%). Early (< 6 weeks) and late (> 6 weeks) complications included cerebrospinal fluid leak ($n = 36$, 17.3%) and endocrinopathy ($n = 43$, 20.7%). Mean follow-up time was 37 months (0.5-180 months), with 86.5% showing no evidence of disease and 2.1% having died from disease at last follow-up. Conclusion: Endoscopic skull base surgery has been shown to be a safe and effective method of treating a variety of pediatric skull base tumors. If appropriately employed,

the minimally invasive approach can provide optimal results in the pediatric population.

Shinthia N, **Otero R**, Mansour L, **Miller M** and **Todd B** (2019). "The impact of electronic medical record alerts on emergency physician workflow and clinical decision making." *Annals of Emergency Medicine* 74(4): S35-S36.

[Full Text](#)

Department of Emergency Medicine

OUWB Medical Student Author

Siljander MP, **Cross J**, Koueiter DM, Sobh A, **Moore D** and **Karadsheh MS** (2019). "Order of total hip or total knee arthroplasty does not affect length of stay or discharge disposition in patients with coexisting hip and knee arthritis." *Orthopedics* 42(6): E528-E531.

[Request Form](#)

Department of Orthopaedic Surgery

OUWB Medical Student Author

Primary total joint arthroplasty (TJA) of the hip and knee are effective procedures for improving pain and function in patients with arthritis. This study examined whether order of surgery (TKA or THA first) affects length of stay (LOS) and discharge disposition among patients with coexisting knee and hip arthritis. A total joint arthroplasty database review was performed to collect all available data for arthroplasties performed at 2 campuses of a single institution between July 2013 and April 2017. Inclusion criteria were patients who underwent both primary THA and TKA within 18 months and were age 18 years or older. Patients were divided into 2 groups based on whether THA or TKA was performed first. For all procedures, the following data were collected: age, body mass index (BMI), time between cases, LOS, discharge disposition, and the number of 90-day adverse postoperative events. Adverse 90-day events included deep infection, fracture, hardware failure, urinary tract infection, other return to the operating room, emergency department visit, readmission, or death. A total of 211 patients underwent both THA and TKA within 18 months; 124 patients underwent THA first and 87 underwent TKA first. There was no difference in age or BMI between the 2 groups. There was a significantly longer time between the first and second arthroplasty in patients with TKA first by a mean of 2 months ($P=.001$). There was no difference in 90-day adverse postoperative events following THA whether done first or second ($P=.371$), and no difference in 90-day events following TKA whether done first or second ($P=.524$). There was no difference in discharge disposition ($P=.833$ and $P=.395$) or LOS ($P=.695$ and $P=.473$) between groups for the first or second procedure, respectively. In a patient with coexisting hip and knee arthritis, the current results do not support recommending THA or TKA first based on cost related to LOS and discharge disposition.

Smythe MA, Parker D, Garwood CL, Cuker A and Messe SR (2019). "Timing of initiation of oral anticoagulation after acute ischemic stroke in patients with atrial fibrillation." *Pharmacotherapy*. ePub Ahead of Print.

[Full Text](#)

Department of Foundational Medical Studies (BH)

Patients with atrial fibrillation (AF) who suffer an acute ischemic stroke are at risk for both hemorrhagic transformation and recurrent ischemic stroke in the acute post-stroke period. Oral anticoagulants are recommended for secondary stroke prevention in patients with AF. The optimal time to initiate anticoagulant therapy after acute ischemic stroke in patients with AF is uncertain. There is concern that early initiation increases the risk of hemorrhagic transformation, whereas delayed initiation leaves the patient at risk for recurrent ischemic stroke. In this article, we provide a review of the risk of hemorrhagic transformation of acute ischemic stroke as well as review the literature and major guidelines addressing the timing of anticoagulation initiation after an acute ischemic stroke in patients with AF. Relevant articles published from 1990 to the present were identified using the PubMed and Embase databases. The majority of available literature is observational data. Large ischemic lesions, cerebral microbleeds, thrombolytic therapy, and other clinical factors may increase the risk of hemorrhagic transformation of an acute ischemic stroke. Parenteral anticoagulation within 48 hours is associated with an increased risk of hemorrhagic transformation and is not recommended. Insufficient data exist to support the safety of routine oral anticoagulant (direct oral anticoagulants or warfarin) initiation within 48 hours of an acute ischemic stroke. Direct oral anticoagulant initiation within 2 days of an acute ischemic stroke is associated with a 5% rate of hemorrhagic transformation. Infarct size and presence of hemorrhage are important factors in identifying the optimal time

to initiation and should guide decisions when available. A recommended framework for patient decision making is provided. Randomized controlled trials in this area are needed to identify the optimal timing of anticoagulation initiation, and such trials are under way.

Stem MS, Wa CA, Todorich B, Woodward MA, Walsh MK and **Wolfe JD** (2019). "27-gauge sutureless intrascleral fixation of intraocular lenses with haptic flanging: Short-term clinical outcomes and a disinsertion force study." Retina 39(11): 2149-2154.

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Department of Ophthalmology

Purpose: To determine whether haptic flanging during 27-gauge sutureless intrascleral fixation of intraocular lenses (IOLs) increases IOL stability and to report the short-term clinical outcomes of sutureless intrascleral surgery using 27-gauge trocar cannulas with haptic flanging. Methods: Retrospective surgical case series using live and cadaveric human eyes. Results: In the cadaveric experiment using five eyes, flanged haptics required more force to dislocate the IOL compared with unflanged haptics (14 ± 4 vs. 3 ± 1 g, $P = 0.03$). The clinical series included 52 eyes from 52 patients. The average age at the time of surgery was 73 ± 14 years, with a mean follow-up of 27 ± 19 weeks. The most common indication for surgery was IOL dislocation/subluxation ($n = 43$, 83%). Mean visual acuity improved from 20/140 preoperatively to 20/50 at postoperative Month 1 ($P < 0.001$). The most common postoperative issue was intraocular pressure elevation ($n = 12$, 23%). Two patients (4%) needed a reoperation for IOL dislocation. Conclusion: Haptic flanging during 27-gauge sutureless intrascleral surgery creates a more stable scleral-fixated IOL compared with the traditional unflanged technique based on a cadaveric human eye study. In addition, this variation of sutureless intrascleral surgery seems safe and effective for patients who require secondary IOLs.

Syed Z and **Chisti MM** (2019). "Disseminated intravascular coagulation and Coombs-negative hemolytic anemia caused by disseminated cytomegalovirus infection in an immunocompromised female successfully treated with Ganciclovir." Anticancer Research 39(10): 5850-5850.

[Request Form](#)

Department of Internal Medicine

Talia N, **Miller M**, Mishkoo A, Chen NW, **Otero R** and **Swor R** (2019). "Frequency of early rapid response team activation in emergency department patients with missing vital signs." Annals of Emergency Medicine 74(4): S33.

[Full Text](#)

OUWB Medical Student Author

Department of Emergency Medicine

Study Objectives: Abnormal vital signs (VS) in the emergency department (ED) have been associated with early rapid response team (eRRT) activation after admission. The absence of at least one VS in inpatients has been linked to adverse events. We postulated that patients for whom VS are missing at the time of transfer to the floor might also be at risk for deterioration and eRRT activation. Our primary objective was to document the association of eRRT within 6 hours of admission from the ED with missing VS just before admission. Secondary objectives were to explore the association between missing VS in the ED and different diagnoses as well as length of hospitalization. Methods: A retrospective observational study was conducted on RRT activations for the time period between January 1, 2017-June 30, 2017 in adult patients admitted from the ED to a regular floor at a single health center. Study sample included patients who were identified for activation within the first 6 hours of admission. Exclusions included obstetric, pediatric and mental health patients. To assess the association of variables, bivariate analyses were performed to summarize findings using frequencies and percentages for categorical variables and an association was examined with Chi-squared tests where appropriate, otherwise Fisher's exact tests were used. For continuous variables, measured characteristics were summarized using means and compared by t tests and Wilcoxon tests for normally and non-normally distributed data, respectively. Results: A total of 395 patients were identified to meet inclusion criteria. The most commonly undocumented VS was temperature (290/395 patients). Out of 395 patients who had RRT activation within 6 hours of arrival to the floor, 25 patients (6.33%) with a missing blood pressure (BP) at time of admission ($p=0.001$) and 32 (8.1%) with a missing heart rate (HR) ($p=0.02$) had a significantly higher association with RRT activation within 1 hour. Moreover, there was an increased mean length of hospitalization with the addition of 1 day in patients with a missing BP (7.3 vs 6, $p=0.03$) and

approximately 1.5 days in patients with a missing HR (7.52 vs 5.97, $p=0.04$). Of 33 patients (8.35%) with sepsis who had RRT activation, 6 were missing HR ($p=0.01$), 7 were missing BP ($p=0.002$), and 9 were missing oxygen saturation ($p<0.001$). Compared to non-sepsis patients, more sepsis patients (61%) had RRT activation within 2 hours of arrival to floor ($p=0.01$). Conclusion: There is a statistically significant association between undocumented BP and HR at time of admission from the ED with RRT activation within 6 hours of arrival to the floor as well as with increased length of hospitalization. Patients diagnosed with sepsis in the ED who had RRT activation tended to have missing VS prior to admission, namely HR, BP, and oxygen saturation and over half of sepsis patients had RRT activation within 2 hours after arriving to the floor. A larger cohort may further support the suggestion that a complete set of VS at the time of transfer to the medical ward should be obtained and reviewed before leaving the ED to minimize risk of eRRT.

Thangathurai D, Vitug S and **Ravi V** (2019). "Spirituality of physicians." *Southern Medical Journal* 112(12): 619-619.

[Request Form](#)

OUWB Medical Student Author

Thanos A, Lau-Sickon LK, **Wolfe JD** and **Hassan TS** (2019). "Three port sutureless posterior chamber intraocular lens intrascleral fixation: A novel approach." *Retina* 39: 16-20.

[Full Text](#)

Department of Ophthalmology

Thanos A, Shwayder T, Papakostas TD, Corradetti G, **Capone A, Jr.**, Sarraf D, Shields CL and **Trese MT** (2019). "Retinal vascular abnormalities in phakomatosis pigmentovascularis." *Ophthalmology Retina* 3(12): 1098-1104.

[Request Form](#)

Department of Ophthalmology

Purpose: To describe the spectrum of retinal vascular abnormalities in patients with phakomatosis pigmentovascularis (PPV). Design: Multicenter, retrospective, noncomparative, consecutive case series. Methods: Eligible patients underwent detailed retinal examination including indirect ophthalmoscopy. Ultra-widefield fundus imaging, including color fundus photography and angiography, was performed using standardized protocols, and findings were recorded and reviewed and analyzed. Participants: Three patients with a clinical diagnosis of PPV are presented. Results: Evaluation of all patients ($n = 6$ eyes of 3 patients) with widefield fluorescein angiography showed several retinal vascular abnormalities, including peripheral retinal nonperfusion ($n = 3$ eyes), peripheral vascular leakage ($n = 3$ eyes), aberrant retinal vessels ($n = 1$ eyes), vascular tortuosity ($n = 1$ eyes), and disruption of the foveal avascular zone including fovea plana ($n = 3$ eyes). In addition, 2 eyes demonstrated peripheral retinal vascular straightening and leakage similar to the features of familial exudative vitreoretinopathy. One of the patients was a carrier of a somatic GNA11 R183C pathogenic variant that has been associated with PPV. Conclusions: Fluorescein angiography, especially with widefield capability, reveals numerous retinal vascular abnormalities in patients with PPV. Considering the association of GNA11 pathogenic variants with PPV and allied disorders, these observations may suggest a role of guanine-binding proteins (G-proteins) in retinal vascular development. Supplemental material available at www.ophtalmologyretina.org.

Thanos A, Todorich B, Pasadhika S, Khundkar T, Xu D, Jain A, Ung C, **Faia LJ**, Capone A, **Williams GA**, Yonekawa Y, Sarraf D and **Wolfe JD** (2019). "Degenerative peripheral retinoschisis: Observations from ultra-widefield fundus imaging." *Ophthalmic Surgery Lasers & Imaging Retina* 50(9): 557-+.

[Request Form](#)

Department of Ophthalmology

Background and Objective: To describe the ultra-widefield (UWF) imaging characteristics of patients with degenerative peripheral retinoschisis (DPR) using Optomap technology. Patients and Methods: In this multicenter, retrospective, noncomparative, consecutive case series, eligible patients underwent detailed retinal examination including indirect ophthalmoscopy. UWF fundus imaging, including color fundus photography, autofluorescence, and angiography, was performed using standardized protocols and findings were recorded and reviewed and analyzed. Results: A total of 35 patients (58 eyes) with DPR were identified who underwent 55 sessions of UWF imaging. Mean age was 65 years, and the inferotemporal quadrant was most commonly affected (74% of eyes). Of these patients, 31 underwent fluorescein angiography and 90% of

these studies illustrated abnormalities in the area affected by the schisis. The most common finding was retinal vascular leakage originating from the deep capillary plexus observed in 29 eyes (93.5%). Conclusions: UWF imaging enables a more detailed identification of the clinical features associated with DPR and provides simple, practical, and noninvasive tools to monitor progression of disease. The breadth of retinal vascular complications identified with fluorescein angiography may suggest an important vascular component associated with the pathogenesis of this entity.

Todorich B, Thanos A, Yonekawa Y, Korot E, **Trese MT, Drenser KA and Capone A, Jr.** (2019). "Surgical management of tractional retinoschisis associated with vitreous hemorrhage in retinopathy of prematurity." *Retinal Cases & Brief Reports* 13(1): 72-74.

[Request Form](#)

Department of Ophthalmology

Purpose: The tractional retinoschisis is a poorly understood, rare, and likely underappreciated entity in retinopathy of prematurity. The purpose of this article is to describe clinical findings and surgical management of tractional retinoschisis in retinopathy of prematurity, masquerading as Stage 4 retinopathy of prematurity retinal detachment. Methods: A retrospective review of a single case with literature review and case discussion. Results: In this report, we describe a child with retinopathy of prematurity and tractional schisis, who initially presented with vitreous hemorrhage and was effectively managed by vitrectomy and inner wall retinectomy. At 5 months after vitrectomy, the child demonstrated complete collapse of the retinoschisis with intact posterior pole and brisk light perception. Conclusion: Vitrectomy with or without inner wall retinectomy is effective in the management of tractional retinoschisis.

Tuma F and **Al-Wahab Z** (2019). "Rectovaginal Fistula." *StatPearls*. Treasure Island (FL): StatPearls Publishing.

[Full Text](#)

Department of Obstetrics & Gynecology

A fistula is an abnormal connection between 2 epithelial surfaces. This is a general definition that applies to most of the known fistula but not all of them. The general description differentiates fistulae from sinuses,[1] abscesses, and other forms of luminal tracts or extra-luminal collections. Fistula connects 2 surfaces or lumens. It begins on the offending side and makes its way to an adjacent lumen or surface. It follows the easiest and shortest path to the adjacent organ. Recto-vaginal fistula starts from the rectum and extends to the vagina. It is not a healthy situation or physiological status. There is usually an underlying pathology, injury, or surgical event. Characteristics of rectovaginal fistula (RVF), for example, site, size, length, activity, and symptoms, vary depending on the cause of the fistula, patient factors, and the treatment received. It is a potentially challenging surgical condition for both the patient and health care team. The underlying etiology determines the method of assessment, management, and prognosis. This article reviews rectovaginal fistula under the general category of fistulae.

Turkoglu O, Cital A, Katar C, Mert I, Kumar P, Yilmaz A, Uygur DS, Erkaya S, **Graham SF and Bahado-Singh RO** (2019). "Metabolomic identification of novel diagnostic biomarkers in ectopic pregnancy." *Metabolomics* 15(11).

[Full Text](#)

Department of Obstetrics & Gynecology

Introduction: Ectopic pregnancy (EP) is a potentially life-threatening condition and early diagnosis still remains a challenge, causing a delay in management leading to tubal rupture. Objectives: To identify putative plasma biomarkers for the detection of tubal EP and elucidate altered biochemical pathways in EP compared to intrauterine pregnancies. Methods: This case-control study included prospective recruitment of 39 tubal EP cases and 89 early intrauterine pregnancy controls. Plasma samples were biochemically profiled using proton nuclear magnetic resonance spectroscopy (1H NMR). To avoid over-fitting, datasets were randomly divided into a discovery group (26 cases vs 60 controls) and a test group (13 cases and 29 controls). Logistic regression models were developed in the discovery group and validated in the independent test group. Area under the receiver operating characteristics curve (AUC), 95% confidence interval (CI), sensitivity, and specificity values were calculated. Results: In total 13 of 43 (30.3%) metabolite concentrations were significantly altered in EP plasma ($p < 0.05$). Metabolomic profiling yielded significant separation between EP and controls ($p < 0.05$). Independent validation of a two-metabolite model consisting of lactate and acetate, achieved an AUC (95% CI) = 0.935 (0.843–1.000) with a sensitivity of 92.3%

and specificity of 96.6%. The second metabolite model (d-glucose, pyruvate, acetoacetate) performed well with an AUC (95% CI) = 0.822 (0.657–0.988) and a sensitivity of 84.6% and specificity of 86.2%. Conclusion: We report novel metabolomic biomarkers with a high accuracy for the detection of EP. Accurate biomarkers could potentially result in improved early diagnosis of tubal EP cases.

van den Hoogen IJ, van Rosendael AR, Lin FY, Lu Y, Dimitriu-Leen AC, Smit JM, Scholte A, Achenbach S, Al-Mallah MH, Andreini D, Berman DS, Budoff MJ, Cademartiri F, Callister TQ, Chang HJ, **Chinnaiyan K**, Chow BJW, Cury RC, DeLago A, Feuchtner G, Hadamitzky M, Hausleiter J, Kaufmann PA, Kim YJ, Leipsic JA, Maffei E, Marques H, de Araujo Goncalves P, Pontone G, **Raff GL**, Rubinshtein R, Villines TC, Gransar H, Jones EC, Pena JM, Shaw LJ, Min JK and Bax JJ (2019). "Coronary atherosclerosis scoring with semiquantitative CCTA risk scores for prediction of major adverse cardiac events: Propensity score-based analysis of diabetic and non-diabetic patients." Journal of Cardiovascular Computed Tomography. ePub Ahead of Print.

[Full Text](#)

Department of Internal Medicine

Aims: We aimed to compare semiquantitative coronary computed tomography angiography (CCTA) risk scores - which score presence, extent, composition, stenosis and/or location of coronary artery disease (CAD) - and their prognostic value between patients with and without diabetes mellitus (DM). Risk scores derived from general chest-pain populations are often challenging to apply in DM patients, because of numerous confounders. **Methods:** Out of a combined cohort from the Leiden University Medical Center and the CONFIRM registry with 5-year follow-up data, we performed a secondary analysis in diabetic patients with suspected CAD who were clinically referred for CCTA. A total of 732 DM patients was 1:1 propensity-matched with 732 non-DM patients by age, sex and cardiovascular risk factors. A subset of 7 semiquantitative CCTA risk scores was compared between groups: 1) any stenosis $\geq 50\%$, 2) any stenosis $\geq 70\%$, 3) stenosis-severity component of the coronary artery disease-reporting and data system (CAD-RADS), 4) segment involvement score (SIS), 5) segment stenosis score (SSS), 6) CT-adapted Leaman score (CT-LeSc), and 7) Leiden CCTA risk score. Cox-regression analysis was performed to assess the association between the scores and the primary endpoint of all-cause death and non-fatal myocardial infarction. Also, area under the receiver-operating characteristics curves were compared to evaluate discriminatory ability. **Results:** A total of 1,464 DM and non-DM patients (mean age 58 +/- 12 years, 40% women) underwent CCTA and 155 (11%) events were documented after median follow-up of 5.1 years. In DM patients, the 7 semiquantitative CCTA risk scores were significantly more prevalent or higher as compared to non-DM patients ($p \leq 0.022$). All scores were independently associated with the primary endpoint in both patients with and without DM ($p \leq 0.020$), with non-significant interaction between the scores and diabetes (interaction $p \geq 0.109$). Discriminatory ability of the Leiden CCTA risk score in DM patients was significantly better than any stenosis $\geq 50\%$ and $\geq 70\%$ ($p = 0.003$ and $p = 0.007$, respectively), but comparable to the CAD-RADS, SIS, SSS and CT-LeSc that also focus on the extent of CAD ($p \geq 0.265$). **Conclusion:** Coronary atherosclerosis scoring with semiquantitative CCTA risk scores incorporating the total extent of CAD discriminate major adverse cardiac events well, and might be useful for risk stratification of patients with DM beyond the binary evaluation of obstructive stenosis alone.

van Rosendael AR, Shaw LJ, Xie JX, Dimitriu-Leen AC, Smit JM, Scholte AJ, van Werkhoven JM, Callister TQ, DeLago A, Berman DS, Hadamitzky M, Hausleiter J, Al-Mallah MH, Budoff MJ, Kaufmann PA, **Raff G**, **Chinnaiyan K**, Cademartiri F, Maffei E, Villines TC, Kim YJ, Feuchtner G, Lin FY, Jones EC, Pontone G, Andreini D, Marques H, Rubinshtein R, Achenbach S, Dunning A, Gomez M, Hindoyan N, Gransar H, Leipsic J, Narula J, Min JK and Bax JJ (2019). "Superior risk stratification with coronary computed tomography angiography using a comprehensive atherosclerotic risk score." JACC: Cardiovascular Imaging 12(10): 1987-1997.

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Department of Internal Medicine

Objectives: This study was designed to assess the prognostic value of a new comprehensive coronary computed tomography angiography (CTA) score compared with the stenosis severity component of the Coronary Artery Disease-Reporting and Data System (CAD-RADS). **Background:** Current risk assessment with coronary CTA is mainly focused on maximal stenosis severity. Integration of plaque extent, location, and composition in a comprehensive model may improve risk stratification. **Methods:** A total of 2,134 patients with suspected but without known CAD were included. The predictive value of the comprehensive CTA score

(ranging from 0 to 42 and divided into 3 groups: 0 to 5, 6 to 20, and >20) was compared with the CAD-RADS combined into 3 groups (0% to 30%, 30% to 70% and \geq 70% stenosis). Its predictive performance was internally and externally validated (using the 5-year follow-up dataset of the CONFIRM [Coronary CT Angiography Evaluation for Clinical Outcomes: An International Multicenter Registry], n = 1,971). Results: The mean age of patients was 55 ± 13 years, mean follow-up 3.6 ± 2.8 years, and 130 events (myocardial infarction or death) occurred. The new, comprehensive CTA score showed strong and independent predictive value using the Cox proportional hazard analysis. A model including clinical variables plus comprehensive CTA score showed better discrimination of events compared with a model consisting of clinical variables plus CAD-RADS (0.768 vs. 0.742, p = 0.001). Also, the comprehensive CTA score correctly reclassified a significant proportion of patients compared with the CAD-RADS (net reclassification improvement 12.4%, p < 0.001). Good predictive accuracy was reproduced in the external validation cohort. Conclusions: The new comprehensive CTA score provides better discrimination and reclassification of events compared with the CAD-RADS score based on stenosis severity only. The score retained similar prognostic accuracy when externally validated. Anatomic risk scores can be improved with the addition of extent, location, and compositional measures of atherosclerotic plaque. (Comprehensive CTA risk score calculator is available at: <http://18.224.14.19/calcApp/>)

Vicini FA, Cecchini RS, White JR, Arthur DW, Julian TB, Rabinovitch RA, Kuske RR, Ganz PA, Parda DS, Scheier MF, Winter KA, Paik S, Kuerer HM, Vallow LA, Pierce LJ, Mamounas EP, McCormick B, Costantino JP, Bear HD, Germain I, **Gustafson G**, Grossheim L, Petersen IA, Hudes RS, Curran WJ, Jr., Bryant JL and Wolmark N (2019). "Long-term primary results of accelerated partial breast irradiation after breast-conserving surgery for early-stage breast cancer: A randomised, phase 3, equivalence trial." *Lancet* 394(10215): 2155-2164.

[Full Text](#)

Department of Radiation Oncology

Background: Whole-breast irradiation after breast-conserving surgery for patients with early-stage breast cancer decreases ipsilateral breast-tumour recurrence (IBTR), yielding comparable results to mastectomy. It is unknown whether accelerated partial breast irradiation (APBI) to only the tumour-bearing quadrant, which shortens treatment duration, is equally effective. In our trial, we investigated whether APBI provides equivalent local tumour control after lumpectomy compared with whole-breast irradiation. Methods: We did this randomised, phase 3, equivalence trial (NSABP B-39/RTOG 0413) in 154 clinical centres in the USA, Canada, Ireland, and Israel. Adult women (>18 years) with early-stage (0, I, or II; no evidence of distant metastases, but up to three axillary nodes could be positive) breast cancer (tumour size \leq 3 cm; including all histologies and multifocal breast cancers), who had had lumpectomy with negative (ie, no detectable cancer cells) surgical margins, were randomly assigned (1:1) using a biased-coin-based minimisation algorithm to receive either whole-breast irradiation (whole-breast irradiation group) or APBI (APBI group). Whole-breast irradiation was delivered in 25 daily fractions of 50 Gy over 5 weeks, with or without a supplemental boost to the tumour bed, and APBI was delivered as 34 Gy of brachytherapy or 38.5 Gy of external beam radiation therapy in 10 fractions, over 5 treatment days within an 8-day period. Randomisation was stratified by disease stage, menopausal status, hormone-receptor status, and intention to receive chemotherapy. Patients, investigators, and statisticians could not be masked to treatment allocation. The primary outcome of invasive and non-invasive IBTR as a first recurrence was analysed in the intention-to-treat population, excluding those patients who were lost to follow-up, with an equivalency test on the basis of a 50% margin increase in the hazard ratio (90% CI for the observed HR between 0.667 and 1.5 for equivalence) and a Cox proportional hazard model. Survival was assessed by intention to treat, and sensitivity analyses were done in the per-protocol population. This trial is registered with ClinicalTrials.gov, NCT00103181. Findings: Between March 21, 2005, and April 16, 2013, 4216 women were enrolled. 2109 were assigned to the whole-breast irradiation group and 2107 were assigned to the APBI group. 70 patients from the whole-breast irradiation group and 14 from the APBI group withdrew consent or were lost to follow-up at this stage, so 2039 and 2093 patients respectively were available for survival analysis. Further, three and four patients respectively were lost to clinical follow-up (ie, survival status was assessed by phone but no physical examination was done), leaving 2036 patients in the whole-breast irradiation group and 2089 in the APBI group evaluable for the primary outcome. At a median follow-up of 10.2 years (IQR 7.5-11.5), 90 (4%) of 2089 women eligible for the primary outcome in the APBI group and 71 (3%) of 2036 women in the whole-breast irradiation group had an IBTR (HR 1.22, 90% CI 0.94-1.58). The 10-year cumulative incidence of IBTR

was 4.6% (95% CI 3.7-5.7) in the APBI group versus 3.9% (3.1-5.0) in the whole-breast irradiation group. 44 (2%) of 2039 patients in the whole-breast irradiation group and 49 (2%) of 2093 patients in the APBI group died from recurring breast cancer. There were no treatment-related deaths. Second cancers and treatment-related toxicities were similar between the two groups. 2020 patients in the whole-breast irradiation group and 2089 in APBI group had available data on adverse events. The highest toxicity grade reported was: grade 1 in 845 (40%), grade 2 in 921 (44%), and grade 3 in 201 (10%) patients in the APBI group, compared with grade 1 in 626 (31%), grade 2 in 1193 (59%), and grade 3 in 143 (7%) in the whole-breast irradiation group. Interpretation: APBI did not meet the criteria for equivalence to whole-breast irradiation in controlling IBTR for breast-conserving therapy. Our trial had broad eligibility criteria, leading to a large, heterogeneous pool of patients and sufficient power to detect treatment equivalence, but was not designed to test equivalence in patient subgroups or outcomes from different APBI techniques. For patients with early-stage breast cancer, our findings support whole-breast irradiation following lumpectomy; however, with an absolute difference of less than 1% in the 10-year cumulative incidence of IBTR, APBI might be an acceptable alternative for some women. Funding: National Cancer Institute, US Department of Health and Human Services.

Wanamaker BL, Seth MM, Sukul D, **Dixon SR**, Bhatt DL, Madder RD, Rumsfeld JS and Gurm HS (2019). "Relationship between troponin on presentation and In-hospital mortality in patients with ST-segment-elevation myocardial infarction undergoing primary percutaneous coronary intervention." Journal of the American Heart Association 8(19): 1-9.

[Full Text](#)

Department of Internal Medicine

Background: Troponin release in ST-segment-elevation myocardial infarction (STEMI) has predictable kinetics with early levels reflective of ischemia duration. Little research has examined the value of admission troponin levels in STEMI patients undergoing primary percutaneous coronary intervention. We investigated the relationship between troponin on presentation and mortality in a large, real-world cohort of STEMI patients undergoing primary percutaneous coronary intervention. Methods and Results: We used multivariable adaptive regression modeling to examine the association between admission troponin levels and in-hospital mortality for patients who underwent primary percutaneous coronary intervention for STEMI. We adjusted for known clinical risk factors using a validated mortality risk model derived from the NCDR (National Cardiovascular Data Registry) CathPCI database, and this same model was used to calculate patients' predicted mortality based on clinical and demographic factors. Patients were then stratified by troponin groups to compare predicted versus observed mortality. Of the 14 061 patients included in the cohort, 47.2% had initial troponin levels that were undetectable or within the reference range. Admission troponin was an independent predictor of in-hospital mortality, and any value above the reference range was associated with increased mortality (1.8% versus 5.1%, [standardized difference, 18.2%]). Patients with the highest predicted risk for mortality (13% predicted) in the highest admission troponin grouping experienced an observed mortality of 19.5%. Patients in low troponin groupings consistently demonstrated lower than predicted mortality based on their clinical and demographic risk profile. Conclusions: Nearly half of patients undergoing primary percutaneous coronary intervention had normal troponin on presentation and had a relatively good outcome. Mortality increases with elevated admission troponin levels, regardless of baseline clinical risk. The substantial number of patients who present with markedly elevated troponin and their relatively worse outcomes highlights the need for continued improvement in prehospital STEMI detection and care.

Wang HJ, Tyagi P, Chen YM, **Chancellor MB** and Chuang YC (2019). "Low energy shock wave therapy inhibits inflammatory molecules and suppresses prostatic pain and hypersensitivity in a capsaicin induced prostatitis model in rats." International Journal of Molecular Sciences 20(19): 4777.

[Full Text](#)

Department of Urology

The effect of low energy shock wave (LESW) therapy on the changes of inflammatory molecules and pain reaction was studied in a capsaicin (10 mM, 0.1 cc) induced prostatitis model in rats. Intraprostatic capsaicin injection induced a pain reaction, including closing of the eyes, hypolocomotion, and tactile allodynia, which effects were ameliorated by LESW treatment. LESW therapy (2Hz, energy flux density of 0.12 mJ/mm²) at 200 and 300 shocks significantly decreased capsaicin-induced inflammatory reactions, reflected by a reduction of

tissue edema and inflammatory cells, COX-2 and TNF- α stained positive cells, however, the therapeutic effects were not observed at 100 shocks treated group. Capsaicin-induced IL-1 β , COX-2, IL-6, caspase-1, and NGF upregulation on day 3 and 7, while NALP1 and TNF- α upregulation was observed on day 7. LESW significantly suppressed the expression of IL-1 β , COX-2, caspase-1, NGF on day 3 and IL-1 β , TNF- α , COX-2, NALP1, caspase-1, NGF expression on day 7 in a dose-dependent fashion. LESW has no significant effect on IL-6 expression. Intraprostatic capsaicin injection activates inflammatory molecules and induces prostatic pain and hypersensitivity, which effects were suppressed by LESW. These findings might be the potential mechanisms of LESW therapy for nonbacterial prostatitis in humans.

Wasserman JA, Navin MC and Vercler CJ (2019). "Pediatric assent and treating children over objection." *Pediatrics* 144(5): e20190382.

[Request Form](#)

Department of Foundational Medical Studies (OU)

Watchko JF and **Maisels MJ** (2019). "Avoiding harm from hyperbilirubinemia screening." *JAMA Pediatrics* 173(12): 1209-1209.

[Full Text](#)

Department of Pediatrics

To the Editor: It was with great interest and some alarm that we read the Grosse et al Viewpoint entitled "Screening for Neonatal Hyperbilirubinemia: First Do No Harm?" The authors assert that the "relevant question for screening policy and practice is the balance of benefits and harms associated with treatments after screening," an appropriate concern. We have other concerns about neonatal jaundice. Screening for hyperbilirubinemia serves an important purpose beyond identifying infants who might require treatment, namely, identifying those who are at risk for developing subsequent severe hyperbilirubinemia. Surely the authors do not suggest forgoing jaundice screening, the minimum standard of care for decades in identifying hyperbilirubinemia in neonates? Unfortunately, the clinical diagnosis of jaundice in infants who are younger than 48 hours is simply too imprecise to allow a judgment regarding the need for additional investigation, intervention, or timely follow-up, and we now have much more robust, noninvasive bilirubin screening available, such as transcutaneous bilirubin measurement. The issue Grosse et al raise is how to act on the screening result, something the 2009 American Academy of Pediatrics updated guideline sets forth in detail. In this regard, raising phototherapy treatment thresholds will necessitate more vigilant bilirubin surveillance, not less.

White JL, Hollander JE, Chang AM, Nishijima DK, Lin AL, Su E, Weiss RE, Yagapen AN, Malveau SE, Adler DH, **Bastani A**, Baugh CW, Caterino JM, **Clark CL**, Diercks DB, Nicks BA, Shah MN, Stiffler KA, Storrow AB, Wilber ST and Sun BC (2019). "Orthostatic vital signs do not predict 30-day serious outcomes in older emergency department patients with syncope: A multicenter observational study." *American Journal of Emergency Medicine* 37(12): 2215-2223.

[Full Text](#)

Department of Emergency Medicine

Background: Syncope is a common chief complaint among older adults in the Emergency Department (ED), and orthostatic vital signs are often a part of their evaluation. We assessed whether abnormal orthostatic vital signs in the ED are associated with composite 30-day serious outcomes in older adults presenting with syncope. Methods: We performed a secondary analysis of a prospective, observational study at 11 EDs in adults \geq 60 years who presented with syncope or near syncope. We excluded patients lost to follow up. We used the standard definition of abnormal orthostatic vital signs or subjective symptoms of lightheadedness upon standing to define orthostasis. We determined the rate of composite 30-day serious outcomes, including those during the index ED visit, such as cardiac arrhythmias, myocardial infarction, cardiac intervention, new diagnosis of structural heart disease, stroke, pulmonary embolism, aortic dissection, subarachnoid hemorrhage, cardiopulmonary resuscitation, hemorrhage/anemia requiring transfusion, with major traumatic injury from fall, recurrent syncope, and death) between the groups with normal and abnormal orthostatic vital signs. Results: The study cohort included 1974 patients, of whom 51.2% were male and 725 patients (37.7%) had abnormal orthostatic vital signs. Comparing those with abnormal to those with normal orthostatic vital signs, we did not find a difference in composite 30-serious outcomes (111/725 (15.3%) vs 184/1249 (14.7%); unadjusted odds ratio, 1.05 [95%CI, 0.81–1.35], $p = 0.73$). After adjustment for

gender, coronary artery disease, congestive heart failure (CHF), history of arrhythmia, dyspnea, hypotension, any abnormal ECG, physician risk assessment, medication classes and disposition, there was no association with composite 30-serious outcomes (adjusted odds ratio, 0.82 [95%CI, 0.62–1.09], $p = 0.18$). Conclusions: In a cohort of older adult patients presenting with syncope who were able to have orthostatic vital signs evaluated, abnormal orthostatic vital signs did not independently predict composite 30-day serious outcomes.

Wilson TG, Hanna A, **Recknagel J**, Pruetz BL, Baschnagel AM and **Wilson GD** (2019). "Prognostic significance of MTOR expression in HPV positive and negative head and neck cancers treated by chemoradiation." Head and Neck- Journal for the Sciences and Specialties of the Head and Neck. ePub Ahead of Print.

[Full Text](#)

OUWB Medical Student Author

Department of Radiation Oncology

Background: The mechanistic target of rapamycin (MTOR) plays a key role in regulating cell growth and metabolism and is commonly overexpressed in head and neck cancer (HNSCC). This study investigated the association of MTOR with clinical outcome in human papilloma virus (HPV) positive and negative HNSCC patients treated by chemoradiation. Methods: A tissue microarray (TMA) consisting of cores from 109 HNSCC patients treated by definitive chemoradiation was constructed and stained with antibodies against p16 and MTOR and expression correlated with clinicopathological features and clinical outcome. Results: MTOR varied widely between tumor cores and was not associated with HPV status or clinicopathological features. There was a positive correlation with pre-treatment FDG uptake. ($P = .01$). In HPV negative patients, MTOR predicted for shorter locoregional control ($P = .02$), diseases free survival ($P = .02$), and overall survival ($P = .04$). MTOR expression was not associated with outcome in HPV positive patients. Conclusions: Prognostic significance of MTOR expression depends on HPV status.

Wood EH, Rao P and **Mahmoud TH** (2019). "Nanovitreoretinal subretinal gateway device to displace submacular hemorrhage: Access to the subretinal space without vitrectomy." Retina. ePub Ahead of Print.

[Request Form](#)

Department of Ophthalmology

Yin W, Kumar T, Lai Z, Zeng X, **Kanaan HD**, **Li W** and **Zhang PL** (2019). "Kidney injury molecule-1, a sensitive and specific marker for identifying acute proximal tubular injury, can be used to predict renal functional recovery in native renal biopsies." International Urology and Nephrology 51(12): 2255-2265.

[Full Text](#)

Department of Pathology

Kidney injury molecule-1 (KIM-1) staining has been shown to be very useful in identifying acute proximal tubular injury, but its sensitivity, specificity and predicting values for the recovery of renal function after injury in renal biopsies have not been well established. In the first study, we randomly selected 184 renal biopsies from a wide age range of patients (children to elderly) with various renal diseases. KIM-1 staining scores were significantly correlated with serum creatinine (sCr) levels ($P < 0.05$) in all age groups. Receiver-operating characteristic curve (ROC) was generated to evaluate true-positive rate (sensitivity) and true-negative rate (1-specificity). The area under the curve (AUC) in pediatric cases was 0.74, which demonstrated KIM-1 was a fair index in correlating with sCr. In adults, the AUC was 0.87, indicating that KIM-1 was an even better index in the adult population in correlating to sCr. The second study was to determine whether KIM-1 could be a potential predictor of the recovery of acute kidney injury (AKI), and 51 indicated native biopsies with acute tubular injury were randomly selected for KIM-1 staining and sCr follow-up over a 6-month period. A higher KIM-1/sCr ratio (0.57 ± 0.06) was significantly and positively associated with a better reduction in sCr over 6 months. In summary, our data demonstrated that KIM-1 staining in renal biopsies is a sensitive and specific marker to identify acute tubular injury and KIM-1/sCr ratio is useful for predicting the recovery of renal function after injury, although some patients' sCr levels cannot return to their baseline levels.

Yu P, Venkat P, Chopp M, Zacharek A, Shen Y, Ning R, Liang L, **Li W**, Zhang L, Landschoot-Ward J, Jiang R and Chen J (2019). "Role of microRNA-126 in vascular cognitive impairment in mice." Journal of Cerebral Blood Flow and

Metabolism 39(12): 2497-2511.

[Full Text](#)

Department of Pathology

Vascular dementia (VaD) affects cognition and memory. MicroRNA-126 (miR-126) is an angiogenic microRNA that regulates vascular function. In this study, we employ a multiple microinfarction (MMI) model to induce VaD in mice, and investigate VaD-induced cognitive dysfunction, white matter (WM) damage, glymphatic dysfunction and the role of miR-126 in mediating these effects. Male six-to eight-months old C57/BL6 mice (WT) were subject to MMI model, and cerebral blood flow (CBF), vessel patency, glymphatic function, cognitive function, and serum miR-126 expression were measured. Mice were sacrificed at 28 days after MMI. To investigate the role of miR-126 in VaD, cognitive function, water channel integrity and glymphatic function were assessed in male, six-to eight months old conditional-knockout endothelial cell miR-126 (miR-126EC^{-/-}), and control (miR-126fl/fl) mice. MMI in WT mice induces significant cognitive deficits, decreases CBF and vessel patency; evokes astrocytic and microglial activation, increases inflammation, axonal/WM damage; decreases synaptic plasticity and dendritic spine density, instigates water channel and glymphatic dysfunction, and decreases serum miR-126 expression. MiR-126EC^{-/-} mice exhibit significant cognitive impairment, decreased CBF, myelin density and axon density, increased inflammation, and significant water channel and glymphatic dysfunction compared to miR-126fl/fl mice. Reduction of endothelial miR-126 expression may mediate cognitive impairment in MMI-induced VaD.

Zakaria HM, Mansour T, Telemi E, Xiao SJ, Bazydlo M, Schultz L, Nerenz D, **Perez-Cruet M**, Seyfried D, Aleem IS, **Easton R**, Schwalb JM, Abdulhak M and Chang V (2019). "Patient demographic and surgical factors that affect completion of patient-reported outcomes 90 days and 1 year after spine surgery: Analysis from the Michigan Spine Surgery Improvement Collaborative (MSSIC)." World Neurosurgery 130: E259-E271.

[Full Text](#)

Department of Neurosurgery

Department of Orthopaedic Surgery

Background: The Michigan Spine Surgery Improvement Collaborative is a statewide multicenter quality improvement registry. Because missing data can affect registry results, we used MSSIC to find demographic and surgical characteristics that affect the completion of patient-reported outcomes (PROs) at 90 days and 1 year. Methods: A total of 24,404 patients who had lumbar surgery (17,813 patients) or cervical surgery (6591 patients) were included. Multivariate logistic regression models of patient disease were constructed to identify risk factors for failure to complete scheduled PRO surveys. Results: Patients \geq 65 years old and female patients were both more likely to respond at 90 days and 1 year. Increasing education was associated with greater response rate at 90 days and 1 year. Whites and African Americans had no differences in response rates. Calling provided the highest response rate at 90 days and 1 year. For cervical spine patients, only discharge to rehabilitation increased completion rates, at 90 days but not 1 year. For lumbar spine patients, spondylolisthesis or stenosis (vs. herniated disc) had a greater response rate at 1 year. Patients with leg (vs. back) pain had a greater response only at 1 year. Patients with multilevel surgery had an increased response at 1 year. Patients who underwent fusion were more likely to respond at 90 days, but not 1 year. Discharge to rehabilitation increased response at 90 days and 1 year. Conclusions: A multivariate analysis from a multi-center prospective database identified surgical factors that affect PRO follow-up, up to 1 year. This information can be helpful for imputing missing PRO data and could be used to strengthen data derived from large prospective databases.

Zhang KJ, **Wilson GD**, Kara S, Majeske A, **Zhang PL** and **Hafron JM** (2019). "Diagnostic role of kidney injury molecule-1 in renal cell carcinoma." International Urology and Nephrology. 51(11): 1893-1902.

[Full Text](#)

Department of Radiation Oncology

Department of Pathology

Department of Urology

Despite rapid advances in diagnostic and therapeutic medicine, renal cell carcinoma (RCC) continues to cause significant morbidity and mortality in patients. While there has been a shift towards earlier detection, approximately 16% of patients present with metastatic disease at the time of diagnosis. Kidney injury molecule-1 (KIM-1) is a glycoprotein that has been shown to be a robust and reliable biomarker of acute

proximal tubular injury. As KIM-1 is mainly expressed in RCC derived from the proximal tubules, it is a reliable marker to differentiate between proximal tubular primary RCC and distal nephron primary RCC. Several studies have investigated urinary KIM-1 (uKIM-1) in RCC and demonstrated that it is a sensitive and specific marker for detecting localized RCC, as patients had markedly reduced uKIM-1 levels following nephrectomy, with uKIM-1 levels correlating with tumor size and grade. In addition, levels of KIM-1 present in plasma have also shown utility as a biomarker of RCC with levels being elevated in RCC cases at least 5 years before diagnosis. This review focuses on a progressive understanding of KIM-1 in the diagnosis of RCC using biopsies, urine, and plasma samples, and it will also provide some insight into potential roles of KIM-1 in the growth and spread of RCC.