

OAKLAND UNIVERSITY WILLIAM BEAUMONT SCHOOL OF MEDICINE  
PUBLICATION LIST  
July – September 2020

We compiled this bibliography to recognize the school's scholarly activity and to provide ease of access to the journal articles, published meeting abstracts, book chapters, books, and other works written by OUWB faculty, students and staff. We created the list by searching the institutional affiliation fields in PubMed, Scopus, Web of Science, EMBase, CINAHL, MedEd Portal, Google Scholar and Google Books. Because of search limitations, it does not represent an exhaustive collection of all published works by OUWB authors. If we inadvertently missed your publication, please email the citation to the Medical Library at [medref@oakland.edu](mailto:medref@oakland.edu), and we will add it to the next quarter's list.

Click the "Full-Text" link to download the articles available through the OUWB Medical Library. If the full-text is not available, you may request a copy by clicking the "Request Form" link or calling us at 248-370-3772. If you would us to add you to the automatic distribution list to receive quarterly updates via email, or if you have any questions or comments, please contact David Stewart at [davidstewart@oakland.edu](mailto:davidstewart@oakland.edu).

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## Articles related to the COVID-19 Pandemic

In the midst of our ongoing pandemic, we thought it worthy to recognize those articles pertaining to COVID-19 and the efforts of our faculty and staff to educate the world on its effects as well as how the virus has affected healthcare practices. Please click on the article title to jump to its relevant citation in the report.

Nour Chams, Sana Chams, Reina Badran, Ali Shams, Abdallah Araji, Mohamad Raad, Sanjay Mukhopadhyay, Edana Stroberg, Eric J. Duval, Lisa M. Barton, and **Inaya Hajj Hussein** – [COVID-19: A multidisciplinary review](#)

Ananias C. Diokno and Jeffrey M. Devries – [The impact of COVID-19 on urologic practice, medical education, and training](#)

**Michael J. Gallagher**, Richard Bloomingdale, **Aaron D. Berman**, **Brian D. Williamson**, **Simon R. Dixon**, and **Robert D. Safian** – [Strategic deployment of cardiology fellows in training using the Accreditation Council for Graduate Medical Education Coronavirus Disease 2019 framework](#)

**Alexandra Halalau**, **Jeffrey Ditkoff**, Jessica Hamilton, **Aryana Sharrak**, **Aimen Vanood**, **Amr Abbas**, and **James Ziadeh** – [Emergency center curbside screening during the COVID-19 Pandemic: Retrospective cohort study](#)

Ankur Kalra, Erin D Michos, and **Kavitha Chinnaiyan** – [COVID-19 and the healthcare workers](#)

Raul Macias Gil, Jasmine R. Marcelin, Brenda Zuniga-Blanco, Carina Marquez, **Trini Mathew**, and Damani A. Piggott - [COVID-19 pandemic: Disparate health impact on the Hispanic/Latinx population in the United States](#)

**Girish B. Nair** and Michael S. Niederman – [Updates on community acquired pneumonia management in the ICU](#)

Maria del Carmen Pamplona and **Pablo Antonio Ysunza** - [Speech pathology telepractice for children with cleft palate in the times of COVID-19 pandemic](#)

Aditya Pandey, **Jeffrey M. Wilseck**, **Chris D. Kazmierczak**, **James M. Mick**, et al. - [Letter: COVID-19 pandemic-The bystander effect on stroke care in Michigan](#)

Tina Q. Tan, Ravina Kullar, Talia H. Swartz, **Trini A. Mathew**, Damani A. Piggott, and Vladimir Berthaud - [Location matters: Geographic disparities and impact of Coronavirus Disease 2019 \(COVID-19\)](#)

**George D. Wilson**, Minesh P. Mehta, James S. Welsh, Arnab Chakravarti, C. Leland Rogers, and **James Fontanesi** - [Investigating low-dose thoracic radiation as a treatment for COVID-19 patients to prevent respiratory failure](#)

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Ahmed K, Zaidi SF, Mati Ur R, **Rehman R** and Kondo T (2020). "Hyperthermia and protein homeostasis: Cytoprotection and cell death." *Journal of Thermal Biology* 91: 102615.

[Full Text](#)

*OUWB Medical Student Author*

Protein homeostasis or proteostasis, the correct balance between production and degradation of proteins, is an essential pillar for proper cellular function. Among the several cellular mechanisms that disrupt homeostatic conditions in cancer cells, hyperthermia (HT) has shown promising anti-tumor effects. However, cancer cells are also capable of thermoresistance. Indeed, HT-induced protein denaturation and aggregation results in the up regulation of heat shock proteins, a group of molecular chaperones with cytoprotective and anti-apoptotic properties via stress-inducible transcription factor, heat shock factor 1(HSF1). Heat shock proteins assist in the refolding of misfolded proteins and aids in their elimination if they become irreversibly damaged by various stressors. Furthermore, HSF1 also initiates the unfolded protein response in the endoplasmic reticulum (ER) to assist in the protein folding capacity of ER and also promotes the translation of pro-survival proteins' mRNA such as activating transcription factor 4 (ATF 4). Moreover, HT associated induction of microRNAs is also involved in thermal resistance of cancer cells via up-regulation of anti-apoptotic Bcl-2 proteins and down regulation of pro-apoptotic Bax and caspase 3 activities. Another cellular protection in response to stressors is Autophagy, which is regulated by the Mammalian target of rapamycin (mTOR) protein. Kinase activity in mTOR phosphorylates HSF1 and promotes its nuclear translocation for heat shock protein synthesis. Over-expression of heat shock proteins are reported to up-regulate Beclin-1, an autophagy initiator. Moreover, HT-induced reactive oxygen species (ROS) generation is sensitized by transcription factor NF-E2 related factor 2 (Nrf2) and activates the cellular expression of antioxidants and autophagy gene. Furthermore, ROS also potentiates autophagy via activation of Beclin-1. Inhibition of thermotolerance can potentiate HT-induced apoptosis. Here, we outlined that heat stress alters cellular proteins which activates cellular homeostatic processes to promote cell survival and make cancer cells thermotolerant.

**Al-Hadidi A**, Alslaim H, Ghawanmeh M, Alfarajat F, Habra H, Brahmamdam P and **Novotny N** (2020). "Short-term surgical trips: Local collaboration and its effects on complications and patient satisfaction." *Pediatric Surgery International* 36(8): 977-981.

[Full Text](#)

*OUWB Medical Student Author*

*Department of Surgery*

Purpose: Short-term surgical missions can provide communities in need with desired expertise; however, it is uncertain who will manage the complications after visiting experts leave. Poor outcomes, decreased patient satisfaction, and tension on the healthcare system develop when local providers, often excluded from the initial patient care, are unable to cope with subsequent morbidity. Methods: Two-year retrospective review of pediatric general, plastic, and reconstructive surgery, and urology cases performed by a relief organization in the developing world. Case complexity and postoperative complications were analyzed. Phone interviews conducted with patients/families to quantify postoperative outcomes and satisfaction. Results: 474 surgeries were performed on pediatric patients with 60% response rate. Respondents stratified into three levels of complexity: 159 simple, 72 intermediate, and 54 advanced surgeries. Six (2.1%) high-level complications

occurred. No association between the complexity of the surgery and the occurrence of a complications. 83.5% were satisfied with outcomes and > 92% were happy with the provided support. Conclusion: Facilitating visiting and local surgeons performing cases together increases the expertise of local providers, strengthens infrastructure, and establishes clear follow-up. Despite complications, patients and families continued to recommend care to family and friends by the relief organization and were happy with support from local providers. Engaging local providers is the gold-standard for short-term trips.

Al-Katib AM, Gaith H, Sano D, **Al-Katib S**, Bonnett M and Kafri Z (2020). "Emergence of overt myeloma in a patient with chronic lymphocytic leukemia on ibrutinib therapy." Clinical Case Reports 8(9): 1797-1801.

[Full Text](#)

*Department of Diagnostic Radiology and Molecular Imaging*

Ibrutinib is approved for chronic lymphocytic leukemia (CLL). However, its role in the treatment of multiple myeloma (MM) is not clear and is under investigation. We report a case of CLL that developed MM while on therapy with ibrutinib indicating that this drug may not be active against MM.

Al-Khadra Y, Sattar Y, Ullah W, Moussa Pacha H, Baibars M, Darmoch F, Abu-Mahfouz M, Afonso L, **Glazier JJ**, Devireddy C, Anwaruddin S, Sorajja P, Ajmal R, Shing Kwok C, Asfour AI, Zehr K, Mamas MA and Alraies MC (2020). "Temporal trends and outcomes in utilization of transcatheter and surgical aortic valve therapies in aortic valve stenosis patients with heart failure." International Journal of Clinical Practice: e13711.

[Full Text](#)

*Department of Internal Medicine*

Introductions & Aims: Heart failure (HF) is a common comorbidity in patients undergoing surgical aortic valve replacement (SAVR) and transcatheter aortic valve replacement (TAVR). We sought to access the temporal trends and outcomes of TAVR or SAVR in HF patients. Method: The NIS database from 2011-2014 was queried for patients that underwent TAVR or SAVR and were subsequently diagnosed with HF. Temporal trends in the utilization of TAVR or SAVR in HF patients were analyzed. Results: Among 27,982 patients who were diagnosed with HF of whom 17,681 (63.2%) had heart failure with reduced ejection fraction (HFrEF) while 10,301 (36.8%) had heart failure with preserved ejection fraction (HFpEF), 9,049 (32.3%) underwent TAVR and 16,933 (76.7%) underwent SAVR. Patients with HFrEF and HFpEF had higher utilization of TAVR compared to SAVR over the course of the study period (p trend < 0.001). TAVR was associated with lower mortality [2.8% in 2012 and 1.8% in 2014 (p 0.013)] compared with SAVR. Similarly, multiple logistic regression showed a statistically significant lower in-hospital mortality in the TAVR group compared to SAVR (aOR 0.634; CI 0.504, 0.798, P < 0.001). Conclusion: For patients with severe aortic valve stenosis and heart failure who undergo aortic valve intervention, TAVR is associated with less odds of in-hospital mortality compared with SAVR.

Almahariq MF, **Chen PY**, Dekhne N and **Dilworth JT** (2020). "ASO author reflections: Omission of axillary lymph node dissection for breast cancer patients with residual N1 nodal disease following neoadjuvant chemotherapy: Not ready for primetime?" Annals of Surgical Oncology. ePub Ahead of Print.

[Full Text](#)

*OUWB Medical Student Author*

*Department of Radiation Oncology*

Almahariq MF, Levitin R, Quinn TJ, **Chen PY**, Dekhne N, Kiran S, Desai A, Benitez P, **Jawad MS**, **Gustafson GS** and **Dilworth JT** (2020). "Omission of axillary lymph node dissection is associated with inferior survival in breast cancer patients with residual N1 nodal disease following neoadjuvant chemotherapy." Annals of Surgical Oncology. ePub Ahead of Print.

[Full Text](#)

*Department of Radiation Oncology*

Background: The appropriateness of substituting sentinel lymph node dissection (SLND) and regional nodal irradiation (RNI) for axillary lymph node dissection (ALND) in patients with residual lymph node (LN) disease following neoadjuvant chemotherapy (NAC) is unknown. We used the National Cancer Database (NCDB) to compare survival following SLND and ALND in breast cancer patients with residual LN disease. Methods: We analyzed NCDB patients, treated between 2006 and 2014, with cT1-3, cN1, cM0 breast cancer and residual

disease in 1-3 axillary LNs (ypN1) following NAC. Patients were grouped into those who received SLND (defined as removal of  $\leq 4$  LNs) and RNI, or ALND and RNI. Patients were matched for all patient, tumor, and treatment characteristics. Results: We identified 1313 eligible patients in the ALND group and 304 patients in the SLND group. For the matched cohorts, SLND was associated with significantly lower survival in both univariate and doubly robust multivariable analyses (MVA) (HR 1.7, 95% CI 1.3-2.2,  $P < 0.001$  for MVA), with estimated 5-year OS of 71%, compared with 77% in the ALND group ( $P = 0.01$ ). Exploratory subgroup analyses showed that SLND was comparable with ALND in patients with luminal A or B tumors with a single metastatic LN (HR 1.03, 95% CI 0.59-1.8, ( $P = 0.91$ )). Conclusions: Our analysis suggests that, while an ALND may not be needed for patients with limited residual nodal burden and biologically favorable tumors, SLND should not be routinely substituted for ALND in patients with ypN1 disease following NAC until its efficacy is confirmed by prospective trials.

Almahariq MF, Quinn TJ, Arden JD, Roskos PT, **Wilson GD**, Marples B, **Grills IS**, **Chen PY**, **Krauss DJ**, **Chinnaiyan P** and **Dilworth JT** (2020). "Pulsed radiation therapy for the treatment of newly diagnosed glioblastoma." Neuro Oncology. ePub Ahead of Print.

[Full Text](#)

*Department of Radiation Oncology*

Background: Pulsed radiation therapy (PRT) has shown effective tumor control and superior normal-tissue sparing ability compared to standard radiotherapy (SRT) in pre-clinical models and retrospective clinical series. This is the first prospective trial to investigate PRT in the treatment of patients with newly diagnosed glioblastoma (GBM). Methods: This is a single-arm, prospective study. Patients with newly diagnosed GBM underwent surgery, followed by 60 Gy of PRT with concurrent temozolomide (TMZ). Each daily, 2-Gy fraction was divided into ten 0.2-Gy pulses, separated by 3-minute intervals. Patients received maintenance TMZ. Neurocognitive function (NCF) and quality of life (QOL) were monitored for two years using the Hopkins Verbal Learning Test-Revised, and EORTC QLQ-C30 QOL questionnaire. Change in NCF was evaluated based on a minimal clinically important difference (MCID) threshold of 0.5 standard deviations. Results: Twenty patients were enrolled with a median follow-up of 21 months. Median age was 60 years. Forty percent underwent subtotal resection, and 60% underwent gross total resection. One patient had an IDH-mutated tumor. Median PFS and OS were 10.7 and 20.9 months, respectively. In a post-hoc comparison, mOS for the prospective cohort was longer, compared to a matched cohort treated with SRT (20.9 vs 14 months,  $P=0.042$ ). There was no decline in QOL, and changes in NCF scores did not meet the threshold of a MCID. Conclusions: Treatment of newly diagnosed GBM with PRT is feasible and produces promising effectiveness while maintaining neurocognitive function and QOL. Validation of our results in a larger prospective trial warrants consideration.

Anderson RE, Keihani S, Moses RA, Nocera AP, Selph JP, Castillejo Becerra CM, Baradaran N, Glavin K, Broghammer JA, Arya CS, Sensenig RL, **Rezaee ME**, Morris BJ, Majercik S, **Hewitt T**, **Burks FN**, Schwartz I, Elliott SP, Luo-Owen X, Mukherjee K, Thomsen PB, Erickson BA, Miller BD, Santucci RA, Allen L, Norwood S, Fick CN, Smith BP, Piotrowski J, Dodgion CM, DeSoucy ES, Zakaluzny S, Kim DY, Breyer BN, Okafor BU, Askari R, Lucas JW, Simhan J, Khabiri SS, Nirula R and Myers JB (2020). "Current management of extraperitoneal bladder injuries: Results from the Multi-Institutional Genito-Urinary Trauma Study (MiGUTS)." The Journal of Urology 204(3): 538-544.

[Full Text](#)

*Department of Urology*

*OUWB Medical Student Author*

Purpose: We studied the current management trends for extraperitoneal bladder injuries and evaluated the use of operative repair versus catheter drainage, and the associated complications with each approach. Materials and Methods: We prospectively collected data on bladder trauma from 20 level 1 trauma centers across the United States from 2013 to 2018. We excluded patients with intraperitoneal bladder injury and those who died within 24 hours of hospital arrival. We separated patients with extraperitoneal bladder injuries into 2 groups (catheter drainage vs operative repair) based on their initial management within the first 4 days and compared the rates of bladder injury related complications among them. Regression analyses were used to identify potential predictors of complications. Results: From 323 bladder injuries we included 157 patients with extraperitoneal bladder injuries. Concomitant injuries occurred in 139 (88%) patients with pelvic fracture seen in 79%. Sixty-seven patients (43%) initially underwent operative repair for

their extraperitoneal bladder injuries. The 3 most common reasons for operative repair were severity of injury or bladder neck injury (40%), injury found during laparotomy (39%) and concern for pelvic hardware contamination (28%). Significant complications were identified in 23% and 19% of the catheter drainage and operative repair groups, respectively (p=0.55). The only statistically significant predictor for complications was bladder neck or urethral injury (RR 2.69, 95% 1.21-5.97, p=0.01). Conclusions: In this large multi-institutional cohort, 43% of patients underwent surgical repair for initial management of extraperitoneal bladder injuries. We found no significant difference in complications between the initial management strategies of catheter drainage and operative repair. The most significant predictor for complications was concomitant urethral or bladder neck injury.

Arora A, **Jacob M** and **Cappell MS** (2020). "Novel videoendoscopy demonstrating irregular, pulsatile GI bleeding from left atrium through an esophageal fistula after pulmonary vein isolation and catheter ablation for atrial fibrillation (with video)." Gastrointestinal Endoscopy 92(1): 211-212.

[Full Text](#)

*Department of Internal Medicine*

**Bahl A**, **Hijazi M**, Chen NW, Lachapelle-Clavette L and **Price J** (2020). "Ultralong versus standard long peripheral intravenous catheters: A randomized controlled trial of ultrasonographically guided catheter survival." Annals of Emergency Medicine 76(2): 134-142.

[Full Text](#)

*Department of Emergency Medicine*

*OUWB Medical Student Author*

Study Objective: Ultrasonographically guided intravenous peripheral catheters have dismal dwell time, with most intravenous lines failing before completion of therapy. Catheter length in the vein is directly related to catheter longevity. We investigate the survival of an ultralong ultrasonographically guided intravenous peripheral catheter compared with a standard long one. Methods: We conducted a single-site, nonblinded, randomized trial of catheter survival. Adult patients presenting to the emergency department with difficult vascular access were recruited and randomized to receive either standard long, 4.78-cm, 20-gauge ultrasonographically guided intravenous peripheral catheters or ultralong, 6.35-cm, 20-gauge ultrasonographically guided intravenous peripheral catheters. The primary outcome was duration of catheter survival. The secondary outcome was the optimal length of the catheter in the vein to maximize survival. Additional intravenous-related endpoints included first-stick success, time to insertion, number of attempts, thrombosis, and infection. Results: Between October 2018 and March 2019, 257 patients were randomized, with 126 in the standard long ultrasonographically guided intravenous peripheral catheter group and 131 in the ultralong group. Kaplan-Meier estimate of catheter median survival time in the ultralong group was 136 hours (95% confidence interval [CI] 116 to 311 hours) compared with 92 hours (95% CI 71 to 120 hours) in the standard long group, for a difference of 44 hours (95% CI 2 to 218 hours). The optimal catheter length in the vein was 2.75 cm, and intravenous lines with greater than 2.75 cm inserted had a median survival of 129 hours (95% CI 102 to 202 hours) compared with 75 hours (95% CI 52 to 116 hours) for intravenous lines with less than or equal to 2.75 cm, for a difference of 54 hours (95% CI 10 to 134 hours). Insertion characteristics were similar between the groups: 74.1% versus 79.4% first-stick success (95% CI for the difference -2% to 5%), 1.4 versus 1.3 for number of attempts (95% CI for the difference -0.1 to 0.3), and 6.9 versus 5.9 minutes to completion (95% CI for the difference -1.3 to 3.4) with ultralong versus standard long, respectively. There were no cases of infection or thrombosis. Conclusion: This study demonstrated increased catheter survival when the ultralong compared with the standard long ultrasonographically guided intravenous peripheral catheter was used, whereas insertion characteristics and safety appeared similar.

Bajaj JS, Brenner DM, Cai Q, Cash BD, Crowell M, Dibaise J, Gallegos-Orozco JF, Gardner TB, Gyawali CP, Ha C, Holtmann G, **Jamil LH**, Kaplan GG, Karsan HA, Kinoshita Y, Lebwohl B, Leontiadis GI, Lichtenstein GR, Longstreth GF, Muthusamy VR, Oxentenko AS, Pimentel M, Pisegna JR, Rubenstein JH, Russo MW, Saini SD, Samadder NJ, Shaikat A, Simren M, Stevens T, Valdovinos M, Vargas H, Spiegel B and Lacy BE (2020). "Major trends in gastroenterology and hepatology between 2010 and 2019: An overview of advances from the past decade selected by the editorial board of the American Journal of Gastroenterology." American Journal of Gastroenterology 115(7): 1007-1018.

[Full Text](#)

*OUWB Medical Student Author*

**Barbat A, Oska S, Partiali B, Folbe A** and Jacob J (2020). "Gender and ethnic diversity in diagnostic and interventional radiology trainees, 2014-2019: Has the recently introduced Integrated Interventional Radiology program changed anything?" [Academic Radiology](#). ePub Ahead of Print.

[Request Form](#)

*Department of Surgery*

*OUWB Medical Student Author*

**Barbat A, Partiali B, Oska S** and **Folbe A** (2020). "Head, face, and neck fractures secondary to ladder-related injuries treated in United States emergency departments in 2009-2018." [Journal of Emergency Medicine \(0736-4679\)](#) 59(2): 186-192.

[Full Text](#)

*Department of Surgery*

*OUWB Medical Student Author*

Background: Ladders are a commonly used piece of equipment; however, their use is accompanied by a significant potential for injury. Fractures of the head, face, and neck are potential consequences of ladder use and can be devastating due to potential for severe sequelae. Objectives: To describe the frequency and pattern of ladder-related head, face, and neck fractures from 2009-2018. Methods: The National Electronic Injury Surveillance System (NEISS) was searched for ladder-related head, face, and neck fractures treated in U.S. emergency departments. Demographics, mechanism of injury, fracture type, setting in which fracture occurred, and patient disposition were analyzed. Results: There were 601 total cases (weighted national estimate of 20,450 total cases) of ladder-related head, face, and neck fractures obtained from the NEISS from 2009 to 2018. The mean age of injury was 53 years, and the majority of cases occurred in home settings. Approximately 25% of the cases were patients aged older than 65 years. The majority of fractures in individuals younger than 18 years and older than 46 years of age resulted in admission. The most commonly fractured locations included the face (51.0%), followed by cervical spine (28.3%) and cranial (20.7%) fractures. Conclusions: Admission rates for ladder-related head, face, and neck fractures are substantially higher than those previously reported for all types of ladder-related injuries. Injury and admission patterns vary by age. Rigorous safety precautions may be indicated for the high-risk groups identified by this study, especially the elderly.

Berry C, Khabele D, Johnson-Mann C, Henry-Tillman R, Joseph KA, Turner P, Pugh C, Fayanju OM, Backhus L, Sweeting R, Newman EA, Oseni T, Hasson RM, White C, Cobb A, Johnston FM, **Stallion A**, Karpeh M, Nwariaku F, Rodriguez LM and Jordan AH (2020). "A call to action: Black/African American women surgeon scientists, where are they?" [Annals of Surgery](#) 272(1): 24-29.

[Full Text](#)

*Department of Surgery*

Objective: To determine the representation of Black/AA women surgeons in academic medicine among U.S. medical school faculty and to assess the number of NIH grants awarded to Black/AA women surgeon-scientists over the past 2 decades. Summary of Background Data: Despite increasing ethnic/racial and sex diversity in U.S. medical schools and residencies, Black/AA women have historically been underrepresented in academic surgery. Methods: A retrospective review of the Association of American Medical Colleges 2017 Faculty Roster was performed and the number of grants awarded to surgeons from the NIH (1998-2017) was obtained. Data from the Association of American Medical Colleges included the total number of medical school surgery faculty, academic rank, tenure status, and department Chair roles. Descriptive statistics were performed. Results: Of the 15,671 U.S. medical school surgical faculty, 123 (0.79%) were Black/AA women surgeons with only 11 (0.54%) being tenured faculty. When stratified by academic rank, 15 (12%) Black/AA women surgeons were instructors, 73 (59%) were assistant professors, 19 (15%) were associate professors, and 10 (8%) were full professors of surgery. Of the 372 U.S. department Chairs of surgery, none were Black/AA women. Of the 9139 NIH grants awarded to academic surgeons from 1998 and 2017, 31 (0.34%) grants were awarded to fewer than 12 Black/AA women surgeons. Conclusion: A significant disparity in the number of Black/AA women in academic surgery exists with few attaining promotion to the rank of professor with tenure and none ascending to the role of department Chair of surgery. Identifying and removing



structural barriers to promotion, NIH grant funding, and academic advancement of Black/AA women as leaders and surgeon-scientists is needed.

Bradley CJ and **Haines DE** (2020). "Pulsed field ablation for pulmonary vein isolation in the treatment of atrial fibrillation." Journal of Cardiovascular Electrophysiology 31(8): 2136-2147.

[Full Text](#)

*Department of Internal Medicine*

Pulsed-field ablation (PFA) is a promising new ablation modality for the treatment of atrial fibrillation. This energy form employs a train of microsecond duration high amplitude electrical pulses that ablate myocardium by electroporation of the sarcolemmal membrane without measurable tissue heating. The ablation pulse waveform has multiple variable components that can affect ablation efficacy, thus each proprietary system has unique properties that cannot be generalized to other systems. Success with PFA depends upon the proximity of the electrode to the target tissue, but not necessarily upon contact. A unique feature of PFA is tissue specificity. Myocardium is very susceptible to irreversible injury whereas the esophagus, phrenic nerves, pulmonary veins, and coronary arteries are relatively resistant to injury. The tissue specificity of PFA may result in a wide therapeutic range and improved safety profile during atrial fibrillation ablation. Vein isolation can be achieved very rapidly (seconds) promising that PFA may reduce procedure time to 1 hour or less. This attractive new technology promises to be a major advance in the field of atrial fibrillation ablation.

Brown EC, **Franklin BA**, Regensteiner JG and Stewart KJ (2020). "Effects of single bout resistance exercise on glucose levels, insulin action, and cardiovascular risk in type 2 diabetes: A narrative review." Journal of Diabetes Complications 34(8): 107610.

[Full Text](#)

*Department of Internal Medicine*

**Aims:** Previous studies have reported beneficial effects of chronic resistance exercise in the prevention and treatment of type 2 diabetes. To clarify potential modulators of acute responses to resistance exercise, we reviewed the literature to determine the effects of a single bout of resistance exercise on cardiometabolic risk factors in type 2 diabetes. **Methods:** Pubmed and Embase were searched for studies investigating the effects of single bouts of resistance exercise on glucose and insulin levels, and cardiovascular disease risk in people with diabetes. Fourteen reports were identified and reviewed to formulate evidence-based resistance exercise prescription recommendations. **Results:** Glucose and insulin levels appear to decrease with resistance exercise with effects lasting up to 24 and 18 h, respectively. Bouts of resistance exercise may outperform aerobic exercise in reducing ambulatory blood pressure, with effects lasting up to 24 h. Moreover, resistance exercise after rather than before a meal may be more effective in reducing glucose, insulin, and triacylglycerol levels. However, reducing injectable insulin dosage prior to resistance exercise may blunt its favorable effects on glucose levels. **Conclusions:** This review suggests that a single bout of resistance exercise may be effective for acutely improving cardiometabolic markers in people with diabetes.

Campos A, Ernest EV, Cash RE, Rivard MK, Panchal AR, Clemency BM, **Swor RA** and Crowe RP (2020). "The association of death notification and related training with burnout among emergency medical services professionals." Prehospital Emergency Care. ePub Ahead of Print.

Request Form

*Department of Emergency Medicine*

**Introduction:** Death notification is a difficult task commonly encountered during prehospital care and may lead to burnout among EMS professionals. Lack of training could potentiate the relationship between death notification and burnout. The first objective of this study was to describe EMS professionals' experience with death notification and related training. The secondary objective was to assess the associations between death notification delivery, training, and burnout. **Methods:** We administered an electronic questionnaire to a random sample of nationally-certified EMS professionals. Work-related burnout was measured using the validated Copenhagen Burnout Inventory. Analysis was stratified by certification level to basic life support (BLS) and advanced life support (ALS). The association between the number of adult ( $\geq 18$  years) patient death notifications delivered in the prior 12 months and burnout was assessed using multivariable logistic regression to adjust for confounding variables. Multivariable logistic regression modelling was used to assess

the adjusted association between training and burnout among those who reported delivering at least one death notification in the prior 12 months. Adjusted odds ratios (aOR) and 95% confidence intervals are reported (95% CI). Results: We received 2,333/19,330 (12%) responses and 1,514 were included in the analysis. Most ALS respondents (77%) and one-third of BLS respondents (33%) reported at least one adult death notification in the past year. Approximately half of respondents reported receiving death notification training as part of their initial EMS education program (51% BLS; 52% ALS) and fewer reported receiving continuing education (30% BLS; 44% ALS). Delivering a greater number of death notifications was associated with increased odds of burnout. Among those who delivered at least one death notification, continuing education was associated with reduced odds of burnout. Conclusion: Many EMS professionals reported delivering at least one death notification within the past year. Yet, fewer than half reported training related to death notification during initial EMS education and even fewer reported receiving continuing education. More of those who delivered death notifications experienced burnout, while continuing education was associated with reduced odds of burnout. Future work is needed to develop and evaluate death notification training specifically for EMS professionals.

**Cappell MS** (2020). "Improving the safety of endoscopy in pregnancy: Approaching gravidity with gravitas." Digestive Diseases and Sciences. ePub Ahead of Print.

[Full Text](#)

*Department of Internal Medicine*

Cardenas V, **Mankuzhy N**, Mody R, McCaffery H, Fontana RJ and DiPaola F (2020). "Incidence and sequelae of liver injury among children treated for solid tumors: Analysis of a large single-center prospective cohort." Journal of Pediatric Gastroenterology & Nutrition 71(2): 197-202.

[Full Text](#)

*OUWB Medical Student Author*

Objectives: Pediatric oncology patients are at risk of adverse drug events. The incidence and etiologies of liver injury in this population are not well characterized. We utilized a large, single-center pediatric oncology registry to investigate the incidence, causes, and outcomes of liver injury during treatment for solid tumor malignancies. Methods: We reviewed all young individuals (age <25 years) who received treatment for any solid tumor at the University of Michigan between January 2004 and July 2016. Subjects with liver injury meeting predetermined laboratory criteria were identified. Cases were independently reviewed by 2 expert hepatologists to assign a cause of liver injury. Clinical characteristics of drug-induced liver injury (DILI) and non-DILI cases were compared. Cases of liver injury occurring after bone marrow or liver transplant were excluded. Results: Of 1136 solid tumor patients, 160 (14%) experienced liver injury, and the overall frequency of DILI was 4%. DILI was the leading identified cause of liver injury (31%), followed by infection (17%), metastatic/malignant biliary disease (13%), and perioperative liver injury (13%). Most DILI cases (>90%) were mild acute hepatocellular injury episodes that did not result in modification to the chemotherapy plan, and all DILI eventually resolved. Severe presentations involving jaundice and/or prolonged hospital course were significantly more common among non-DILI versus DILI cases (23% vs 2%,  $P < 0.001$ ). Conclusions: DILI is the leading cause of liver injury events among pediatric solid tumor patients. In our registry, DILI was of mild severity and did not result in an alteration of the treatment plan in most patients. In contrast, non-DILI-related liver injury events, including infection, were more likely to have a more severe presentation and a complicated course with a greater mortality during follow-up.

**Challa JA**, Kasir R and **Taranikanti V** (2020). "Abnormal anatomical and radiological changes in a rare presentation of adult developmental dysplasia of the hip." Cureus 12(8): e9938.

[Full Text](#)

*OUWB Medical Student Author*

*Department of Foundational Medical Studies (OU)*

Adult presentation of bilateral dysplasia and dislocation is an extremely rare presentation. The management of adult hip dysplasia is to preserve the hip and reduce pain through surgical intervention. Hence, early diagnosis provides more options as the treatment dilemma with the late presentation is very complicated with debatable prognosis. The case presented is a 53-year old woman who complained of persistent pain in the hip region. On radiology, dysplasia and dislocation of both the hip joints were observed along with soft



tissue abnormalities around the joint. In this case report, we discuss the underlying pathophysiology that might have led to the abnormal radiological and anatomical changes in the hip region and the possible treatment options in a conservatively managed case of developmental dysplasia of the hip (DDH).

Chams N, Chams S, Badran R, Shams A, Araji A, Raad M, Mukhopadhyay S, Stroberg E, Duval EJ, Barton LM and **Hajj Hussein I** (2020). "COVID-19: A multidisciplinary review." Front Public Health 8: 383.

[Full Text](#)

*Department of Foundational Medical Studies (OU)*

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is a novel coronavirus that is responsible for the 2019-2020 pandemic. In this comprehensive review, we discuss the current published literature surrounding the SARS-CoV-2 virus. We examine the fundamental concepts including the origin, virology, pathogenesis, clinical manifestations, diagnosis, laboratory, radiology, and histopathologic findings, complications, and treatment. Given that much of the information has been extrapolated from what we know about other coronaviruses including severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV), we identify and provide insight into controversies and research gaps for the current pandemic to assist with future research ideas. Finally, we discuss the global response to the coronavirus disease-2019 (COVID-19) pandemic and provide thoughts regarding lessons for future pandemics.

Chang AM, Hollander JE, Su E, Weiss RE, Yagapen AN, Malveau SE, Adler DH, **Bastani A**, Baugh CW, Caterino JM, **Clark CL**, Diercks DB, Nicks BA, Nishijima DK, Shah MN, Stiffler KA, Storrow AB, Wilber ST and Sun BC (2020). "The accuracy of interqual criteria in determining the observation versus inpatient status in older adults with syncope." Journal of Emergency Medicine 59(2): 193-200.

[Full Text](#)

*Department of Emergency Medicine*

Background: McKesson's InterQual criteria are widely used in hospitals to determine if patients should be classified as observation or inpatient status, but the accuracy of the criteria is unknown. Objective: We sought to determine whether InterQual criteria accurately predicted length of stay (LOS) in older patients with syncope. Methods: We conducted a secondary analysis of a cohort study of adults  $\geq 60$  years of age who had syncope. We calculated InterQual criteria and classified the patient as observation or inpatient status. Outcomes were whether LOS were less than or greater than 2 midnights. Results: We analyzed 2361 patients; 1227 (52.0%) patients were male and 1945 (82.8%) were white, with a mean age of 73.2 +/- 9.0 years. The median LOS was 32.6 h (interquartile range 24.2-71.8). The sensitivity of InterQual criteria for LOS was 60.8% (95% confidence interval 57.9-63.6%) and the specificity was 47.8% (95% confidence interval 45.0-50.5%). Conclusions: In older adults with syncope, those who met InterQual criteria for inpatient status had longer LOS compared with those who did not; however, the accuracy of the criteria to predict length of stay over 2 days is poor, with a sensitivity of 60% and a specificity of 48%. Future research should identify criteria to improve LOS prediction.

Chen CJ, Lee CC, Kano H, Kearns KN, Ding D, Tzeng SW, Atik AF, Joshi K, Huang PP, Kondziolka D, Ironside N, Mathieu D, Iorio-Morin C, **Grills IS**, Quinn TJ, Siddiqui ZA, Marvin K, Feliciano C, Starke RM, Faramand A, Barnett G, Lunsford LD and Sheehan JP (2020). "Radiosurgery for unruptured intervention-naïve pediatric brain arteriovenous malformations." Neurosurgery 87(2): 368-376.

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*Department of Radiation Oncology*

Background: Long-term data regarding stereotactic radiosurgery (SRS) as a standalone therapy for unruptured pediatric brain arteriovenous malformations (AVMs) are incompletely defined. Objective: To evaluate, in a multicenter, retrospective cohort study, the outcomes after SRS for unruptured, intervention-naïve pediatric AVMs. Methods: To retrospectively analyze the International Radiosurgery Research Foundation pediatric AVM database from 1987 to 2018. Pediatric patients with unruptured, previously untreated AVMs who underwent SRS were included. The primary endpoint was a composite of hemorrhagic stroke, death, or permanently symptomatic radiation-induced changes. Results: The study cohort comprised 101 patients (mean follow-up 80.8 mo). The primary endpoint occurred in 14%, comprising hemorrhagic stroke, death, and permanent radiation-induced changes in 6%, 3%, and 8%, respectively. Estimated

probabilities of the primary endpoint were 5.2%, 10.8%, and 23.0% at 2, 5, and 10 yr, respectively. Estimated probabilities of AVM obliteration at 5 and 10 yr were 64% and 82%, respectively. Single SRS treatment ( $P = .007$ ) and higher margin dose ( $P = .005$ ) were predictors of obliteration. Subgroup analysis of Spetzler-Martin grade I-III AVMs estimated primary endpoint probabilities of 3.7%, 8.4%, and 18.7% at 2, 5, and 10 yr, respectively. Conclusion: Treatment of unruptured, intervention-naïve AVMs in the pediatric population with SRS carries an approximately 2% annual risk of morbidity and mortality, which appears to plateau after 10 yr. The poorly described natural history of pediatric AVMs renders any comparison of SRS vs conservative management imperfect.

Chen JY, Galwankar NS, Emch HN, Menon SS, **Cortes C**, Thurman JM, Merrill SA, Brodsky RA and Ferreira VP (2020). "Properdin is a key player in lysis of red blood cells and complement activation on endothelial cells in hemolytic anemias caused by complement dysregulation." *Frontiers in Immunology* 11: 1460.

[Full Text](#)

*Department of Foundational Medical Studies (OU)*

The complement system alternative pathway (AP) can be activated excessively in inflammatory diseases, particularly when there is defective complement regulation. For instance, deficiency in complement regulators CD55 and CD59, leads to paroxysmal nocturnal hemoglobinuria (PNH), whereas Factor H mutations predispose to atypical hemolytic uremic syndrome (aHUS), both causing severe thrombohemolysis. Despite eculizumab being the treatment for these diseases, benefits vary considerably among patients. Understanding the molecular mechanisms involved in complement regulation is essential for developing new treatments. Properdin, the positive AP regulator, is essential for complement amplification by stabilizing enzymatic convertases. In this study, the role of properdin in red blood cell (RBC) lysis and endothelial cell opsonization in these AP-mediated diseases was addressed by developing in vitro assays using PNH patient RBCs and human primary endothelial cells, where the effects of inhibiting properdin, using novel monoclonal antibodies (MoAbs) that we generated and characterized, were compared to other complement inhibitors. In in vitro models of PNH, properdin inhibition prevented hemolysis of patient PNH type II and III RBCs more than inhibition of Factor B, C3, and C5 (>17-fold, or >81-fold, or >12-fold lower molar IC90 values, respectively). When tested in an in vitro aHUS hemolysis model, the anti-properdin MoAbs had 11-fold, and 86-fold lower molar IC90 values than inhibition of Factor B, or C3, respectively ( $P < 0.0001$ ). When comparing target/inhibitor ratios in all hemolysis assays, inhibiting properdin was at least as efficient as the other complement inhibitors in most cases. In addition, using in vitro endothelial cell assays, the data indicate a critical novel role for properdin in promoting complement activation on human endothelial cells exposed to heme (a hemolysis by-product) and rH19-20 (to inhibit Factor H cell-surface protection), as occurs in aHUS. Inhibition of properdin or C3 in this system significantly reduced C3 fragment deposition by 75%. Altogether, the data indicate properdin is key in promoting RBC lysis and complement activation on human endothelial cells, contributing to the understanding of PNH and aHUS pathogenesis. Further studies to determine therapeutic values of inhibiting properdin in complement-mediated diseases, in particular those that are characterized by AP dysregulation, are warranted.

Conte E, Dwivedi A, Mushtaq S, Pontone G, Lin FY, Hollenberg EJ, Lee SE, Bax J, Cademartiri F, **Chinnaiyan K**, Chow BJW, Cury RC, Feuchtner G, Hadamitzky M, Kim YJ, Baggiano A, Leipsic J, Maffei E, Marques H, Plank F, **Raff GL**, van Rosendaal AR, Villines TC, Weirich HG, Al'Aref SJ, Baskaran L, Cho I, Danad I, Han D, Heo R, Lee JH, Stuijzand WJ, Gransar H, Lu Y, Sung JM, Park HB, Al-Mallah MH, de Araújo Gonçalves P, Berman DS, Budoff MJ, Samady H, Shaw LJ, Stone PH, Virmani R, Narula J, Min JK, Chang HJ and Andreini D (2020). "Age- and sex-related features of atherosclerosis from coronary computed tomography angiography in patients prior to acute coronary syndrome: Results from the ICONIC study." *European Heart Journal of Cardiovascular Imaging*. ePub Ahead of Print.

[Full Text](#)

*Department of Internal Medicine*

**Aims:** Although there is increasing evidence supporting coronary atherosclerosis evaluation by coronary computed tomography angiography (CCTA), no data are available on age and sex differences for quantitative plaque features. The aim of this study was to investigate sex and age differences in both qualitative and quantitative atherosclerotic features from CCTA prior to acute coronary syndrome (ACS). **Methods and Results:** Within the ICONIC study, in which 234 patients with subsequent ACS were propensity

matched 1:1 with 234 non-event controls, our current subanalysis included only the ACS cases. Both qualitative and quantitative advance plaque analysis by CCTA were performed by a core laboratory. In 129 cases, culprit lesions identified by invasive coronary angiography at the time of ACS were co-registered to baseline CCTA precursor lesions. The study population was then divided into subgroups according to sex and age (<65 vs. ≥ 65 years old) for analysis. Older patients had higher total plaque volume than younger patients. Within specific subtypes of plaque volume, however, only calcified plaque volume was higher in older patients ( $135.9 \pm 163.7$  vs.  $63.8 \pm 94.2$  mm<sup>3</sup>,  $P < 0.0001$ , respectively). Although no sex-related differences were recorded for calcified plaque volume, females had lower fibrous and fibrofatty plaque volume than males (Fibrofatty volume  $29.6 \pm 44.1$  vs.  $75.3 \pm 98.6$  mm<sup>3</sup>,  $P = 0.0001$ , respectively). No sex-related differences in the prevalence of qualitative high-risk plaque features were found, even after separate analyses considering age were performed. Conclusion: Our data underline the importance of age- and sex-related differences in coronary atherosclerosis presentation, which should be considered during CCTA-based atherosclerosis quantification.

**DiMagno AN, Hajj-Hussein I, Othmani AE, Stasch J, Sayeed Z and El-Othmani MM (2020).** "Chronic kidney disease impact on total joint arthroplasty outcomes: A national inpatient sample-based study." Journal of Orthopaedic Surgery 28(3): 2309499020916129.

[Full Text](#)

*Department of Foundational Medical Studies (OU)*

*OUWB Medical Student Author*

Introduction: In the United States, chronic kidney disease (CKD) affects roughly 11% of the population or 19.2 million people. As the prevalence of CKD and demand for total joint arthroplasty (TJA) continue to rise, it is critical to assess the impact of CKD on postoperative clinical and economic outcomes. Methods: Discharge data from 2006 to 2011 National Inpatient Sample were used for this study. A total of 851,150 TJA patients were divided into three cohorts: group 1 included no CKD, CKD stage I, and CKD stage II; group 2 included CKD stage III and stage IV; group 3 included CKD stage V. Inverse probability of treatment weighting/propensity score weighting was used to predict outcome variables as a function of age, sex, and Elixhauser comorbidities. Patients were compared against group I for in-hospital postoperative outcomes. Results: Stage III/IV CKD patients undergoing primary TJA had higher odds of any complication (odds ratio (OR), 2.63;  $p < 0.0001$ ), longer length of stay (LOS), and higher total charge (LOS, 4.34 vs. 3.48 days; total charge, US\$56,003 vs. US\$46,115;  $p < 0.0001$ ) when compared to patients with no CKD/stage I or II. Similarly, stage V CKD patients undergoing primary TJA had higher odds of any complication (OR, 1.64;  $p < 0.0001$ ), longer LOS, and higher total charges (LOS, 5.81 vs. 3.48 days; total charge, US\$59,869 vs. US\$46,115) than their counterparts with no CKD/stage I or II CKD. Discussion: Our results indicate that stage III, IV, or V CKD, compared with those with no CKD, stage I or II patients are at a greater risk for postoperative complications and consume more resources following TJA.

**Diokno AC and Devries JM (2020).** "The impact of COVID-19 on urologic practice, medical education, and training." International Urology and Nephrology 52(7): 1195-1198.

[Full Text](#)

*Department of Urology*

*Department of Pediatrics*

Ferraro RA, van Rosendael AR, Lu Y, Andreini D, Al-Mallah MH, Cademartiri F, **Chinnaiyan K**, Chow BJW, Conte E, Cury RC, Feuchtner G, de Araújo Gonçalves P, Hadamitzky M, Kim YJ, Leipsic J, Maffei E, Marques H, Plank F, Pontone G, **Raff GL**, Villines TC, Lee SE, Al'Aref SJ, Baskaran L, Cho I, Danad I, Gransar H, Budoff MJ, Samady H, Stone PH, Virmani R, Narula J, Berman DS, Chang HJ, Bax JJ, Min JK, Shaw LJ and Lin FY (2020). "Non-obstructive high-risk plaques increase the risk of future culprit lesions comparable to obstructive plaques without high-risk features: The ICONIC study." European Heart Journal of Cardiovascular Imaging 21(9): 973-980.

[Full Text](#)

*Department of Internal Medicine*

Aims: High-risk plaque (HRP) and non-obstructive coronary artery disease independently predict adverse events, but their importance to future culprit lesions has not been resolved. We sought to determine in patients prior to confirmed acute coronary syndrome (ACS) the association between lesion percent diameter

stenosis (%DS), and the absolute number and prevalence of HRP. The secondary objective was to examine the relative importance of non-obstructive HRP in future culprit lesions. Methods and Results: Within the ICONIC study, a nested case-control study of patients undergoing coronary computed tomographic angiography (coronary CT), we included ACS cases with culprit lesions confirmed by invasive coronary angiography and coregistered to baseline coronary CT. Quantitative CT was used to evaluate obstructive ( $\geq 50\%$ ) and non-obstructive ( $< 50\%$ ) diameter stenosis, with HRP defined as  $\geq 2$  features of spotty calcification, positive remodelling, or low-attenuation plaque at baseline. A total of 234 patients with downstream ACS over 54 (interquartile range 5-525.5) days exhibited 198/898 plaques with HRP on coronary CT. While HRP was less prevalent in non-obstructive (19.7%, 161/819) than obstructive lesions (46.8%, 37/79,  $P < 0.001$ ), non-obstructive plaque comprised 81.3% (161/198) of HRP lesions overall. Among the 128 patients with identifiable culprit lesion precursors, the adjusted hazard ratio (HR) was 1.85 [95% confidence interval (CI) 1.26-2.72] for HRP, with no interaction between %DS and HRP ( $P = 0.82$ ). Compared to non-obstructive HRP lesions, obstructive lesions without HRP exhibited a non-significant HR of 1.41 (95% CI 0.61-3.25,  $P = 0.42$ ). Conclusions: While HRP is more prevalent among obstructive lesions, non-obstructive HRP lesions outnumber those that are obstructive and confer risk clinically approaching that of obstructive lesions without HRP. Published on behalf of the European Society of Cardiology. All rights reserved.

Foster CC, Fan M, Lee NY, Yom SS, Heaton CM, **Deraniyagala R**, Amdur R, Weichselbaum RR and Haraf DJ (2020). "Is it worth it? Consequences of definitive head and neck reirradiation." *Seminars in Radiation Oncology* 30(3): 212-217.

[Full Text](#)

*Department of Radiation Oncology*

Locally recurrent head and neck malignancies after definitive radiation or chemoradiation represent challenging clinical scenarios requiring careful consideration of individualized risks and benefits before deciding upon the next best course of therapy. Herein, a case-based approach to personalized decision making highlights the expert opinions of leaders in head and neck oncology. Topics of interest include optimal candidacy for reirradiation or salvage surgical resection, the judicious use of chemotherapy as induction therapy or as a radiosensitizing agent, the incorporation of immunotherapy into the treatment paradigm for locally recurrent disease, and the impact of various treatment modalities on quality of life and functional outcomes. Interestingly, the lack of consensus among the experts on topics as fundamental as the appropriateness of offering reirradiation at all and as nuanced as target volume delineation for the reirradiated field suggests that there is no straightforward approach in this scenario. Common to all opinions is a desire to maximize the therapeutic ratio for a patient potentially facing a grim prognosis, and honest discussions about goals of care and expectations for post-treatment quality of life should be central to the clinical approach to this and similar cases.

Foster CC, Seiwert TY, MacCracken E, Blair EA, Agrawal N, Melotek JM, Portugal L, **Brisson RJ**, Gooi Z, Spiotto MT, Vokes EE and Haraf DJ (2020). "Dose and volume de-escalation for human papillomavirus-positive oropharyngeal cancer is associated with favorable posttreatment functional outcomes." *International Journal of Radiation Oncology, Biology, Physics* 107(4): 662-671.

[Full Text](#)

*OUWB Medical Student Author*

Purpose: To report functional outcomes for patients with human papillomavirus-positive oropharyngeal cancer treated on a phase 2 protocol of risk- and induction chemotherapy response-adapted dose and volume de-escalated radiation therapy (RT)/chemoradiation (CRT). Methods and Materials: Patients were stratified as low risk (LR) or high risk (HR) according to T/N-stage and smoking history. Induction chemotherapy was followed by radiographic response assessment. LR patients with  $\geq 50\%$  response received 50 Gy RT (RT50), whereas LR patients with 30% to 50% response or HR patients with  $\geq 50\%$  response received 45 Gy CRT (CRT45). All other patients received 75 Gy CRT (CRT75) with RT limited to the first echelon of uninvolved nodes. Pre- and post-RT/CRT modified barium swallow studies were performed. Percutaneous endoscopic gastrostomy (PEG) tube placement, body mass index (BMI), and narcotic use were recorded. Statistical comparisons used linear or logistic regression, the Mann-Whitney U test, the  $\chi^2$  test, or Fisher's exact test as appropriate. Results: Twenty-eight LR and 34 HR patients were enrolled; 49 completed RT50/CRT45 and 11 completed CRT75. PEG-tube dependency at the end of RT/CRT and 3 months post-RT/CRT significantly differed according to risk and treatment groups (all  $P < .05$ ). Treatment intensity was

independently associated with 3-month PEG status while adjusting for risk group (P = .002). The CRT75 group had a median -8.42% change from baseline BMI at 1 year post-RT/CRT versus -2.54% for the RT50/CRT45 group (P = .01). At the end of RT/CRT, CRT75 patients were less likely to tolerate a normal diet, more likely to have swallowing performance status scale scores  $\geq 4$ , more likely to have Rosenbek's penetration-aspiration scores  $\geq 7$ , more likely to have developed trismus, and more likely to require narcotics >2 months (all P < .05). Conclusions: Induction chemotherapy followed by risk- and response-adapted dose and volume de-escalated RT/CRT is associated with clinically meaningful functional outcomes including (1) improved swallowing function, (2) higher BMI, and (3) shorter narcotic use for patients receiving de-escalation.

**Gallagher MJ**, Bloomingdale R, **Berman AD**, **Williamson BD**, **Dixon SR** and **Safian RD** (2020). "Strategic deployment of cardiology fellows in training using the Accreditation Council for Graduate Medical Education Coronavirus Disease 2019 framework." *Journal of the American Heart Association* 9(14): 1-16.

[Full Text](#)

*Department of Internal Medicine*

Coronavirus disease 2019 is a global pandemic affecting >3 million people in >170 countries, resulting in >200 000 deaths; 35% to 40% of patients and deaths are in the United States. The coronavirus disease 2019 crisis is placing an enormous burden on health care in the United States, including residency and fellowship training programs. The balance between mitigation, training and education, and patient care is the ultimate determinant of the role of cardiology fellows in training during the coronavirus disease 2019 crisis. On March 24, 2020, the Accreditation Council for Graduate Medical Education issued a formal response to the pandemic crisis and described a framework for operation of graduate medical education programs. Guidance for deployment of cardiology fellows in training during the coronavirus disease 2019 crisis is based on the principles of a medical mission, and adherence to preparation, protection, and support of our fellows in training. The purpose of this review is to describe our departmental strategic deployment of cardiology fellows in training using the Accreditation Council for Graduate Medical Education framework for pandemic preparedness.

Gill I, Edhi AI and **Cappell MS** (2020). "Proposed characterization of the syndrome of epidural pneumatosis (pneumorrhachis) in patients with forceful vomiting from diabetic ketoacidosis as a clinico-radiologic pentad based on systematic literature review & an illustrative case report." *Medicine (Baltimore)* 99(35): e21001.

[Full Text](#)

*Department of Internal Medicine*

Background: Previous literature on epidural pneumatosis (pneumorrhachis, or air in epidural cavity) associated with forceful vomiting in a patient with diabetic ketoacidosis (DKA) has consisted of individual case reports without comprehensive syndrome characterization due to syndromic rarity, with the largest previous literature review comprising 6 cases. Presumed pathophysiology is air escaping from alveolar rupture from forceful vomiting via tissue planes to cause epidural pneumatosis. Aim: Systematically review literature to facilitate syndromic diagnosis, evaluation, and treatment. A new illustrative case is reported. Methods: Systematic review of literature using 2 independent readers, 2 computerized databases, and the following medical terms/keywords: ["epidural pneumatosis" OR "pneumorrhachis"] AND ["diabetes" OR "diabetic ketoacidosis" OR "DKA"]. Discrepancies between 2 readers were resolved by consensus using prospectively developed study inclusion criteria. Two readers independently abstracted case report. Prospective review protocol and patients, problems, intervene, comparison group, outcomes discussed in Methods section of paper. Results-Systematic-Literature-Review: Revealed 10 previously reported cases plus 1 new case (see below) that shows this syndrome presents rather stereotypically with the tentatively proposed following pentad (% of patients fulfilling individual criterion): 1-forceful vomiting (100%), 2-during DKA (100%), 3-pneumomediastinum from forceful alveolar rupture (100%), 4-epidural pneumatosis from air escape from pneumomediastinum (100%), and 5-no complications of Boerhaave syndrome or of focal neurological deficits (100%). Pentad is pathophysiologically reasonable because forceful vomiting can cause alveolar rupture, pneumomediastinum, and air entry into epidural space. Results-Illustrative-Case-Report: Epidural pneumatosis occurred in a 33-year-old-male with poorly controlled diabetes mellitus type 1 who presented with forceful vomiting while in DKA. Radiologic findings also included subcutaneous emphysema, pneumomediastinum, and small pneumothorax. The patient rapidly improved while receiving acute therapy



for DKA, and was discharged after 2 hospital days. Study Limitations: Limited number of analyzed, retrospectively reported cases. Case reports subject to reporting bias. Specificity, positive predictive value, and negative predictive value not meaningfully analyzed in this homogeneous population. Conclusions: Based on systematic review, syndrome is tentatively proposed as a pentad with: 1-forceful vomiting, 2-during DKA, 3- pneumomediastinum, 4-epidural pneumatosis, and 5-no complications of Boerhaave syndrome or focal neurological deficits. Proposed pentad should be prospectively tested in a larger population including patients with this versus closely related syndromes.

Goldman JJ, **Huynh KA**, Elfallal W, Chaiyasate K and **Fahim DK** (2020). "Cervical spine and craniocervical junction reconstruction with a vascularized fibula free flap: A case report." World Neurosurgery. ePub Ahead of Print.

[Full Text](#)

*Department of Neurosurgery*

*OUIB Medical Student Author*

Long-term stabilization of the cervical spine after extensive multilevel tumor resection is difficult to achieve. The current standard approach of instrumentation combined with allograft or nonvascularized autograft is limited in settings of increased risk of nonunion or delayed union (i.e. prior radiation therapy or poorly vascularized wound beds). In such cases, vascularized bone grafting is a viable alternative to achieve lasting stability because of hastened fusion time, limited reliance on osseous remodeling, and incorporation into the axial skeleton with strut strength. We report the first time that a vascularized fibular free flap has been used to reconstruct the cervical column across five vertebral levels, from the craniocervical junction to the lower cervical spine. We describe a transoral approach to the area and compare this method to other reconstructive options.

**Goldstein JA** and **Hanson I** (2020). "Impella RP for treatment of right ventricular shock: Appropriate unloading never gets old." Catheterization and Cardiovascular Interventions 96(2): 382-383.

[Full Text](#)

*Department of Internal Medicine*

Rapid restoration of hemodynamics is key to successful shock management. The failing right ventricular (RV) is resilient and recovers if hemodynamics are supported while the underlying insulting cause is alleviated. Inotropic/vasopressor drugs constitute a "double-edged sword" that augment hemodynamics, but exacerbate myocardial and multiorgan injury. Impella RP mechanical support for RV shock stabilizes hemodynamics and is associated with favorable clinical outcomes.

Gralow JR, Barlow WE, Paterson AHG, M'lao 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 (2020). "Phase III randomized trial of bisphosphonates as adjuvant therapy in breast cancer: S0307." Journal of National Cancer Institute 112(7): 698-707.

[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 randomly assigned to 3 years of intravenous zoledronic acid, oral clodronate, or oral ibandronate. The primary endpoint was disease-free survival (DFS) with overall survival as a secondary outcome. All statistical tests were two-sided. Results: A total of 6097 patients enrolled. Median age was 52.7 years. Prior to being randomly assigned, 73.2% patients indicated preference for oral vs intravenous formulation. DFS did not differ across arms in a log-rank test ( $P = .49$ ); 5-year DFS was 88.3% (zoledronic acid: 95% confidence interval [CI] = 86.9% to 89.6%), 87.6% (clodronate: 95% CI = 86.1% to 88.9%), and 87.4% (ibandronate: 95% CI = 85.6% to 88.9%). Additionally, 5-year overall survival did not differ between arms (log rank  $P = .50$ ) and was 92.6% (zoledronic acid: 95% CI = 91.4% to 93.6%), 92.4% (clodronate: 95% CI = 91.2% to 93.5%), and 92.9% (ibandronate: 95% CI = 91.5% to 94.1%). Bone as first site of recurrence did not differ between arms ( $P = .93$ ). 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 was highest for zoledronic acid (1.26%) compared with 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 osteonecrosis of the jaw 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 United States should be considered.

Greive J, Cooke A, Nanda A, Epstein SZ, Wasan AN, Shepard KV, II, Capão-Filipe M, Nish A, Rubin M, Gregory KL, **Dass K**, Blessing-Moore J and Randolph C (2020). "Work group report: Perspectives in diagnosis and management of exercise-induced bronchoconstriction in athletes." Journal of Allergy and Clinical Immunology 8(8): 2542-2555.

[Full Text](#)

*Department of Internal Medicine*

Exercise-induced bronchoconstriction, otherwise known as exercise-induced bronchoconstriction with asthma or without asthma, is an acute airway narrowing that occurs as a result of exercise and can occur in patients with asthma. A panel of members from the American Academy of Allergy, Asthma & Immunology Sports, Exercise, & Fitness Committee reviewed the diagnosis and management of exercise-induced bronchoconstriction in athletes of all skill levels including recreational athletes, high school and college athletes, and professional athletes. A special emphasis was placed on the recommendations and regulations set forth by professional athletic organizations after a detailed review of their collective bargaining agreements, substance abuse policies, antidoping program manuals, and the World Anti-Doping Agency antidoping code. The recommendations in this review are based on currently available evidence in addition to providing guidance for athletes of all skill levels as well as their treating physicians to better understand which pharmaceutical and nonpharmaceutical management options are appropriate as well as which medications are permitted or prohibited, and the proper documentation required to remain compliant.

Guzzardo G and **Gowans LK** "A 21-year-old with right lower extremity edema." Clinical Pediatrics. ePub Ahead of Print.

[Full Text](#)

*Department of Pediatrics*

Haight M, Bahner I, Belovich AL, Bonaminio G, Brenneman A, Brooks WS, Chinn C, El-Sawi N, Haudek SB, **McAuley RJ**, Rowe R, Slivkoff MD and Vari RC (2020). "How is health science education tackling the opioid crisis?" Medical Science Educator 30(3): 1295-1297.

[Full Text](#)

*Department of Foundational Medical Studies (OU)*

**Halalau A, Ditkoff J**, Hamilton J, **Sharrak A, Vanood A, Abbas A** and **Ziadeh J** (2020). "Emergency center curbside screening during the COVID-19 pandemic: Retrospective cohort study." JMIR Public Health and Surveillance 6(3): e20040.

[Full Text](#)

*OUWB Medical Student Author*

*Department of Emergency Medicine*

*Department of Internal Medicine*

Background: Coronavirus disease (COVID-19) is a global pandemic that has placed a significant burden on health care systems in the United States. Michigan has been one of the top states affected by COVID-19. Objective: We describe the emergency center curbside testing procedure implemented at Beaumont Hospital, a large hospital in Royal Oak, MI, and aim to evaluate its safety and efficiency. Methods: Anticipating a surge in patients requiring testing, Beaumont Health implemented curbside testing, operated by a multidisciplinary team of health care workers, including physicians, advanced practice providers, residents, nurses, technicians, and registration staff. We report on the following outcomes over a period of 26 days (March 12, 2020, to April 6, 2020): time to medical decision, time spent documenting electronic medical records, overall screening time, and emergency center return evaluations. Results: In total, 2782 patients received curbside services. A nasopharyngeal swab was performed on 1176 patients (41%), out of whom 348 (29.6%) tested positive. The median time for the entire process (from registration to discharge)

was 28 minutes (IQR 17-44). The median time to final medical decision was 15 minutes (IQR 8-27). The median time from medical decision to discharge was 9 minutes (IQR 5-16). Only 257 patients (9.2%) returned to the emergency center for an evaluation within 7 or more days, of whom 64 were admitted to the hospital, 11 remained admitted, and 4 expired. Conclusions: Our curbside testing model encourages the incorporation of this model at other high-volume facilities during an infectious disease pandemic.

Hamera JA, **Bryant NB**, Shievitz MS and **Berger DA** (2020). "Systemic thrombolysis for refractory cardiac arrest due to presumed myocardial infarction." [American Journal of Emergency Medicine](#). ePub Ahead of Print.

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*Department of Emergency Medicine*

The empiric usage of systemic thrombolysis for refractory out of hospital cardiac arrest (OHCA) is considered for pulmonary embolism (PE), but not for undifferentiated cardiac etiology [1, 2]. We report a case of successful resuscitation after protracted OHCA with suspected non-PE cardiac etiology, with favorable neurological outcome after empiric administration of systemic thrombolysis. A 47-year-old male presented to the emergency department (ED) after a witnessed OHCA with no bystander cardiopulmonary resuscitation (CPR). His initial rhythm was ventricular fibrillation (VF) which had degenerated into pulseless electrical activity (PEA) by ED arrival. Fifty-seven minutes into his arrest, we gave systemic thrombolysis which obtained return of spontaneous circulation (ROSC). He was transferred to the coronary care unit (CCU) and underwent therapeutic hypothermia. On hospital day (HD) 4 he began following commands and was extubated on HD 5. Subsequent percutaneous coronary intervention (PCI) revealed non-obstructive stenosis in distal LAD. He was discharged home directly from the hospital, with one-month cerebral performance category (CPC) score of one. He was back to work three months post-arrest. Emergency physicians (EP) should be aware of this topic since we are front-line health care professionals for OHCA. Thrombolytics have the advantage of being widely available in ED and therefore offer an option on a case-by-case basis when intra-arrest PCI and ECPR are not available. This case report adds to the existing literature on systemic thrombolysis as salvage therapy for cardiac arrest from an undifferentiated cardiac etiology. The time is now for this treatment to be reevaluated.

Han D, Berman DS, Miller RJH, Andreini D, Budoff MJ, Cademartiri F, **Chinnaiyan K**, Choi JH, Conte E, Marques H, de Araújo Gonçalves P, Gottlieb I, Hadamitzky M, Leipsic J, Maffei E, Pontone G, Shin S, Kim YJ, Lee BK, Chun EJ, Sung JM, Lee SE, Virmani R, Samady H, Stone P, Narula J, Bax JJ, Shaw LJ, Lin FY, Min JK and Chang HJ (2020). "Association of cardiovascular disease risk factor burden with progression of coronary atherosclerosis assessed by serial coronary computed tomographic angiography." [JAMA Network Open](#) 3(7): e2011444.

[Full Text](#)

*Department of Internal Medicine*

Importance: Several studies have reported that the progression of coronary atherosclerosis, as measured by serial coronary computed tomographic (CT) angiography, is associated with the risk of future cardiovascular events. However, the cumulative consequences of multiple risk factors for plaque progression and the development of adverse plaque characteristics have not been well characterized. Objectives: To examine the association of cardiovascular risk factor burden, as assessed by atherosclerotic cardiovascular disease (ASCVD) risk score, with the progression of coronary atherosclerosis and the development of adverse plaque characteristics. Design, Setting, and Participants: This cohort study is a subgroup analysis of participant data from the prospective observational Progression of Atherosclerotic Plaque Determined by Computed Tomographic Angiography Imaging (PARADIGM) study, which evaluated the association between serial coronary CT angiography findings and clinical presentation. The PARADIGM international multicenter registry, which includes 13 centers in 7 countries (Brazil, Canada, Germany, Italy, Portugal, South Korea, and the US), was used to identify 1005 adult patients without known coronary artery disease who underwent serial coronary CT angiography scans (median interscan interval, 3.3 years; interquartile range [IQR], 2.6-4.8 years) between December 24, 2003, and December 16, 2015. Based on the 10-year ASCVD risk score, the cardiovascular risk factor burden was classified as low (<7.5%), intermediate (7.5%-20.0%), or high (>20.0%). Data were analyzed from February 8, 2019, to April 17, 2020. Exposures: Association of baseline ASCVD risk burden with plaque progression. Main Outcomes and Measures: Noncalcified plaque, calcified plaque, and total plaque volumes (mm<sup>3</sup>) were measured. Noncalcified plaque was subclassified using predefined Hounsfield unit thresholds for fibrous, fibrofatty, and low-attenuation plaque. The percent atheroma volume

(PAV) was defined as plaque volume divided by vessel volume. Adverse plaque characteristics were defined as the presence of positive remodeling, low-attenuation plaque, or spotty calcification. Results: In total, 1005 patients (mean [SD] age, 60 [8] years; 575 men [57.2%]) were included in the analysis. Of those, 463 patients (46.1%) had a low 10-year ASCVD risk score (low-risk group), 373 patients (37.1%) had an intermediate ASCVD risk score (intermediate-risk group), and 169 patients (16.8%) had a high ASCVD risk score (high-risk group). The annualized progression rate of PAV for total plaque, calcified plaque, and noncalcified plaque was associated with increasing ASCVD risk ( $r = 0.26$  for total plaque,  $r = 0.23$  for calcified plaque, and  $r = 0.11$  for noncalcified plaque;  $P < .001$ ). The annualized PAV progression of total plaque, calcified plaque, and noncalcified plaque was significantly greater in the high-risk group compared with the low-risk and intermediate-risk groups (for total plaque, 0.99% vs 0.45% and 0.58%, respectively;  $P < .001$ ; for calcified plaque, 0.61% vs 0.23% and 0.36%;  $P < .001$ ; and for noncalcified plaque, 0.38% vs 0.22% and 0.23%;  $P = .01$ ). When further subclassified by noncalcified plaque type, the annualized PAV progression of fibrofatty and low-attenuation plaque was greater in the high-risk group (0.09% and 0.02%, respectively) compared with the low- to intermediate-risk group ( $n = 836$ ; 0.02% [ $P = .02$ ] and 0.001% [ $P = .008$ ], respectively). The interval development of adverse plaque characteristics was greater in the high-risk group compared with the low-risk and intermediate-risk groups (for new positive remodeling, 73 patients [43.2%] vs 151 patients [32.6%] and 133 patients [35.7%], respectively;  $P = .02$ ; for new low-attenuation plaque, 26 patients [15.4%] vs 44 patients [9.5%] and 35 patients [9.4%];  $P = .02$ ; and for new spotty calcification, 37 patients [21.9%] vs 52 patients [11.2%] and 54 patients [14.5%];  $P = .002$ ). The progression of noncalcified plaque subclasses and the interval development of adverse plaque characteristics did not significantly differ between the low-risk and intermediate-risk groups. Conclusions and Relevance: Progression of coronary atherosclerosis occurred across all ASCVD risk groups and was associated with an increase in 10-year ASCVD risk. The progression of fibrofatty and low-attenuation plaques and the development of adverse plaque characteristics was greater in patients with a high risk of ASCVD.

Han D, Klein E, Friedman J, Gransar H, Achenbach S, Al-Mallah MH, Budoff MJ, Cademartiri F, Maffei E, Callister TQ, **Chinnaiyan K**, Chow BJW, DeLago A, Hadamitzky M, Hausleiter J, Kaufmann PA, Villines TC, Kim YJ, Leipsic J, Feuchtner G, Cury RC, Pontone G, Andreini D, Marques H, Rubinshtein R, Chang HJ, Lin FY, Shaw LJ, Min JK and Berman DS (2020). "Prognostic significance of subtle coronary calcification in patients with zero coronary artery calcium score: From the CONFIRM registry." *Atherosclerosis* 309: 33-38.

[Full Text](#)

*Department of Internal Medicine*

Background and Aims: The Agatston coronary artery calcium score (CACS) may fail to identify small or less dense coronary calcification that can be detected on coronary CT angiography (CCTA). We investigated the prevalence and prognostic importance of subtle calcified plaques on CCTA among individuals with CACS 0. Methods: From the prospective multicenter CONFIRM registry, we evaluated patients without known CAD who underwent CAC scan and CCTA. CACS was categorized as 0, 1–10, 11–100, 101–400, and >400. Patients with CACS 0 were stratified according to the visual presence of coronary plaques on CCTA. Plaque composition was categorized as non-calcified (NCP), mixed (MP) and calcified (CP). The primary outcome was a major adverse cardiac event (MACE) which was defined as death and myocardial infarction. Results: Of 4049 patients, 1741 (43%) had a CACS 0. NCP and plaques that contained calcium (MP or CP) were detected by CCTA in 110 patients (6% of CACS 0) and 64 patients (4% of CACS 0), respectively. During a 5.6 years median follow-up (IQR 5.1–6.2 years), 413 MACE events occurred (13%). Patients with CACS 0 and MP/CP detected by CCTA had similar MACE risk compared to patients with CACS 1–10 ( $p = 0.868$ ). In patients with CACS 0, after adjustment for risk factors and symptom, MP/CP was associated with an increased MACE risk compared to those with entirely normal CCTA (HR 2.39, 95% CI [1.09–5.24],  $p = 0.030$ ). Conclusions: A small but non-negligible proportion of patients with CACS 0 had identifiable coronary calcification, which was associated with increased MACE risk. Modifying CAC image acquisition and/or scoring methods could improve the detection of subtle coronary calcification.

Hansen TWR, **Jeffrey Maisels M**, Ebbesen F, Vreman HJ, Stevenson DK, Wong RJ and Bhutani VK (2020). "Sixty years of phototherapy for neonatal jaundice: from serendipitous observation to standardized treatment and rescue for millions." *Journal of Perinatology* 40(10): 1582-1583.

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*Department of Pediatrics*

Haque A, **Cortes C**, Alam MN, Sreedhar M, Ferreira VP and Pangburn MK (2020). "Characterization of binding properties of individual functional sites of human complement factor H." *Frontiers in Immunology* 11: 1728.

[Full Text](#)

*Department of Foundational Medical Studies (OU)*

Factor H exists as a 155,000 dalton, extended protein composed of twenty small domains which is flexible enough that it folds back on itself. Factor H regulates complement activation through its interactions with C3b and polyanions. Three binding sites for C3b and multiple polyanion binding sites have been identified on Factor H. In intact Factor H these sites appear to act synergistically making their individual contributions difficult to distinguish. Recombinantly expressed fragments of human Factor H were examined using surface plasmon resonance (SPR) for interactions with C3, C3b, iC3b, C3c, and C3d. Eleven recombinant proteins of lengths from one to twenty domains were used to show that the three C3b-binding sites exhibit 100-fold different affinities for C3b. The N-terminal site [complement control protein (CCP) domains 1-6] bound C3b with a K<sub>d</sub> of 0.08 μM and this interaction was not influenced by the presence or absence of domains 7 and 8. Full length Factor H similarly exhibited a K<sub>d</sub> for C3b of 0.1 μM. Unexpectedly, the N-terminal site (CCP 1-6) bound native C3 with a K<sub>d</sub> of 0.4 μM. The C-terminal domains (CCP 19-20) exhibited a K<sub>d</sub> of 1.7 μM for C3b. We localized a weak third C3b binding site in the CCP 13-15 region with a K<sub>d</sub> estimated to be ~15 μM. The C-terminal site (CCP 19-20) bound C3b, iC3b, and C3d equally well with a K<sub>d</sub> of 1 to 2 μM. In order to identify and compare regions of Factor H that interact with polyanions a family of 18 overlapping three domain recombinant proteins spanning the entire length of Factor H were expressed and purified. Immobilized heparin was used as a model polyanion and SPR confirmed the presence of heparin binding sites in CCP 6-8 (K<sub>d</sub> 1.2 μM) and in CCP 19-20 (4.9 μM) and suggested the existence of a weak third polyanion binding site in the center of Factor H (CCP 11-13). Our results unveil the relative contributions of different regions of Factor H to its regulation of complement, and may contribute to the understanding of how defects in certain Factor H domains lead to disease.

Howard B, **Haines DE**, Verma A, Packer D, Kirchhof N, Barka N, Onal B, Fraasch S, Miklavčič D and Stewart MT (2020). "Reduction in pulmonary vein stenosis and collateral damage with pulsed field ablation compared with radiofrequency ablation in a canine model." *Circulation: Arrhythmia & Electrophysiology* 13(9): e008337.

[Full Text](#)

*Department of Internal Medicine*

Background: Pulmonary vein (PV) stenosis is a highly morbid condition that can result after catheter ablation for PV isolation. We hypothesized that pulsed field ablation (PFA) would reduce PV stenosis risk and collateral injury compared with irrigated radiofrequency ablation (IRF). Methods: IRF and PFA deliveries were randomized in 8 dogs with 2 superior PVs ablated using one technology and 2 inferior PVs ablated using the other technology. IRF energy (25-30 W) or PFA was delivered (16 pulse trains) at each PV in a proximal and in a distal site. Contrast computed tomography scans were collected at 0, 2, 4, 8, and 12-week (termination) time points to monitor PV cross-sectional area at each PV ablation site. Results: Maximum average change in normalized cross-sectional area at 4-weeks was -46.1±45.1% post-IRF compared with -5.5±20.5% for PFA (P≤0.001). PFA-treated targets showed significantly fewer vessel restrictions compared with IRF (P≤0.023). Necropsy showed expansive PFA lesions without stenosis in the proximal PV sites, compared with more confined and often incomplete lesions after IRF. At the distal PV sites, only IRF ablations were grossly identified based on focal fibrosis. Mild chronic parenchymal hemorrhage was noted in 3 left superior PV lobes after IRF. Damage to vagus nerves as well as evidence of esophagus dilation occurred at sites associated with IRF. In contrast, no lung, vagal nerve, or esophageal injury was observed at PFA sites. Conclusions: PFA significantly reduced risk of PV stenosis compared with IRF postprocedure in a canine model. IRF also caused vagus nerve, esophageal, and lung injury while PFA did not.

Hung YC, Lee CC, Yang HC, Mohammed N, Kearns KN, Nabeel AM, Karim KA, Emad Eldin RM, El-Shehaby AMN, Reda WA, Tawadros SR, Liscak R, Jezkova J, Lunsford LD, Kano H, Sisterson ND, Álvarez RM, Martínez Moreno NE, Kondziolka D, Golfinos JG, **Grills I**, Thompson A, Borghesi-Razavi H, Maiti TK, Barnett GH, McInerney J, Zacharia BE, Xu Z and Sheehan JP (2020). "The benefit and risk of stereotactic radiosurgery for prolactinomas: An international multicenter cohort study." *Journal of Neurosurgery* 133(3): 717-726.

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*Department of Radiation Oncology*

Objective: The most common functioning pituitary adenoma is prolactinoma. Patients with medically refractory or residual/recurrent tumors that are not amenable to resection can be treated with stereotactic radiosurgery (SRS). The aim of this multicenter study was to evaluate the role of SRS for treating prolactinomas. Methods: This retrospective study included prolactinomas treated with SRS between 1997 and 2016 at ten institutions. Patients' clinical and treatment parameters were investigated. Patients were considered to be in endocrine remission when they had a normal level of prolactin (PRL) without requiring dopamine agonist medications. Endocrine control was defined as endocrine remission or a controlled PRL level  $\leq 30$  ng/ml with dopamine agonist therapy. Other outcomes were evaluated including new-onset hormone deficiency, tumor recurrence, and new neurological complications. Results: The study cohort comprised 289 patients. The endocrine remission rates were 28%, 41%, and 54% at 3, 5, and 8 years after SRS, respectively. Following SRS, 25% of patients (72/289) had new hormone deficiency. Sixty-three percent of the patients (127/201) with available data attained endocrine control. Three percent of patients (9/269) had a new visual complication after SRS. Five percent of the patients (13/285) were recorded as having tumor progression. A pretreatment PRL level  $\leq 270$  ng/ml was a predictor of endocrine remission ( $p = 0.005$ , adjusted HR 0.487). An increasing margin dose resulted in better endocrine control after SRS ( $p = 0.033$ , adjusted OR 1.087). Conclusions: In patients with medically refractory prolactinomas or a residual/recurrent prolactinoma, SRS affords remarkable therapeutic effects in endocrine remission, endocrine control, and tumor control. New-onset hypopituitarism is the most common adverse event.

Ionescu F, Petrescu I and **Marin M** (2020). "Unusual behaviour of an unusual tumour: Calcitriol-induced hypercalcaemia in metastatic oesophageal neuroendocrine carcinoma." *BMJ Case Reports* 13(8): e235209.

[Full Text](#)

*Department of Internal Medicine*

Hypercalcaemia in malignancy is most commonly caused by paraneoplastic secretion of parathyroid hormone-related protein or osteolytic metastases. Very rarely (<1% of cases), the mechanism behind increased serum calcium is increased production of calcitriol (1,25-dihydroxyvitamin D) and even rarer is the occurrence of this phenomenon in solid malignancies, with few such instances reported in the literature. We present a case of a neuroendocrine malignancy originating in the oesophagus associated with calcitriol-induced hypercalcaemia, a phenomenon that has not been previously described. We review the pathophysiology of calcitriol-induced hypercalcaemia and previously reported cases of solid tumours with this presentation. ©

Jackson WC, Hartman HE, Dess RT, Birer SR, Soni PD, Hearn JWD, Reichert ZR, Kishan AU, Mahal BA, Zumsteg ZS, Efstathiou JA, Kaffenberger S, Morgan TM, Mehra R, Showalter TN, **Krauss DA**, Nguyen PL, Schipper MJ, Feng FY and Sandler HM (2020). "Addition of androgen-deprivation therapy or brachytherapy boost to external beam radiotherapy for localized prostate cancer: A network meta-analysis of randomized trials." *Journal of Clinical Oncology* 38(26): 3024-3031.

[Full Text](#)

*Department of Radiation Oncology*

Purpose: In men with localized prostate cancer, the addition of androgen-deprivation therapy (ADT) or a brachytherapy boost (BT) to external beam radiotherapy (EBRT) have been shown to improve various oncologic end points. Practice patterns indicate that those who receive BT are significantly less likely to receive ADT, and thus we sought to perform a network meta-analysis to compare the predicted outcomes of a randomized trial of EBRT plus ADT versus EBRT plus BT. Materials and Methods: A systematic review identified published randomized trials comparing EBRT with or without ADT, or EBRT (with or without ADT) with or without BT, that reported on overall survival (OS). Standard fixed-effects meta-analyses were performed for each comparison, and a meta-regression was conducted to adjust for use and duration of ADT. Network meta-analyses were performed to compare EBRT plus ADT versus EBRT plus BT. Bayesian analyses were also performed, and a rank was assigned to each treatment after Markov Chain Monte Carlo analyses to create a surface under the cumulative ranking curve. Results: Six trials compared EBRT with or without ADT ( $n = 4,663$ ), and 3 compared EBRT with or without BT ( $n = 718$ ). The addition of ADT to EBRT improved OS (hazard ratio [HR], 0.71 [95% CI, 0.62 to 0.81]), whereas the addition of BT did not significantly



improve OS (HR, 1.03 [95% CI, 0.78 to 1.36]). In a network meta-analysis, EBRT plus ADT had improved OS compared with EBRT plus BT (HR, 0.68 [95% CI, 0.52 to 0.89]). Bayesian modeling demonstrated an 88% probability that EBRT plus ADT resulted in superior OS compared with EBRT plus BT. Conclusion: Our findings suggest that current practice patterns of omitting ADT with EBRT plus BT may result in inferior OS compared with EBRT plus ADT in men with intermediate- and high-risk prostate cancer. ADT for these men should remain a critical component of treatment regardless of radiotherapy delivery method until randomized evidence demonstrates otherwise.

Kadri AN, Bernardo M, Assar SZ, Werns S and **Abbas AE** (2020). "Surgical versus transcatheter aortic valve replacement in patients with malignancy." Cardiovascular Revascularization Medicine. ePub Ahead of Print.

[Full Text](#)

*Department of Internal Medicine*

Background: Patients with aortic stenosis (AS) and malignancy experience poor clinical outcomes with challenging decisions regarding aortic valve replacement (AVR). We sought to compare the outcomes of transcatheter (TAVR) versus surgical (SAVR) AVR in patients with AS and malignancy. Methods: Based on the Nationwide Readmission Database, we compared all patients with malignancy who underwent isolated SAVR vs. TAVR in 2016 for severe AS. We performed univariate and multivariate analyses for baseline characteristics and clinical outcomes. A total of 2566 patients were included, 1952 (76%) had TAVR and the remaining 614 (24%) had isolated SAVR. Patients who underwent TAVR were older (82 vs 72 years,  $p < .001$ ), had more metastasis (19 vs 14%,  $p = .004$ ), heart failure (72% vs 34%,  $p < .001$ ), coronary artery disease (72% vs 52%,  $p < .001$ ), anemia (28% vs 22%,  $p = .006$ ), chronic lung (30% vs 22%,  $p < .001$ ) and renal disease (35% vs 14%,  $p < .001$ ), and shorter length of stay (3 vs 7 days,  $p < .001$ ). Results: In multivariate regression, TAVR and SAVR had similar in-patient mortality (HR = 1.08; 95%CI 0.61\_ 1.94) and 30-day readmission (HR = 1.26; 95%CI 0.95\_ 1.67). TAVR was associated with lower vascular complications (HR = 0.59; 95%CI 0.41\_ 0.86), acute deep venous thrombosis (HR = 0.25, 95%CI 0.1\_ 0.59), acute kidney injury (HR = 0.24, 95%CI 0.17\_ 0.33), blood transfusion (HR = 0.22, 95%CI 0.16\_ 0.3), cardiogenic shock (HR = 0.48, 95%CI 0.26\_ 0.89), and respiratory complications (HR = 0.26, 95%CI 0.2\_ 0.35). Conclusions: In patients with malignancy, TAVR is a viable and safe option compared to SAVR with better clinical outcomes, especially thromboembolic events.

Kalra A, Michos ED and **Chinnaiyan KM** (2020). "COVID-19 and the healthcare workers." European Heart Journal 41(31): 2936-2937.

[Full Text](#)

*Department of Internal Medicine*

Kant S, Kesarwani P, Guastella AR, Kumar P, **Graham SF**, Buelow KL, Nakano I and **Chinnaiyan P** (2020). "Perhexiline demonstrates FYN-mediated antitumor activity in glioblastoma." Molecular Cancer Therapeutics 19(7): 1415-1422.

[Full Text](#)

*Department of Obstetrics and Gynecology*

*Department of Radiation Oncology*

Glioblastoma is the most common primary malignant brain tumor in adults. Despite aggressive treatment, outcomes remain poor with few long-term survivors. Therefore, considerable effort is being made to identify novel therapies for this malignancy. Targeting tumor metabolism represents a promising therapeutic strategy and activation of fatty acid oxidation (FAO) has been identified as a central metabolic node contributing toward gliomagenesis. Perhexiline is a compound with a long clinical track record in angina treatment and commonly described as an FAO inhibitor. We therefore sought to determine whether this compound might be repurposed to serve as a novel therapy in glioblastoma. Perhexiline demonstrated potent in vitro cytotoxicity, induction of redox stress and apoptosis in a panel of glioblastoma cell lines. However, the antitumor activity of perhexiline was distinct when compared with the established FAO inhibitor etomoxir. By evaluating mitochondrial respiration and lipid dynamics in glioblastoma cells following treatment with perhexiline, we confirmed this compound did not inhibit FAO in our models. Using in silico approaches, we identified FYN as a probable target of perhexiline and validated the role of this protein in perhexiline sensitivity. We extended studies to patient samples, validating the potential of FYN to serve as therapeutic target in glioma. When evaluated in vivo, perhexiline demonstrated the capacity to cross the



blood-brain barrier and antitumor activity in both flank and orthotopic glioblastoma models. Collectively, we identified potent FYN-dependent antitumor activity of perhexiline in glioblastoma, thereby, representing a promising agent to be repurposed for the treatment of this devastating malignancy.

Kerwin M, Saado J, Pan J, Ailawadi G, Mazimba S, Salerno M and **Mehta N** (2020). "New-onset atrial fibrillation and outcomes following isolated coronary artery bypass surgery: A systematic review and meta-analysis." Clinical Cardiology 43(9): 928-934.

[Full Text](#)

*OUWB Medical Student Author*

Prior meta-analyses have shown that new-onset atrial fibrillation (NOAF) occurs in up to 40% of patients following cardiac surgery and is associated with substantial major adverse cardiovascular events. The stroke and mortality implications of NOAF in isolated CABG without concomitant valve surgery is not known. We thought that NOAF would be associated with increased risk of stroke and mortality, even in patients undergoing isolated CABG. A blinded review of studies from MEDLINE, CENTRAL, and Web of Science was done by two independent investigators. Stroke, 30-day/hospital mortality, long-term cardiovascular mortality, and long-term (>1 year) all-cause mortality were analyzed. We used Review Manager Version 5.3 to perform pooled analysis of outcomes. Of 4461 studies identified, 19 studies (n = 129 628) met inclusion criteria. NOAF incidence ranged from 15% to 36%. NOAF was associated with increased risk of stroke (unadjusted OR 2.15 [1.82, 2.53] [P < .00001]; adjusted OR 1.88 [1.02, 3.46] [P = .04]). NOAF was associated with increased 30-day/hospital mortality (OR 2.35 [1.67, 3.32] [P < .00001]) and long-term cardiovascular mortality (OR 2.04 [1.35, 3.09] [P = .0007]) NOAF was associated with increased long-term all-cause mortality (unadjusted OR 1.79 [1.63, 1.96] [P < .00001]; adjusted OR 1.58 [1.24, 2.00] [P = .0002]). We found that the incidence of NOAF following isolated CABG is high and is associated with increased stroke rate and mortality. Early recognition and management of NOAF could improve outcomes.

Klement RJ, Sonke JJ, Allgäuer M, Andratschke N, Appold S, Belderbos J, Belka C, Blanck O, Dieckmann K, Eich HT, Mantel F, Eble M, Hope A, Grosu AL, Nevinny-Stickel M, Semrau S, Sweeney RA, Hörner-Rieber J, Werner-Wasik M, Engenhardt-Cabillic R, Ye H, **Grills I** and Guckenberger M (2020). "Correlating dose variables with local tumor control in stereotactic body radiation therapy for early-stage non-small cell lung cancer: A modeling study on 1500 individual treatments." International Journal of Radiation Oncology Biology Physics 107(3): 579-586.

[Request Form](#)

*Department of Radiation Oncology*

Background: Large variation regarding prescription and dose inhomogeneity exists in stereotactic body radiation therapy (SBRT) for early-stage non-small cell lung cancer. The aim of this modeling study was to identify which dose metric correlates best with local tumor control probability to make recommendations regarding SBRT prescription. Methods and Materials: We combined 2 retrospective databases of patients with non-small cell lung cancer, yielding 1500 SBRT treatments for analysis. Three dose parameters were converted to biologically effective doses (BEDs): (1) the (near-minimum) dose prescribed to the planning target volume (PTV) periphery (yielding BEDmin); (2) the (near-maximum) dose absorbed by 1% of the PTV (yielding BEDmax); and (3) the average between near-minimum and near-maximum doses (yielding BEDave). These BED parameters were then correlated to the risk of local recurrence through Cox regression. Furthermore, BED-based prediction of local recurrence was attempted by logistic regression and fast and frugal trees. Models were compared using the Akaike information criterion. Results: There were 1500 treatments in 1434 patients; 117 tumors recurred locally. Actuarial local control rates at 12 and 36 months were 96.8% (95% confidence interval, 95.8%-97.8%) and 89.0% (87.0%-91.1%), respectively. In univariable Cox regression, BEDave was the best predictor of risk of local recurrence, and a model based on BEDmin had substantially less evidential support. In univariable logistic regression, the model based on BEDave also performed best. Multivariable classification using fast and frugal trees revealed BEDmax to be the most important predictor, followed by BEDave. Conclusions: BEDave was generally better correlated with tumor control probability than either BEDmax or BEDmin. Because the average between near-minimum and near-maximum doses was highly correlated to the mean gross tumor volume dose, the latter may be used as a prescription target. More emphasis could be placed on achieving sufficiently high mean doses within the gross tumor volume rather than the PTV covering dose, a concept needing further validation.

Kokkinos P, Kaminsky LA, Arena R, Zhang J, **Franklin B**, Kraus W, Triantafyllidi H, Benas D, Whellan DJ and Myers J (2020). "New equations for predicting maximum oxygen uptake in patients with heart failure." [American Journal of Cardiology](#) 128: 7-11.

[Full Text](#)

*Department of Internal Medicine*

We obtained directly measured maximal oxygen uptake (VO<sub>2</sub> max) by open-circuit spirometry in 1,453 patients with chronic heart failure (HF) who completed a treadmill test (n = 1,453) or cycle ergometry (n = 1,838), as participants in The Fitness Registry and the Importance of Exercise National Data Base (FRIEND) dataset. We developed a new equation to predict measured VO<sub>2</sub> max in those using a treadmill by randomly sampling 70% of the participants from each of the following age categories: <40, 40 to 50, 50 to 70, and >70 and used the remaining 30% for validation. Multivariable linear regression analysis was applied to identify the most relevant variables and construct the best prediction model for VO<sub>2</sub> max. Treadmill speed and treadmill speed \* grade were considered in the final model as predictors of measured VO<sub>2</sub> max and the following equation was generated: VO<sub>2</sub> max in ml O<sub>2</sub> kg/min = speed (m/min) \* (0.17 + fractional grade \* 0.32) + 3.5. To assess the efficacy of the equation, we applied it to 1,612 patients in the HF-ACTION cohort. To assess the efficacy of the FRIEND cycle ergometry equation developed for healthy individuals we applied it to 1,838 HF patients in the FRIEND cohort and 306 patients in a Greek population of HF patients with directly measured VO<sub>2</sub> max. The FRIEND equations were superior to ACSM equations in predicting VO<sub>2</sub> max regardless of the cohort or exercise mode used (treadmill or cycle ergometry) to access VO<sub>2</sub> max.

Kolderman NC, Cheti DR, Hasbrook CD, Forsyth AJ, Coffey MP, **Nair GB** and Al-Katib SA (2020). "Pneumothorax rate and diagnostic adequacy of computed tomography-guided lung nodule biopsies performed with 18 G versus 20 G needles: A cross-sectional study." [Journal of Thoracic Imaging](#) 35(4): 265-269.

[Full Text](#)

*Department of Internal Medicine*

Purpose: Conflicting data exist with regard to the effect of needle gauge on outcomes of computed tomography (CT)-guided lung nodule biopsies. The purpose of this study was to compare the complication and diagnostic adequacy rates between 2 needle sizes: 18 G and 20 G in CT-guided lung nodule biopsies. Materials and Methods: This retrospective cohort study examined CT-guided lung biopsies performed between March 2014 and August 2016 with a total of 550 patients between the ages of 30 and 94. Biopsies were performed using an 18-G or a 20-G needle. Procedure-associated pneumothorax and other complication rates were compared between the 2 groups. Univariate and multiple logistic regression analyses were performed. Results: There was no significant difference in pneumothorax rate between 18 G (n=125) versus 20 G (n=425) (rates: 25.6% vs. 28.7%; P=0.50; odds ratio [OR]=0.86; 95% confidence interval [CI]=0.54-1.35), chest tube insertion rate (4.8% vs. 5.6%; P=0.71; OR=0.84; 95% CI=0.34-2.11), or diagnostic adequacy (95% vs. 93%; P=0.36; OR=1.51; 95% CI=0.61-3.72). Multiple logistic regression analysis demonstrated emphysema along the biopsy path (OR=3.12; 95% CI=1.63-5.98) and nodule distance from the pleural surface ≥4 cm (OR=1.85; 95% CI=1.05-3.28) to be independent risk factors for pneumothorax. Conclusion: No statistically significant difference in pneumothorax rate or diagnostic adequacy was found between 18-G versus 20-G core biopsy needles. Independent risk factors for pneumothorax include emphysema along the biopsy path and nodule distance from the pleural surface.

Kumar M, Sebai ME, Appleford C and **Dekhne N** (2020). "Myxoma in the axilla of a patient with a history of inflammatory breast cancer." [Breast Journal](#) 26(7): 1400-1401.

[Full Text](#)

*Department of Surgery*

Laucis AM, Jagsi R, Griffith KA, Dominello MM, Walker EM, Abu-Isa EI, **Dilworth JT**, Vicini F, Kocheril PG, Browne CH, Mietzel MA, Moran JM, Hayman JA, Pierce LJ and Michigan Radiation Oncology Quality C (2020). "The role of facility variation on racial disparities in use of hypofractionated whole breast radiation therapy." [International Journal of Radiation Oncology Biology Physics](#) 107(5): 949-958.

[Full Text](#)

*Department of Radiation Oncology*

Purpose: Hypofractionated radiation therapy is a less burdensome and less costly approach that is

efficacious for most patients with early-stage breast cancer. Concerns about racial disparities in adoption of medical advances motivate investigation of the use of hypofractionated radiation in diverse populations. The goal of our study was to determine whether hypofractionated whole breast radiation therapy after breast-conserving surgery was being similarly used across racial groups in the state of Michigan. **Methods and Materials:** A prospectively collected statewide quality consortium database from 25 institutions was queried for patients with breast cancer who completed hypofractionated (HF) or conventionally fractionated whole breast radiation therapy from January 2012 to December 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 9634 patients analyzed, 81% self-reported race as white, 17% as black, and 2% as Asian, similar to statewide and national distributions. In addition, 31.7% of whites were treated at teaching centers compared with 66.7% of blacks and 64.8% of Asians. In 2018, HF was used in 72.7% of whites versus 56.7% of blacks and 67.6% of Asians ( $P = .0411$ ). On patient-level multivariable analysis, black and Asian races were significantly associated with a lower likelihood of HF receipt ( $P < .001$ ), despite accounting for treatment year, age, laterality, body mass index, breast volume, comorbidities, stage, triple-negative status, intensity modulated radiation therapy use, teaching center treatment, and 2011 American Society for Radiation Oncology 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 whole breast radiation therapy less often than whites, despite more frequent treatment at teaching centers. Multilevel modeling eliminated this disparity, suggesting that differences in facility-specific HF use appear to have contributed. Further inquiry is needed to determine whether reduction of facility-level variation may reduce disparities in accessing HF treatment.

Lee SE, Sung JM, Andreini D, Al-Mallah MH, Budoff MJ, Cademartiri F, **Chinnaiyan K**, Choi JH, Chun EJ, Conte E, Gottlieb I, Hadamitzky M, Kim YJ, Lee BK, Leipsic JA, Maffei E, Marques H, de Araújo Gonçalves P, Pontone G, Shin S, Stone PH, Samady H, Virmani R, Narula J, Berman DS, Shaw LJ, Bax JJ, Lin FY, Min JK and Chang HJ (2020). "Per-lesion versus per-patient analysis of coronary artery disease in predicting the development of obstructive lesions: the Progression of Atherosclerotic Plaque Determined by Computed Tomographic Angiography Imaging (PARADIGM) study." *International Journal of Cardiovascular Imaging*. ePub Ahead of Print.

[Full Text](#)

*Department of Internal Medicine*

To determine whether the assessment of individual plaques is superior in predicting the progression to obstructive coronary artery disease (CAD) on serial coronary computed tomography angiography (CCTA) than per-patient assessment. From a multinational registry of 2252 patients who underwent serial CCTA at a  $\geq 2$ -year inter-scan interval, patients with only non-obstructive lesions at baseline were enrolled. CCTA was quantitatively analyzed at both the per-patient and per-lesion level. Models predicting the development of an obstructive lesion at follow up using either the per-patient or per-lesion level CCTA measures were constructed and compared. From 1297 patients (mean age  $60 \pm 9$  years, 43% men) enrolled, a total of 3218 non-obstructive lesions were identified at baseline. At follow-up (inter-scan interval:  $3.8 \pm 1.6$  years), 76 lesions (2.4%, 60 patients) became obstructive, defined as  $> 50\%$  diameter stenosis. The C-statistics of Model 1, adjusted only by clinical risk factors, was 0.684. The addition of per-patient level total plaque volume (PV) and the presence of high-risk plaque (HRP) features to Model 1 improved the C-statistics to 0.825 [95% confidence interval (CI) 0.823-0.827]. When per-lesion level PV and the presence of HRP were added to Model 1, the predictive value of the model improved the C-statistics to 0.895 [95% CI 0.893-0.897]. The model utilizing per-lesion level CCTA measures was superior to the model utilizing per-patient level CCTA measures in predicting the development of an obstructive lesion ( $p < 0.001$ ). Lesion-level analysis of coronary atherosclerotic plaques with CCTA yielded better predictive power for the development of obstructive CAD than the simple quantification of total coronary atherosclerotic burden at a per-patient level. Clinical Trial Registration: ClinicalTrials.gov NCT0280341.

**Lerchenfeldt S, Kamel-ElSayed S, Patino G, Thomas DM and Wagner J** (2020). "Suicide assessment and management team-based learning module." *MedEdPORTAL* 16: 10952.

[Full Text](#)

*Department of Foundational Medical Studies (OU)*

### *Department of Psychiatry*

Introduction: Suicide is a global health problem that health care providers must feel comfortable addressing. Unfortunately, many health care providers are not equipped to assess and treat patients at risk for suicide due to lack of training and education. Interactive resources are needed to educate health professions students about the management of suicidal patients. Methods: The suicide assessment and management team-based learning (TBL) module was developed to address the gap in suicide education. After completing the module, students were able to identify key elements for a comprehensive assessment of a patient's risk for suicide and to discuss clinical management for a suicidal patient. The activity was designed for second-year medical students during a psychopathology course, the last organ-system course prior to clerkships. This module could also be used or modified to meet the educational requirements for other health professions, including medical residents, nurse practitioner students, and physician assistant students. Results: A total of 342 students among 62 teams participated in the TBL over a period of 3 consecutive years. The class averages for the individual Readiness Assurance Test ranged from 80% to 88%. The class averages for the team Readiness Assurance Test and application questions were comparable across all 3 years. Course evaluations showed the TBL helped students think critically and integrate information to prepare them for their future careers. Discussion: Overall, this TBL was an effective educational tool that stimulated high-quality discussion, in which students remained engaged and asked thought-provoking questions.

Li G, **Dietz CJK**, Freundlich RE, Shotwell MS and Wanderer JP (2020). "The impact of an intraoperative clinical decision support tool to optimize perioperative glycemic management." *Journal of Medical Systems* 44(10): 175.

[Full Text](#)

### *OUWB Medical Student Author*

With the transition from Vanderbilt's Perioperative Information Management System (VPIMS) to Epic's Best Practice Advisory (BPA) framework, a replacement intraoperative glucose clinical decision support (CDS) system was designed. We examined changes in the frequency of intraoperative glucose monitoring, hyper- and hypoglycemia rates in the post-anesthesia care unit (PACU), to determine the impact of the changes on glucose management. Data were collected into three phases: 1) VPIMS CDS, 2) No CDS, and 3) BPA CDS. One-way ANOVA was conducted to test the significance of changes in the frequency of glucose monitoring and abnormal glucose across phases. Interrupted time series segmented analysis was performed to assess the autocorrelation and trend over times. A total of 3706 cases were analyzed. The monitoring rate fell from 84.5% in VPIMS CDS to 67.6% in No CDS ( $p < .001$ ) and increased to 83.1% in BPA CDS ( $p < .001$ ). The PACU hyperglycemia rate increased from VPIMS CDS to No CDS (5.2% to 10.4%,  $p < .001$ ) and decreased from No CDS to BPA CDS (10.4% to 7.2%,  $p = 0.031$ ). The segmented analysis demonstrated immediate changes in the intraoperative monitoring frequency ( $p < .001$ ) and postoperative hyperglycemia rate ( $p = 0.002$ ) with the replacement of CDS. The temporary removal of CDS was associated with a significant reduction in intraoperative glucose monitoring and increased hyperglycemia in the PACU. Implementation of the BPA CDS led to a significant improvement in the intraoperative glucose monitoring and glucose management in the PACU.

Lombardo DJ, Siljander MP, Sobh A, **Moore DD** and **Karadsheh MS** (2020). "Periprosthetic fractures about total knee arthroplasty." *Musculoskeletal Surgery* 104(2): 135-143.

[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 DM, Gbadamosi B, **Jaiyesimi I** and **Gaikazian S** (2020). "Medical cannabis in cancer patients: A survey of a community hematology oncology population." *American Journal of Clinical Oncology* 43(9): 636-639.

[Full Text](#)

*Department of Internal Medicine*

Objectives: Cancer patients are using medical cannabis (MC) to address symptoms; however, little data exist to guide clinicians when counseling patients. We seek to define the patterns of MC use among cancer patients, as well as efficacy and safety of MC. Materials and Methods: Cancer patients attending oncology office visits at Beaumont Hospital, Michigan from July to December 2018 were anonymously surveyed. The survey included data regarding demographics, diagnosis, treatment, symptom burden, and MC use. Patients who reported MC use since their cancer diagnosis completed a section on patterns of use, efficacy, and safety. Results: The response rate was 188 of 327 (57.5%). MC use was reported by 46 of 188 (24.5%). A median composite baseline symptom score ranging from 8 (best) to 32 (worst) was higher in patients using MC versus nonusers; 17.5 versus 14.4 ( $P < 0.001$ ). Pain was the symptom with the highest frequency of improvement 34/42 (81%), followed by appetite 34/44 (77.3%), and anxiety 32/44 (73%). MC improved the ability to tolerate treatment in 24/44 (54.5%). Cloudy thinking is the symptom that worsened the most 7/42 (16.7%), with decreased energy being experienced by 4/41 (9.8%) of the users. Conclusions: MC was utilized by a significant portion of cancer patients in this sample, across age, diagnosis, stage, and treatment. Patients with a higher severity of baseline symptoms were more likely to use MC and report a favorable efficacy profile of MC. Minimal toxicity was reported in this cohort. Prospective studies are needed to define the efficacy and safety of MC.

Macias Gil R, Marcelin JR, Zuniga-Blanco B, Marquez C, **Mathew T** and Piggott DA (2020). "COVID-19 pandemic: Disparate health impact on the Hispanic/Latinx population in the United States." Journal of Infectious Diseases. ePub Ahead of Print.

[Full Text](#)

*Department of Internal Medicine*

In December 2019, a novel coronavirus known as SARS-CoV-2, emerged in Wuhan, China, causing the Coronavirus disease 2019 we now refer to as COVID-19. The World Health Organization declared COVID-19 a pandemic on March 12th, 2020. In the United States, the COVID-19 pandemic has exposed pre-existing social and health disparities among several historically vulnerable populations, with stark differences in the proportion of minority individuals diagnosed with and dying from COVID-19. In this article we will describe the emerging disproportionate impact of COVID-19 on the Hispanic/Latinx (henceforth: Hispanic or Latinx) community in the U.S., discuss potential antecedents and consider strategies to address the disparate impact of COVID-19 on this population.

Macor S, Pignatto S, **Capone A, Jr.**, Piermarocchi S and Lanzetta P (2020). "Lens-sparing vitrectomy for stage 4A retinopathy of prematurity in infants with aggressive-posterior ROP: Anatomic and functional results." European Journal of Ophthalmology: 1120672120946938.

[Request Form](#)

*Department of Ophthalmology*

Aim: To assess long-term anatomic and functional outcomes of early lens-sparing vitrectomy (LSV) for stage 4A retinopathy of prematurity (ROP) in infants with aggressive-posterior ROP (AP-ROP) which progressed to retinal detachment despite laser treatment. Methods: Chart review of infants who underwent early 25-gauge LSV for stage 4A ROP. Outcomes were anatomic success, mean visual acuity (VA), development of postoperative complications, and refractive changes. Follow-up examinations were performed at 1, 3, 6, 12, and then every 6 months. Results: Ten eyes of seven preterm infants who underwent LSV were included. Mean follow-up was  $36 \pm 13.4$  months and mean postmenstrual age (PMA) at last follow-up was  $37 \pm 13.7$  months. Mean gestational age (GA) and weight at birth was  $26 \pm 1.4$  weeks and  $639 \pm 180$  g. Two eyes had vitreous hemorrhage 4 and 14 days after surgery, respectively. At last follow-up anatomic success was 100%, mean VA was 20/80 and eight eyes (80%) had high myopic refractive correction (mean spherical equivalent  $-11.25$  D). Conclusion: Early LSV for stage 4A ROP with AP-ROP and progression to retinal detachment is efficacious in terms of anatomic and functional outcomes. Anatomic success is associated with visual improvement despite possible myopic refraction changes during follow-up.

**Mankuzhy NP**, Almahariq MF, Siddiqui ZA, **Thompson AB**, **Grills IS**, **Guerrero TM**, **Lee KC**, **Stevens CW** and Quinn TJ (2020). "The role of postoperative radiation therapy for pN2 non-small-cell lung cancer." Clinical Lung Cancer. ePub Ahead of Print.



[Full Text](#)

*Department of Radiation Oncology*

*OUWB Medical Student Author*

Background: The role for postoperative radiation therapy (PORT) for patients with non-small-cell lung cancer (NSCLC) with mediastinal lymph node (LN) involvement (pN2 disease) is controversial. We compared surgery alone with PORT among patients with pN2 NSCLC. We then performed subset analyses to better delineate patients that might benefit from PORT. Patients and Methods: We conducted a propensity score (PS)-matched, inverse probability of treatment weighting (IPTW) Surveillance, Epidemiology, and End Results (SEER) analysis of patients with pN2 disease from 1989 to 2016 with surgery alone or PORT. Multiple imputation with chained equations was used for missing LN data. Results: A total of 8631 patients were included in this analysis; 4579 underwent surgery alone, and 4052 underwent PORT. Following PS matching and IPTW, there was no difference in overall survival (OS) (hazard ratio [HR], 0.99; P = .76). However, PORT improved OS among a subset of patients with a LN positive to sampled ratio  $\geq 50\%$  (HR, 0.90; P = .01). Moreover, there was a trend towards improved OS among this subset, even with chemotherapy (HR, 0.91; P = .09). Conclusion: PORT is not associated with an improvement or detriment in OS for all patients with pN2 NSCLC. However, patients with a positive to sampled LN ratio  $\geq 50\%$  may benefit, regardless of chemotherapy status. Nevertheless, PORT will remain the standard of care as we await the results of the ongoing LUNG ART trial.

Marlow ED, **Faia LJ**, **Wu D**, Farley N and **Randhawa S** (2020). "Paraneoplastic ocular sarcoidosis in the setting of recurrent rectal carcinoid tumor diagnosed by F(18)-fluorodeoxyglucose PET CT." *American Journal of Ophthalmology Case Reports* 20: 100887.

[Full Text](#)

*Department of Ophthalmology*

*Department of Diagnostic Radiology and Molecular Imaging*

Purpose: Nuclear medicine imaging can provide a noninvasive means of distinguishing inflammatory mass lesions from oncologic intraocular tumors. Observation: We report a case of paraneoplastic ocular sarcoidosis with choroidal mass lesions that was initially concerning for choroidal metastasis of a primary carcinoid tumor. PET CT was utilized with two different tracers to characterize the choroidal mass as being FDG-avid, consistent with a sarcoid-like lesion, and lacking the Gallium (Ga-68) DOTATATE uptake of carcinoid tumor metastases. Conclusions and Importance: Functional imaging is valuable to distinguish clinically similar inflammatory versus oncologic intraocular pathology.

Masuda E, Ozsvath K, Vossler J, Woo K, Kistner R, Lurie F, Monahan D, **Brown W**, Labropoulos N, Dalsing M, Khilnani N, Wakefield T and Gloviczki P (2020). "The 2020 appropriate use criteria for chronic lower extremity venous disease of the American Venous Forum, the Society for Vascular Surgery, the American Vein and Lymphatic Society, and the Society of Interventional Radiology." *Journal of Vascular Surgery-Venous and Lymphatic Disorders* 8(4): 505-+.

[Full Text](#)

*Department of Surgery*

Background: Stimulated by published reports of potentially inappropriate application of venous procedures, the American Venous Forum and its Ethics Task Force in collaboration with multiple other professional societies including the Society for Vascular Surgery (SVS), American Vein and Lymphatic Society (AVLS), and the Society of Interventional Radiology (SIR) developed the appropriate use criteria (AUC) for chronic lower extremity venous disease to provide clarity to the application of venous procedures, duplex ultrasound imaging, timing, and reimbursements. Methods: The AUC were developed using the RAND/UCLA Appropriateness Method, a validated method of developing appropriateness criteria in health care. By conducting a modified Delphi exercise and incorporating best available evidence and expert opinion, AUC were developed and scored. Results: There were 119 scenarios rated on a scale of 1 to 9 by an expert panel, with 1 being never appropriate and 9 being appropriate. The majority of scenarios consisted of symptomatic indications were deemed appropriate for venous intervention. For scenarios with anatomically short segments of reflux and/or symptoms, the indications were rated less appropriate. For the indication of edema, a wide dispersion of ratings was observed especially for short segments of saphenous reflux or stenting for iliac/inferior vena cava disease, noting that there are multifactorial causes of edema, some of which could coexist with venous disease and possibly impact effectiveness of treatment. Several scenarios



were considered never appropriate, including treatment of saphenous veins with no reflux, iliac vein or inferior vena cava stenting for iliac vein compression as an incidental finding by imaging with minimal or no symptoms or signs, and incentivizing sonographers to find reflux. Conclusions: The AUC statements are intended to serve as a guide to patient care, particularly in areas where high-quality evidence is lacking to aid clinicians in making day-to-day decisions for common venous interventions. This may also prove useful when applied on a population level, such as practice patterns, and not necessarily to dictate decision making for individual cases. As a product of a collaborative effort, it is hoped that this could be utilized by physicians and multiple stakeholders committed toward improving patient care and to identify and stimulate future research priorities.

Mein C, Dugel PU, Feiner L, **Drenser K**, Miller D, Benz M, Meunier E, Moro L and Fineman MS (2020). "Patient-reported visual function from the ocriplasmin for treatment for symptomatic vitreomacular adhesion, including macular hole (OASIS) study." *Retina* 40(7): 1331-1338.

[Full Text](#)

*Department of Ophthalmology*

Purpose: To evaluate patient-reported visual function after ocriplasmin through the 25-item National Eye Institute Visual Function Questionnaire (VFQ-25) in patients with symptomatic vitreomacular adhesion/vitreomacular traction including macular hole. Methods: This was a prespecified analysis of a secondary endpoint from the OASIS trial. Patients received a single intravitreal injection of ocriplasmin (0.125 mg) or sham and completed the VFQ-25 questionnaire at baseline and at Months 6, 12, and 24. Clinically meaningful ( $\geq 5$ -point) changes from baseline were assessed. Results: Of the 220 patients enrolled, 146 received ocriplasmin and 74 received sham. At Month 24, the percentage of patients with a  $\geq 5$ -point improvement from baseline in VFQ-25 composite scores was higher with ocriplasmin versus sham (51.4% vs. 30.1%, 95% confidence interval, 8.1-34.5,  $P = 0.003$ ). The percentage of patients with  $\geq 5$ -point worsening at Month 24 was lower with ocriplasmin versus sham (9.5% vs. 15.6%, 95% confidence interval: -15.6 to 3.5,  $P = 0.191$ ). A larger percentage of patients treated with ocriplasmin versus sham experienced a  $\geq 5$ -point improvement in VFQ-25 composite and subscale scores at Month 24 regardless of baseline full-thickness macular hole status. Conclusion: A larger percentage of patients with symptomatic vitreomacular adhesion/vitreomacular traction reported clinically meaningful improvements in self-assessed visual function with ocriplasmin than sham.

Mohammed N, Hung YC, Chen CJ, Xu Z, Schlesinger D, Kano H, Chiang V, Hess J, Lee J, Mathieu D, Kaufmann AM, **Grills IS**, Cifarelli CP, Vargo JA, Chytka T, Janouskova L, Feliciano CE, Mercado RR, Lunsford LD and Sheehan JP (2020). "A proposed grading scale for predicting outcomes after stereotactic radiosurgery for dural arteriovenous fistulas." *Neurosurgery* 87(2): 247-255.

[Full Text](#)

*Department of Radiation Oncology*

Background: There are presently no grading scales that specifically address the outcomes of cranial dural arteriovenous fistula (dAVF) after stereotactic radiosurgery (SRS). Objective: To design a practical grading system that would predict outcomes after SRS for cranial dAVFs. Methods: From the International Radiosurgery Research Foundation (University of Pittsburgh [41 patients], University of Pennsylvania [6 patients], University of Sherbrooke [2 patients], University of Manitoba [1 patient], West Virginia University [2 patients], University of Puerto Rico [1 patient], Beaumont Health System 1 [patient], Na Homolce Hospital [13 patients], the University of Virginia [48 patients], and Yale University [6 patients]) centers, 120 patients with dAVF treated with SRS were included in the study. The factors predicting favorable outcome (obliteration without post-SRS hemorrhage) after SRS were assessed using logistic regression analysis. These factors were pooled with the factors that were found to be predictive of obliteration from 7 studies with 736 patients after a systematic review of literature. These were entered into stepwise multiple regression and the best-fit model was identified. Results: Based on the predictive model, 3 factors emerged to develop an SRS scoring system: cortical venous reflux (CVR), prior intracerebral hemorrhage (ICH), and noncavernous sinus location. Class I (score of 0-1 points) predicted the best favorable outcome of 80%. Class II patients (2 points score) had an intermediate favorable outcome of 57%, and class III (score 3 points) had the least favorable outcome at 37%. The ROC analysis showed better predictability to prevailing grading systems (AUC = 0.69;  $P = .04$ ). Kaplan-Meier analysis showed statistically significant difference between the 3 subclasses of the proposed

grading system for post-SRS dAVF obliteration (P = .001). Conclusion: The proposed dAVF grading system incorporates angiographic, anatomic, and clinical parameters and improves the prediction of the outcomes following SRS for dAVF as compared to the existing scoring systems. Copyright

Moskowitz A, Andersen LW, Rittenberger JC, **Swor R**, Seethala RR, Kurz MC, Berg KM, Chase M, Cocchi MN, Grossestreuer AV, Liu X, Holmberg MJ, Callaway CW and Donnino MW (2020). "Continuous neuromuscular blockade following successful resuscitation from cardiac arrest: A randomized trial." Journal of the American Heart Association: e017171.

[Full Text](#)

*Department of Emergency Medicine*

Background: Neuromuscular blockade (NMB) agents are often administered to control shivering during targeted temperature management following cardiac arrest. In this study, we hypothesized that early, continuous NMB would result in a greater reduction in serum lactate levels among comatose patients after cardiac arrest. Methods and Results: Randomized trial of continuous NMB for 24 hours versus usual care following cardiac arrest conducted at 5 urban centers in the United States. Adult patients who achieved return of spontaneous circulation, remained unresponsive, and underwent targeted temperature management after cardiac arrest were included. The primary outcome was change in lactate over 24 hours. A total of 83 patients were randomized, and 80 were analyzed (37 and 43 in the NMB and usual care arms, respectively). There was no significant interaction between time and treatment group with respect to change in lactate over 24 hours (median lactate change from 4.2 to 2.0 mmol/L [-2.2 mmol/L] in the NMB arm versus 4.0 to 1.7 mmol/L [-2.3 mmol/L] in the usual care arm; geometric mean difference, 1.3 [95% CI, 1.0-1.8]; P=0.07 for the interaction term). There was no difference in hospital survival (38% [NMB] versus 33% [usual care]; P=0.63) or survival with good functional outcome (30% [NMB] versus 21% [usual care]; P=0.35). There were no adverse events in either arm attributed to study interventions. Conclusions: Continuous NMB compared with usual care did not reduce lactate over the first 24 hours after enrollment compared with usual care. There was no difference in overall hospital survival, hospital survival with good neurologic outcome, or adverse events.

Moskowitz A, Huang DT, Hou PC, Gong J, Doshi PB, Grossestreuer AV, Andersen LW, Ngo L, Sherwin RL, Berg KM, Chase M, Cocchi MN, McCannon JB, Hershey M, Hilewitz A, Korotun M, Becker LB, **Otero RM**, Uduman J and Sen A (2020). "Effect of ascorbic acid, corticosteroids, and thiamine on organ injury in septic shock: The ACTS randomized clinical trial." JAMA 324(7): 642-650.

[Full Text](#)

*Department of Emergency Medicine*

Importance: The combination of ascorbic acid, corticosteroids, and thiamine has been identified as a potential therapy for septic shock. Objective: To determine whether the combination of ascorbic acid, corticosteroids, and thiamine attenuates organ injury in patients with septic shock. Design, Setting, and Participants: Randomized, blinded, multicenter clinical trial of ascorbic acid, corticosteroids, and thiamine vs placebo for adult patients with septic shock. Two hundred five patients were enrolled between February 9, 2018, and October 27, 2019, at 14 centers in the United States. Follow-up continued until November 26, 2019. Interventions: Patients were randomly assigned to receive parenteral ascorbic acid (1500 mg), hydrocortisone (50 mg), and thiamine (100 mg) every 6 hours for 4 days (n = 103) or placebo in matching volumes at the same time points (n = 102). Main Outcomes and Measures: The primary outcome was change in the Sequential Organ Failure Assessment (SOFA) score (range, 0-24; 0 = best) between enrollment and 72 hours. Key secondary outcomes included kidney failure and 30-day mortality. Patients who received at least 1 dose of study drug were included in analyses. Results: Among 205 randomized patients (mean age, 68 [SD, 15] years; 90 [44%] women), 200 (98%) received at least 1 dose of study drug, completed the trial, and were included in the analyses (101 with intervention and 99 with placebo group). Overall, there was no statistically significant interaction between time and treatment group with regard to SOFA score over the 72 hours after enrollment (mean SOFA score change from 9.1 to 4.4 [-4.7] points with intervention vs 9.2 to 5.1 [-4.1] points with placebo; adjusted mean difference, -0.8; 95% CI, -1.7 to 0.2; P = .12 for interaction). There was no statistically significant difference in the incidence of kidney failure (31.7% with intervention vs 27.3% with placebo; adjusted risk difference, 0.03; 95% CI, -0.1 to 0.2; P = .58) or in 30-day mortality (34.7% vs 29.3%, respectively; hazard ratio, 1.3; 95% CI, 0.8-2.2; P = .26). The most common serious adverse events were

hyperglycemia (12 patients with intervention and 7 patients with placebo), hyponatremia (11 and 7 patients, respectively), and new hospital-acquired infection (13 and 12 patients, respectively). Conclusions and Relevance: In patients with septic shock, the combination of ascorbic acid, corticosteroids, and thiamine, compared with placebo, did not result in a statistically significant reduction in SOFA score during the first 72 hours after enrollment. These data do not support routine use of this combination therapy for patients with septic shock. Trial Registration: ClinicalTrials.gov Identifier: NCT03389555.

**Nair GB** and Niederman MS (2020). "Updates on community acquired pneumonia management in the ICU." *Pharmacology & Therapeutics*: 107663.

[Full Text](#)

*Department of Internal Medicine*

While the world is grappling with the consequences of a global pandemic related to SARS-CoV-2 causing severe pneumonia, available evidence points to bacterial infection with *Streptococcus pneumoniae* as the most common cause of severe community acquired pneumonia (SCAP). Rapid diagnostics and molecular testing have improved the identification of co-existent pathogens. However, mortality in patients admitted to ICU remains staggeringly high. The American Thoracic Society and Infectious Diseases Society of America have updated CAP guidelines to help streamline disease management. The common theme is use of timely, appropriate and adequate antibiotic coverage to decrease mortality and avoid drug resistance. Novel antibiotics have been studied for CAP and extend the choice of therapy, particularly for those who are intolerant of, or not responding to standard treatment, including those who harbor drug resistant pathogens. In this review, we focus on the risk factors, microbiology, site of care decisions and treatment of patients with SCAP.

Narla S, **Oska S**, Lyons AB, Lim HW and Hamzavi IH (2020). "Association of myalgias with compounded topical Janus kinase inhibitor use in vitiligo." *JAAD Case Reports* 6(7): 637-639.

[Full Text](#)

*OUWB Medical Student Author*

**Nguyen A**, Patel AA, Chandra V and Nazerali RS (2020). "Ultrasound guided liposuction for superficialization of difficult to access arteriovenous fistulas." *Journal of Plastic Reconstructive & Aesthetic Surgery*. ePub Ahead of Print.

[Request Form](#)

*OUWB Medical Student Author*

**Omar H, Yue R, Amen A**, Kowalenko T and **Walters BL** (2020). "Reassessment of violence toward emergency medicine physicians in Michigan." *American Journal of Emergency Medicine* 38(8): 1582-1583.

[Full Text](#)

*Department of Emergency Medicine*

*OUWB Medical Student Author*

**Oska S**, Zarbo A, Yeager D, Friedman BJ and Shwayder T (2020). "Melanoma arising in a patient with ataxia-telangiectasia: A call for full skin examinations in this patient population." *Pediatric Dermatology* 37(4): 767-768.

[Full Text](#)

*OUWB Medical Student Author*

Ataxia-telangiectasia (A-T) is an autosomal recessive, multisystem disorder characterized by cerebellar ataxia and oculocutaneous telangiectasias that present in early childhood. Increased incidence of malignancy is also associated with A-T. Hematopoietic malignancies occur most commonly, with a majority being lymphoid cancers; however, there is a risk for other malignancies, such as breast, gastric, and other solid tumors. Herein, we report the case of a 28-year-old woman with A-T with melanoma.

Pamplona MDC and **Ysunza PA** (2020). "Speech pathology telepractice for children with cleft palate in the times of COVID-19 pandemic." *International Journal of Pediatric Otorhinolaryngology* 138: 110318.

[Full Text](#)

*Department of Physical Medicine & Rehabilitation*

Objective: To study whether providing Speech and Language Pathology (SLP) interventions by telepractice

(TP) could effectively improve speech performance in children with cleft palate (CCP). Methods: Forty-three CCP were treated with TP intervention in 45 min sessions, 2 times per week for a period of one month. Children ages ranged 4-12 years ( $X = 7.04$ ;  $SD = 2.59$ ). All children presented with velopharyngeal insufficiency (VPI) and compensatory articulation (CA) after palatal repair. TP was provided in small groups (5-6 children) following the principles of the Whole Language Model (WLM). Severity of CA was evaluated by a standardized scale at the onset and at the end of the TP period. Results: At the onset of the TP intervention period, 84% of the patients demonstrated severe CA. At the end of the TP period there was a significant improvement in severity of CA ( $p < 0.001$ ). Conclusion: The results of this study suggests that TP can be a safe and reliable tool for improving CA. Considering that the COVID-19 pandemic will radically modify the delivery of Health Care services in the long term, alternate modes of service delivery should be studied and implemented.

Pandey AS, Daou BJ, Tsai JP, Zaidi SF, Salahuddin H, Gemmete JJ, Oliver MJ, Singer J, Elder TA, Mbabuike N, Adel JG, Gujrati Y, Saleemi MA, Siddiqui FM, Elias AE, Rehman MF, Marin H, Chebl AB, Kole M, **Wilseck JM, Kazmierczak CD, Mick JM**, Majhoo AQ, Naravetla BR, Rayes M, Luqman AW, Richards BF, Kelkar P, Burgess R, Thompson BG, Chaudhary N, Mazaris PA, Qahwash O, Razak MA, Jumaa MA and Michigan Stroke Treatment Improvement C (2020). "Letter: COVID-19 pandemic-The bystander effect on stroke care in Michigan." *Neurosurgery* 87(3): E397-E399.

[Full Text](#)

*Department of Diagnostic Radiology and Molecular Imaging*

**Partiali B, Oska S, Barbat A**, Sneij J and **Folbe A** (2020). "Injuries to the head and face from skateboarding: A 10-Year analysis from National Electronic Injury Surveillance System hospitals." *Journal of Oral & Maxillofacial Surgery* 78(9): 1590-1594.

[Full Text](#)

*Department of Surgery*

*OUIWB Medical Student Author*

Purpose: To estimate the incidence of patients presenting to emergency departments (EDs) as a result of facial trauma sustained from skateboarding. Patients and Methods: The National Electronic Injury Surveillance System (NEISS) database was queried for skateboard-related head and face fractures, contusions, abrasions, and lacerations from 2009 through 2018. We identified 2,519 reported injuries, extrapolating to a national incidence of 100,201 injuries. Fractures accounted for 14.1% of these visits. There were 355 ED visits for fractures, extrapolating to an estimated 11,893 visits nationally. Entries were tabulated for demographic information, fracture type, mechanism of injury, and disposition. Results: Patients sustaining injury to the head and face were aged 16 years, on average, and predominantly male patients (85.9%). Most patients sustaining fractures were male patients (87.9%), with a mean age of 18 years. The most common fracture types included unspecified skull fractures (31%), nasal fractures (29%), and mandibular fractures (18%). The most common mechanism of injury was falling off the skateboard while riding (76.9%). Collisions with motor vehicles also accounted for a substantial proportion of the injuries (7.3%). Conclusions: A substantial number of ED visits were a result of skateboarding-related facial trauma. Given the neurologic outcomes of head trauma and functional consequences of facial fractures, especially among adolescents, our findings suggest that injury prevention programs and more aggressive helmet use may be necessary to reduce morbidity and hospitalization.

Patek P, Corcoran J, **Adams L** and **Khandhar P** (2020). "SARS-CoV-2 infection in a 2-week-old male with neutropenia." *Clinical Pediatrics* 59(9-10): 918-920.

[Full Text](#)

*Department of Pediatrics*

*Department of Emergency Medicine*

Patel SN, Starr MR, Obeid A, Ryan EH, Ryan C, Forbes NJ, Soares RR, Ammar M, Patel LG, **Capone A, Jr.**, Emerson GG, Joseph DP, Elliott D, Regillo CD, Gupta OP, Hsu J and Yonekawa Y (2020). "Characteristics and surgical outcomes of rhegmatogenous retinal detachment in older adults: A multicenter comparative cohort study." *Retina*. ePub Ahead of Print.

[Full Text](#)

#### *Department of Ophthalmology*

Purpose: To describe characteristics and outcomes of primary rhegmatogenous retinal detachment (RRD) in older adults (age  $\geq 80$ ). Methods: Consecutive patients with RRD undergoing pars plana vitrectomy (PPV), scleral buckling (SB), or PPV/SB in the Primary Retinal Detachment Outcomes Study were evaluated. Outcome measures included single surgery anatomic success (SSAS) and visual acuity (VA). Results: Of 2144 patients included, 125 (6%) were 80 years or older. Compared to younger patients (age 40-79), older adults were more likely to be pseudophakic ( $P < .001$ ), have macula-off detachments ( $P < .001$ ), and have pre-operative proliferative vitreoretinopathy ( $P = .02$ ). In older adults, initial surgery was PPV in 73%, PPV/SB in 27%, and primary SB in 0%. SSAS was 78% in older adults compared to 84% in younger patients ( $P = .03$ ). In older adults, SSAS was 74% for PPV and 91% for PPV/SB ( $P = .03$ ). Final mean logMAR was lower for older adults (0.79 [20/125] vs 0.40 [20/40], [ $P < .001$ ]). In older adults, final mean logMAR for eyes that underwent PPV was 0.88 (20/160) compared to 0.50 (20/63) for PPV/SB ( $P = .03$ ). Conclusion: Octogenarians and nonagenarians presented with relatively complex pseudophakic RRDs. SSAS and visual outcomes were worse compared to younger patients, and PPV/SB had better outcomes compared to PPV alone.

Porter E, **Fuentes P**, Siddiqui Z, Thompson A, Levitin R, Solis D, Myziuk N and **Guerrero T** (2020). "Hippocampus segmentation on noncontrast CT using deep learning." *Medical Physics* 47(7): 2950-2961.

[Full Text](#)

#### *Department of Radiation Oncology*

*OUWB Medical Student Author*

Purpose: Accurate segmentation of the hippocampus for hippocampal avoidance whole-brain radiotherapy currently requires high-resolution magnetic resonance imaging (MRI) in addition to neuroanatomic expertise for manual segmentation. Removing the need for MR images to identify the hippocampus would reduce planning complexity, the need for a treatment planning MR imaging session, potential uncertainties associated with MRI-computed tomography (CT) image registration, and cost. Three-dimensional (3D) deep convolutional network models have the potential to automate hippocampal segmentation. In this study, we investigate the accuracy and reliability of hippocampal segmentation by automated deep learning models from CT alone and compare the accuracy to experts using MRI fusion. Methods: Retrospectively, 390 Gamma Knife patients with high-resolution CT and MR images were collected. Following the RTOG 0933 guidelines, images were rigidly fused, and a neuroanatomic expert contoured the hippocampus on the MR, then transferred the contours to CT. Using a calculated cranial centroid, the image volumes were cropped to  $200 \times 200 \times 35$  voxels, which were used to train four models, including our proposed Attention-Gated 3D ResNet (AG-3D ResNet). These models were then compared with results from a nested tenfold validation. From the predicted test set volumes, we calculated the 100% Hausdorff distance (HD). Acceptability was assessed using the RTOG 0933 protocol criteria, and contours were considered passing with  $HD \leq 7$  mm. Results: The bilateral hippocampus passing rate across all 90 models trained in the nested cross-fold validation was 80.2% for AG-3D ResNet, which performs with a comparable pass rate ( $P = 0.3345$ ) to physicians during centralized review for the RTOG 0933 Phase II clinical trial. Conclusions: Our proposed AG-3D ResNet's segmentation of the hippocampus from noncontrast CT images alone are comparable to those obtained by participating physicians from the RTOG 0933 Phase II clinical trial.

Possley D, **Baker E**, **Baker K** and **Khalil JG** (2020). "Surface modification techniques to enhance osseointegration of spinal implants." *Journal of the American Academy of Orthopaedic Surgery*. ePub Ahead of Print.

[Request Form](#)

#### *Department of Orthopaedic Surgery*

Biomechanical function, specifically implantation technique and immediate surgical fixation, of orthopaedic implants is the primary consideration during the development of orthopaedic implants. Biologic and material characteristics are additional factors to include in the design process because of the direct impact on short- and long-term implant performance. The body's initial interaction with implant materials can affect protein- and cell-based function, thereby either promoting or impeding osseointegration. An understanding and inclusion of the biologic response, material surface morphology, and material surface chemistry in implant design is crucial because these factors ultimately determine implant function and patient outcomes. Highlighting the biologic- and material-related advantages and inadequacies of current and potential implant materials as well as applications may guide further research and development of implant materials

and designs.

Rao P, Lertjirachai I, Yonekawa Y, Hasbrook M, Thomas BJ, Wood EH, **Mehta N**, Mane G, **Drenser KA**, **Trese MT** and **Capone A, Jr.** (2020). "Etiology and clinical characteristics of macular edema in patients with familial exudative vitreoretinopathy." *Retina* 40(7): 1367-1373.

[Full Text](#)

*Department of Ophthalmology*

*OUIB Medical Student Author*

Purpose: To describe the etiology and clinical characteristics of macular edema (ME) in patients with familial exudative vitreoretinopathy. Methods: Observational, retrospective case series of 30 patients (34 eyes) with ME and familial exudative vitreoretinopathy who underwent spectral-domain optical coherence tomography imaging between 2009 and 2016. Baseline and follow-up optical coherence tomographies were correlated with color fundus photography and fluorescein angiography. Results: The average age was 20.6 years (6.6-68.7). Eighteen eyes exhibited cystoid ME (52.9%), 14 noncystoid ME (41.2%), and 2 eyes (5.9%) with both. Macular edema was foveal in 52.9% (n = 18). Eighteen of 24 eyes (64.3%) with an available fluorescein angiography showed leakage from ME. The most common structural feature was posterior hyaloidal organization/contraction (n = 15). Sixteen eyes were treated with topical or intravitreal steroids (n = 6), intravitreal anti-vascular endothelial growth factor (n = 3), or pars plana vitrectomy with membrane stripping (n = 7). There was no difference between mean preoperative and postoperative LogMAR visual acuity (0.63 [20/85] vs. 0.87 [20/148], P = 0.35) after vitrectomy despite a statistical improvement in the mean central foveal thickness (596  $\mu$ m vs. 303  $\mu$ m, P = 0.04). Conclusion: Macular edema in familial exudative vitreoretinopathy occurs most commonly because of traction. Vitrectomy is effective for relieving tractional forces with anatomical improvement.

Ryan EH, Ryan CM, Forbes NJ, Yonekawa Y, Wagley S, Mitra RA, Parke DW, Joseph DP, Emerson GG, Shah GK, Blinder KJ, Capone A, **Williams GA**, Elliott D, Gupta OP, Hsu J and Regillo CD (2020). "Primary retinal detachment outcomes study report number 2: Phakic retinal detachment outcomes." *Ophthalmology* 127(8): 1077-1085.

[Request Form](#)

*Department of Ophthalmology*

Purpose: Anatomically similar rhegmatogenous retinal detachments (RRDs) can be treated with scleral buckle (SB), pars plana vitrectomy (PPV), or SB combined with PPV (PPV/SB). This study compares moderately complex phakic primary RRD treated with SB, PPV, or PPV/SB to review anatomic and visual outcomes. Design: Multicenter, retrospective, interventional cohort study. Participants: Data were gathered on all patients from multiple retina practices in the United States with RRD in 2015 and >90 days of follow-up. The cohort of phakic patients with moderately complex RRD was analyzed. Methods: A large and detailed database was generated. Eyes with findings that would bias toward PPV (vitreous hemorrhage, dense cataract, proliferative vitreoretinopathy, giant retinal tear, among others) were excluded. Age <40 years (bias toward SB) was excluded. Comparable cases of moderately complex RRD were then chosen naive to surgeon, surgery, and outcome for subgroup analysis. Main Outcome Measures: Single surgery anatomic success (SSAS), defined as retinal attachment with no other RRD surgery within 90 days, is the main outcome measure. Final visual acuity is the secondary outcome measure. Pearson's chi-square and analysis of variance were used to test treatment effect of surgery type on SSAS and vision. Results: Single surgery anatomic success was noted in 155 of 169 SB cases (91.7%), 207 of 249 PPV cases (83.1%), and 271 of 297 PPV/SB cases (91.2%). Scleral buckle and PPV/SB were superior to PPV for SSAS (P = 0.0041). For macula-on or split cases, SB had significantly better visual outcomes than PPV or PPV/SB even after controlling for cataract (cases with minimal cataract at final follow-up or after cataract surgery) (P < 0.001). Conclusions: For phakic moderately complex primary RRDs in this study of PPV versus SB versus PPV/SB, SB had the best visual outcomes, and PPV had the worst SSAS outcomes.

Saeed AM, Khairnar R, Sharma AM, Larson GL, Tsai HK, Wang CJ, Halasz LM, **Chinnaiyan P**, Vargas CE and Mishra MV (2020). "Clinical outcomes in patients with recurrent glioblastoma treated with proton beam therapy reirradiation: Analysis of the Multi-Institutional Proton Collaborative Group Registry." *Advances in Radiation Oncology* 5(5): 978-983.

[Full Text](#)



#### *Department of Radiation Oncology*

Purpose: As a means of limiting normal tissue toxicity, proton-beam therapy (PBT) is an emerging radiation modality for glioblastoma (GBM) reirradiation. However, data for recurrent GBM treated with PBT reirradiation is limited. Therefore, we analyzed treatment patterns, toxicities, and clinical outcomes of patients with recurrent GBM treated with PBT reirradiation using the multi-institutional Proton Collaborative Group registry. Methods and Materials: Prospectively collected data for patients with recurrent GBM who underwent PBT while enrolled in Proton Collaborative Group study 01-009 (NCT01255748) were analyzed. We evaluated overall survival (OS), progression-free survival (PFS), and toxicity. Toxicities were scored per the Common Terminology Criteria for Adverse Events, version 4.0. Descriptive statistics were used to report patient, tumor, and treatment characteristics. Multivariable analyses (MVA) for toxicity were conducted using logistic regression. The Kaplan-Meier method was used to calculate OS and PFS. MVA for OS and PFS was conducted using Cox proportional-hazards models. The SAS statistical software was used for the analysis. Results: We identified 45 recurrent patients with GBM who underwent PBT reirradiation between 2012 and 2018. The median time between initial GBM diagnosis and recurrence was 20.2 months. The median follow-up time from PBT reirradiation was 10.7 months. Median PFS was 13.9 months (95% confidence interval [CI], 8.23-20.0 months) and median OS was 14.2 months (95% CI, 9.6-16.9 months) after PBT reirradiation. One patient experienced an acute grade 3 toxicity, 4 patients experienced late grade 3 toxicity (no grade  $\geq 4$  toxicities). MVA revealed that prior surgery was associated with a 91.3% decreased hazard of death (hazard ratio: 0.087; 95% CI, 0.02-0.42;  $P < .01$ ). No explanatory variables were associated with PFS or grade 3 toxicities. Conclusions: This is the largest series to date reporting outcomes for PBT reirradiation of patients with recurrent GBM. Our analysis indicates that PBT is well tolerated and offers efficacy rates comparable with previously reported photon reirradiation.

Sahu KK, Jindal V, **Anderson J**, Siddiqui AD and **Jaiyesimi IA** (2020). "Current perspectives on diagnostic assays and anti-PF4 antibodies for the diagnosis of heparin-Induced thrombocytopenia." *Journal of Blood Medicine* 11: 267-277.

[Full Text](#)

#### *Department of Internal Medicine*

Heparin-induced thrombocytopenia (HIT) is a recognized clinical entity in patients receiving unfractionated heparin and low-molecular weight heparin. Currently, diagnosing HIT includes the combination of a physician's clinical suspicion based on a clinical scoring system and a series of laboratory tests. In the present article, we discuss challenges in suspecting and diagnosing HIT in consideration of the turnaround time of available tests and recent advances in techniques and methodologies of newer immunoassays and functional assays.

Saleem S and **Berman B** (2020). "Deep vein thrombosis and pulmonary embolism in the setting of mycoplasma infection." *Case Reports in Medicine* 8708417: 1-3.

[Full Text](#)

#### *Department of Pediatrics*

Thirteen-year-old female twins presented one week apart with documented *Mycoplasma pneumoniae* respiratory infection. Each developed venous thrombosis and pulmonary emboli in association with transient self-limited para-infectious anti-phospholipid antibodies. Comprehensive evaluation revealed no identifiable genetic prothrombotic variables. Both children recovered after receiving antibiotics and anticoagulation therapy. Thrombotic complications associated with *Mycoplasma pneumoniae* infections are rare, particularly in children; the occurrence of this complication in identical twins has not been previously reported.

Schwartz AM, Anastasio AT, Farley KX, **Boden S**, Wagner ER and Gottschalk MB (2020). "Complications and mortality in patients with chronic kidney disease undergoing total shoulder arthroplasty." *Seminars in Arthroplasty* 30(2): 96-103.

[Full Text](#)

#### *OUWB Medical Student Author*

Introduction: Shoulder arthroplasty (SA) provides pain relief and functional improvement in patients with shoulder arthritis. With increasing incidence of SA, there is a growing effort to risk-stratify these patients to diminish complication rates. The aim of this study is to quantify complication risk, resource utilization, and mortality of patients with chronic kidney disease (CKD) who are undergoing SA (both non-dialysis

dependent and dialysis dependent) to identify any disease-severity relationship with delirious SA outcomes. Methods: We queried the Nationwide Inpatient Sample database for patients with and without diagnosis of CKD SA from 2007 to 2015. Additional patient comorbidities were stratified using the Elixhauser comorbidity index. Outcomes of interest include mortality, non-surgical and surgical complications, and resource utilization metrics. Multivariate logistical regression was run to determine odds ratios for development of these complications in the non-dialysis dependent (NDD) and dialysis-dependent cohort (DD). Results: Between 2007 and 2015, the prevalence of patients with CKD undergoing SA more than doubled. On univariate analysis, mortality, non-surgical and surgical complications, and all resource-utilization metrics were increased in CKD patients, with a direct disease-severity-dependent relationship; the rate of inpatient mortality in the DD cohort after SA was 32 times higher than patients without CKD ( $p < 0.001$ ). The association between CKD and complication rates, and the disease-severity relationship was conserved on multivariate analysis. The OR for mortality in the DD cohort was 10.6 ( $p < 0.001$ ). Conclusion: Patients with CKD undergoing SA had a far greater risk of mortality, development of postoperative surgical and non-surgical complications, and resource utilization metrics during the postoperative inpatient stay after SA. CKD is an independent risk for a detrimental postoperative course after SA, and this relationship is worsened in patients requiring dialysis. The CKD population represents a potentially hazardous candidate for elective SA. Level of Evidence: Level III

Seiwert TY, Kochanny S, Wood K, Worden FP, Adkins D, Wade JL, Sleckman BG, Anderson D, **Brisson RJ**, Karrison T, Stadler WM and Vokes EE (2020). "A randomized phase 2 study of temsirolimus and cetuximab versus temsirolimus alone in recurrent/metastatic, cetuximab-resistant head and neck cancer: The MAESTRO study." *Cancer* 126(14): 3237-3243.

[Full Text](#)

*OUWB Medical Student Author*

Background: Patients with cetuximab-resistant, recurrent/metastatic head and neck squamous cell carcinoma (HNSCC) have poor outcomes. This study hypothesized that dual blockade of mammalian target of rapamycin and epidermal growth factor receptor (EGFR) would overcome cetuximab resistance on the basis of the role of phosphoinositide 3-kinase signaling in preclinical models of EGFR resistance. Methods: In this multicenter, randomized clinical study, patients with recurrent/metastatic HNSCC with documented progression on cetuximab (in any line in the recurrent/metastatic setting) received 25 mg of temsirolimus weekly plus cetuximab at 400/250 mg/m<sup>2</sup> weekly (TC) or single-agent temsirolimus (T). The primary outcome was progression-free survival (PFS) in the TC arm versus the T arm. Response rates, overall survival, and toxicity were secondary outcomes. Results: Eighty patients were randomized to therapy with TC or T alone. There was no difference for the primary outcome of median PFS (TC arm, 3.5 months; T arm, 3.5 months). The response rate was 12.5% in the TC arm (5 responses, including 1 complete response [2.5%]) and 2.5% in the T arm (1 partial response;  $P = .10$ ). Responses were clinically meaningful in the TC arm (range, 3.6-9.1 months) but not in the T-alone arm (1.9 months). Fatigue, electrolyte abnormalities, and leukopenia were the most common grade 3 or higher adverse events and occurred in less than 20% of patients in both arms. Conclusions: The study did not meet its primary endpoint of improvement in PFS. However, TC induced responses in cetuximab-refractory patients with good tolerability. The post hoc observation of activity in patients with acquired resistance (after prior benefit from cetuximab monotherapy) may warrant further investigation.

**Sellers T, Ghannam M, Asantey K, Klei J, Olive E and Roach VA** (2020). "An early introduction to surgical skills: Validating a low-cost laparoscopic skill training program purpose built for undergraduate medical education." *American Journal of Surgery*. ePub Ahead of Print.

[Full Text](#)

*OUWB Medical Student Author*

*Department of Foundational Medical Studies (OU)*

Background: Medical student exposure to laparoscopy is limited to observation despite the prevalence of minimally invasive techniques in practice. The high cost of laparoscopic simulation equipment, commonly called "box trainers", limits undergraduate exposure to skill training. Methods: Students at a Midwestern medical school were recruited to participate in an experimental laparoscopic skill training program. One cohort ( $n = 17$ ) used a DIY box trainer design freely available on MedEdPORTAL. A second cohort ( $n = 17$ )

used a commercially available equivalent. Pre- and post-training attempts for four tasks were scored and the difference was calculated. The average differences for each cohort were then contrasted statistically. Results: Significant performance improvements (pre- and post-training) were demonstrated regardless of group allocation. The difference in performance between the cohorts was not significant for any task ( $p > 0.05$ ). Conclusions: This low-cost training program using DIY box trainers is as effective as commercially available equivalent box trainers for introducing laparoscopic skills to medical students.

**Seymour ZA, Hamstra DA**, Daignault-Newton S, Bosch W, Michalski J, Gay HA and Pinkawa M (2020). "Long-term follow-up after radiotherapy for prostate cancer with and without rectal hydrogel spacer: A pooled prospective evaluation of bowel-associated quality of life." *BJU International* 126(3): 367-372.

[Full Text](#)

*Department of Radiation Oncology*

Objective: To evaluate the long-term bowel-associated quality of life (QOL) in men after radiotherapy (RT) for prostate cancer with and without the use of rectal hydrogel spacer. Patients and Methods: The patients' QOL was examined using the Expanded Prostate Cancer Index Composite (EPIC) and mean changes from baseline in EPIC domains were evaluated. A total of 215 patients from a randomised multi-institutional trial of RT, with or without hydrogel spacer, with a QOL endpoint were pooled with 165 non-randomised patients from a single institution with prospective QOL collection in patients with or without hydrogel spacer. The proportions of men with minimally important differences (MIDs) relative to pre-treatment baseline in the bowel domain were tested using repeated measure logistic models with a pre-specified threshold for clinically significant declines ( $\geq 5$  equivalent to MIDx1 and  $\geq 10$  equivalent to MIDx2). Results: A total of 380 men were evaluated (64% with spacer and 36% without) with QOL data being available for 199 men with  $>24$  months of follow-up [median (range) 39.5 (31-71.4) months]. Treatment with spacer was associated with less decline in average long-term bowel QOL (89.4 for control and 94.7 for spacer) with differences at  $>24$  months meeting the threshold of a MID difference between cohorts (bowel score difference from baseline: control = -5.1, spacer = 0.3, difference = -5.4;  $P < 0.001$ ). When evaluated over time men without spacer were more likely to have MIDx1 (5 points) declines in bowel QOL ( $P = 0.01$ ). At long-term follow-up MIDx1 was 36% without spacer vs 14% with spacer ( $P < 0.001$ ; odds ratio [OR] 3.5, 95% CI 1.7-6.9) while MIDx2 was seen in 19% vs 6% ( $P = 0.008$ ; OR 3.6, 95% CI 1.4-9.1). The use of spacer was associated with less urgency with bowel movements ( $P = 0.002$ ) and fewer loose stools ( $P = 0.009$ ), as well as less bother with urgency ( $P = 0.007$ ) and frequency of bowel movements ( $P = 0.009$ ). Conclusions: In this pooled analysis of QOL after prostate RT with up to 5 years of follow-up, use of a rectal spacer was associated with preservation of bowel QOL. This QOL benefit was preserved with long-term follow-up.

Shendy NAM, Raghu D, **Roy S**, Perry CH, Safi A, Branco MR, **Homayouni R** and Abell AN (2020). "Coordinated regulation of Rel expression by MAP3K4, CBP, and HDAC6 controls phenotypic switching." *Communications Biology* 3(1): 475.

[Full Text](#)

*Department of Foundational Medical Studies (OU)*

Coordinated gene expression is required for phenotypic switching between epithelial and mesenchymal phenotypes during normal development and in disease states. Trophoblast stem (TS) cells undergo epithelial-mesenchymal transition (EMT) during implantation and placentation. Mechanisms coordinating gene expression during these processes are poorly understood. We have previously demonstrated that MAP3K4-regulated chromatin modifiers CBP and HDAC6 each regulate thousands of genes during EMT in TS cells. Here we show that CBP and HDAC6 coordinate expression of only 183 genes predicted to be critical regulators of phenotypic switching. The highest-ranking co-regulated gene is the NF- $\kappa$ B family member Rel. Although NF- $\kappa$ B is primarily regulated post-transcriptionally, CBP and HDAC6 control Rel transcript levels by binding Rel regulatory regions and controlling histone acetylation. REL re-expression in mesenchymal-like TS cells induces a mesenchymal-epithelial transition. Importantly, REL forms a feedback loop, blocking HDAC6 expression and nuclear localization. Together, our work defines a developmental program coordinating phenotypic switching.

Stephen JR and **Burks FN** (2020). "Buried penis repair: Tips and tricks." *International Brazilian Journal of Urology* 46(4): 519-522.

[Full Text](#)

*Department of Urology*

Obesity is increasing in prevalence worldwide and an increasingly commonly encountered condition is adult acquired buried penis (AABP). We review the current management of AABP and relevant literature. Management of AABP requires a combination of genitourinary reconstructive techniques and plastic surgery techniques that are unique to this condition. We offer our experience and tips and tricks for the treatment of AABP.

Strålin K, Rothman RE, Özenci V, Barkataki K, Brealey D, Dhiman N, Poling L, Kurz MC, Limaye AP, LoVecchio F, Lowery K, Miller LG, Moran GJ, Scott Overcash J, Parekh A, Frank Peacock W, Rivers EP, **Sims M**, Stubbs AM, Sundqvist M, Ullberg M and Carroll KC (2020). "Performance of PCR/electrospray ionization-mass spectrometry on whole blood for detection of bloodstream microorganisms in patients with suspected sepsis." Journal of Clinical Microbiology 58(9).

[Full Text](#)

*Department of Internal Medicine*

Blood culture (BC) often fails to detect bloodstream microorganisms in sepsis. However, molecular diagnostics hold great potential. The molecular method PCR/electrospray ionization-mass spectrometry (PCR/ESI-MS) can detect DNA from hundreds of different microorganisms in whole blood. The aim of the present study was to evaluate the performance of this method in a multicenter study including 16 teaching hospitals in the United States (n = 13) and Europe (n = 3). First, on testing of 2,754 contrived whole blood samples, with or without spiked microorganisms, PCR/ESI-MS produced 99.1% true-positive and 97.2% true-negative results. Second, among 1,460 patients with suspected sepsis (sepsis-2 definition), BC and PCR/ESI-MS on whole blood were positive in 14.6% and 25.6% of cases, respectively, with the following result combinations: BC positive and PCR/ESI-MS negative, 4.3%; BC positive and PCR/ESI-MS positive, 10.3%; BC negative and PCR/ESI-MS positive, 15.3%; and BC negative and PCR/ESI-MS negative, 70.1%. Compared with BC, PCR/ESI-MS showed the following sensitivities (coagulase-negative staphylococci not included): Gram-positive bacteria, 58%; Gram-negative bacteria, 78%; and *Candida* species, 83%. The specificities were 94% for all individual species. Patients who had received prior antimicrobial medications (n = 603) had significantly higher PCR/ESI-MS positivity rates than patients without prior antimicrobial treatment—31% versus 22% (P 0.0001)—with pronounced differences for Gram-negative bacteria and *Candida* species. In conclusion, PCR/ESI-MS showed excellent performance on contrived samples. On clinical samples, it showed high specificities, moderately high sensitivities for Gram-negative bacteria and *Candida* species, and elevated positivity rates during antimicrobial treatment. These promising results encourage further development of molecular diagnostics to be used with whole blood for detection of bloodstream microorganisms in sepsis.

Tan TQ, Kullar R, Swartz TH, **Mathew TA**, Piggott DA and Berthaud V (2020). "Location matters: Geographic disparities and impact of Coronavirus Disease 2019 (COVID-19)." Journal of Infectious Diseases. ePub Ahead of Print.

[Full Text](#)

*Department of Internal Medicine*

The COVID-19 pandemic in the United States has revealed major disparities in the access to testing and messaging about the pandemic based on the geographic location of individuals, particularly in communities of color, rural areas, and areas of low income. This geographic disparity, in addition to deeply rooted structural inequities, have posed additional challenges to adequately diagnose and provide care for individuals of all ages living in these settings. We describe the impact that COVID-19 has had on geographic disparate populations in the United States and share our recommendations to what might be done to ameliorate the current situation.

Tariq T, **Karabon P**, Irfan FB, Sieloff EM, **Patterson R** and **Desai AP** (2020). "National trends and outcomes of nonautoimmune hemolytic anemia in alcoholic liver disease: Analysis of the Nationwide Inpatient Sample." Journal of Clinical Gastroenterology. ePub Ahead of Print.

[Full Text](#)

*Department of Medical Education*

*OUIWB Medical Student Author*

Goal: The aim of this study was to determine the burden of nonautoimmune hemolytic anemia (NAHA) in hospitalized patients with coexisting alcoholic liver disease (ALD), identify risk factors for NAHA in ALD and

describe the hospitalization outcomes. Background: ALD can result in structural and metabolic alterations in the red-blood cell membrane leading to premature destruction of erythrocytes and hemolytic anemia of varying severity. Study: Hospitalized ALD patients with concomitant NAHA were identified in the Nationwide Inpatient Sample database using International Classification of Diseases-9 codes from 2009 to 2014. The primary outcome was to determine the nationwide prevalence and risk factors of NAHA in patients hospitalized with ALD. Results: The prevalence of NAHA was 0.17% (n=3585) among all ALD patients (n=2,125,311) that were hospitalized. Multivariate analysis indicated higher odds of NAHA in ALD patients in the following groups: female gender [adjusted odds ratio (AOR) AOR 1.80, P<0.0001]; highest quartile of median household income (AOR 1.88, P<0.0001); increasing Charlson-Deyo Comorbidity Index (3 to 4 vs. 0, AOR 2.16, P=0.0042) and cirrhosis (AOR 2.74, P<0.0001). Discharges of ALD with anemia had a significantly longer average length of stay (8.8 vs. 6.0 d, P<0.0001), increased hospital charges (\$38,961 vs. \$25,244, P<0.0001) and higher mortality (9.0% vs. 5.6%, P<0.0001) when compared with ALD with no anemia. Conclusion: NAHA in patients with ALD is an important prognostic marker, predicting a longer, costlier hospitalization and increased inpatient mortality in ALD.

Thompson AB, Quinn TJ, Siddiqui ZA, Almahariq MF, **Grills IS** and **Stevens CW** (2020). "Addition of radiotherapy to surgery and chemotherapy improves survival in localized malignant pleural mesothelioma: A Surveillance, Epidemiology, and End Results (SEER) study." Lung Cancer 146: 120-126.

[Full Text](#)

*Department of Radiation Oncology*

Introduction: Malignant pleural mesothelioma (MPM) is a devastating disease with poor survival outcomes for most patients. Optimizing therapeutic approaches is thus vital, but has been hampered by a dearth of randomized trials to guide decision making. We used a population-level database to evaluate the impact of radiotherapy as a component of trimodality therapy on overall survival (OS) in MPM. Methods: We retrospectively reviewed the SEER Radiation/Chemotherapy database for patients with MPM who received surgery and chemotherapy, with or without radiotherapy. A propensity score-matched analysis with inverse probability of treatment weighting (IPTW) was performed. Weight-adjusted univariate KM analysis was performed and doubly robust, IPTW-adjusted multivariable cox proportional hazards regression modeling was also performed to quantify the effect of radiotherapy on OS in trimodality therapy for MPM. Results: 1015 patients were identified. 678 patients received surgery and chemotherapy, and 337 patients received trimodality therapy. For patients with localized disease, OS was significantly improved with trimodality therapy (HR 0.56, CI 0.4 - 0.8, p = 0.001), which persisted with IPTW adjustment (HR 0.65, CI 0.49 - 0.95, p = 0.0248). No significant benefit was seen for patients with regional or distant disease. On multivariate analysis, positive predictors of survival after IPTW adjustment were female sex, diagnosis after 2005, and left-sided disease. Conclusions: These findings support a significant benefit to OS by incorporating radiotherapy as a component of trimodality therapy for patients with localized MPM compared to only surgery and chemotherapy. It does not provide a significant overall survival benefit for patients with regional or metastatic disease.

Tice JA, **Halalau A** and Burke H (2020). "Vitamin D does not prevent cancer or cardiovascular disease: The VITAL Trial " Journal of General Internal Medicine. ePub Ahead of Print.

[Full Text](#)

*Department of Internal Medicine*

**Todd BR**, Traylor S, Heron L and **Turner-Lawrence D** (2020). "SPRINT through tasks: A novel curriculum for improving resident Task management in the emergency department." MedEdPORTAL 16: 10956.

[Full Text](#)

*Department of Emergency Medicine*

Introduction: The emergency department (ED) presents a challenging task-management environment to emergency medicine (EM) trainees. However, equipping residents with a tool to improve task switching (generically known as multitasking) could have positive impacts on patient care and physician emotional state. We designed a task-management tool and educational curriculum with the goal of improving emergency medicine resident task-switching ability. Methods: The task-management tool uses the acronym SPRINT: (1) stabilize critical patients, (2) perform procedures, (3) rack (see new patients in the chart rack), (4)

in or out (reassess and disposition), (5) type it up (chart completion). These tasks and their order were decided on by two seasoned clinicians based on their years of experience in the ED. The SPRINT tool was taught to EM residents through a 1-hour curriculum consisting of an introductory video, a classroom-based workshop with multimedia didactics, and team learning with a card game simulating the use of the SPRINT tool on a shift. Residents were surveyed to evaluate their task-management confidence and perceived effectiveness of the curriculum. Results: A total of 34 EM residents participated in this training on the SPRINT tool. There was an improvement in resident confidence in task management, and residents reporting having a strategy for task prioritization 8 weeks after the workshop. Discussion: The SPRINT curriculum provides EM residents with a tool to manage the complex task-management environment of the ED. Further research in task-management education should focus on patient-oriented outcomes among physicians who have received this training.

Trinh TQ, Leunig M, Larson CM, Clohisy J, Nepple J, **Zaltz I**, Kelly BT, Naimark MB and Bedi A (2020). "Lateral center-edge angle is not predictive of acetabular articular cartilage surface area: Anatomic variation of the lunate fossa." *American Journal of Sports Medicine* 48(8): 1967-1973.

[Full Text](#)

*Department of Orthopaedic Surgery*

Background: Surgical treatment of symptomatic femoroacetabular impingement (FAI) and dysplasia requires careful characterization of acetabular morphology. The lateral center-edge angle (LCEA) is often used to assess lateral acetabular anatomy. Previous work has questioned the LCEA as a surrogate for acetabular contact/articular cartilage surface area because of the variable morphology of the lunate fossa. Hypothesis: We hypothesized that weightbearing articular cartilage of the acetabulum would poorly correlate with LCEA secondary to significant variation in the size of the lunate fossa. Study Design: Cohort study (Diagnosis); Level of evidence, 3. Methods: Patients with 3D CT imaging undergoing either hip arthroscopy or periacetabular osteotomy for FAI or symptomatic hip instability were retrospectively identified. The LCEA and femoral head diameter were measured on an anteroposterior pelvis radiograph. Patients were grouped according to their lateral acetabular coverage as undercoverage (LCEA,  $<25^\circ$ ), normal coverage (LCEA,  $25^\circ$ - $40^\circ$ ), or overcoverage (LCEA,  $>40^\circ$ ). Patients were randomly identified until each group contained 20 patients. The articular surface area was measured from preoperative 3D CT data. Linear regression analysis was performed to examine the relationship between articular surface area and LCEA. Continuous and categorical data were analyzed utilizing analysis of variance and chi-square analysis. Statistical significance was set at  $P < .05$ . Results: No difference in age ( $P = .52$ ), body mass index (BMI) ( $P = .75$ ), or femoral head diameter ( $P = .66$ ) was noted between groups. A significant difference in articular surface area was observed between patients with undercoverage and those with overcoverage (20.4 cm<sup>2</sup> vs 24.5 cm<sup>2</sup>;  $P = .01$ ). No significant difference was identified between the undercoverage and normal groups (20.4 cm<sup>2</sup> vs 23.3 cm<sup>2</sup>;  $P = .09$ ) or the normal and overcoverage groups (23.3 cm<sup>2</sup> vs 24.5 cm<sup>2</sup>;  $P = .63$ ). A moderate positive correlation was observed between LCEA and articular surface area across all patients ( $r = 0.38$ ;  $P = .002$ ) but not when patients with undercoverage were excluded ( $r = 0.02$ ;  $P = .88$ ). Significant variation in surface area was observed within each group such that no patient in any group was outside of 2 SDs of the means of the other groups. When patients were categorized into quartiles established by the articular surface area for the entire population, 40% of patients with overcoverage were observed in the first or second quartile (lower area). Conclusion: Lateral acetabular undercoverage based on the LCEA ( $<25^\circ$ ) correlates with decreased acetabular surface area. Normal or increased acetabular coverage (LCEA,  $>25^\circ$ ), however, is not predictive of increased, normal, or decreased acetabular surface area.

van Rosendael AR, Lin FY, Ma X, van den Hoogen IJ, Gianni U, Al Hussein O, Al'Aref SJ, Peña JM, Andreini D, Al-Mallah MH, Budoff MJ, Cademartiri F, **Chinnaiyan K**, Choi JH, Conte E, Marques H, de Araújo Gonçalves P, Gottlieb I, Hadamitzky M, Leipsic JA, Maffei E, Pontone G, **Raff GL**, Shin S, **Kim YJ**, **Lee BK**, Chun EJ, Sung JM, Lee SE, Berman DS, Virmani R, Samady H, Stone PH, Narula J, Bax JJ, Shaw LJ, Min JK and Chang HJ (2020). "Percent atheroma volume: Optimal variable to report whole-heart atherosclerotic plaque burden with coronary CTA, the PARADIGM study." *Journal of Cardiovascular Computed Tomography* 14(5): 400-406.

Request Form

*Department of Radiation Oncology*

Background and Aims: Different methodologies to report whole-heart atherosclerotic plaque on coronary



computed tomography angiography (CCTA) have been utilized. We examined which of the three commonly used plaque burden definitions was least affected by differences in body surface area (BSA) and sex. Methods: The PARADIGM study includes symptomatic patients with suspected coronary atherosclerosis who underwent serial CCTA >2 years apart. Coronary lumen, vessel, and plaque were quantified from the coronary tree on a 0.5 mm cross-sectional basis by a core-lab, and summed to per-patient. Three quantitative methods of plaque burden were employed: (1) total plaque volume (PV) in mm<sup>3</sup>, (2) percent atheroma volume (PAV) in % [which equaled: PV/vessel volume \* 100%], and (3) normalized total atheroma volume (TAVnorm) in mm<sup>3</sup> [which equaled: PV/vessel length \* mean population vessel length]. Only data from the baseline CCTA were used. PV, PAV, and TAVnorm were compared between patients in the top quartile of BSA vs the remaining, and between sexes. Associations between vessel volume, BSA, and the three plaque burden methodologies were assessed. Results: The study population comprised 1479 patients (age 60.7 ± 9.3 years, 58.4% male) who underwent CCTA. A total of 17,649 coronary artery segments were evaluated with a median of 12 (IQR 11–13) segments per-patient (from a 16-segment coronary tree). Patients with a large BSA (top quartile), compared with the remaining patients, had a larger PV and TAVnorm, but similar PAV. The relation between larger BSA and larger absolute plaque volume (PV and TAVnorm) was mediated by the coronary vessel volume. Independent from the atherosclerotic cardiovascular disease risk (ASCVD) score, vessel volume correlated with PV (P < 0.001), and TAVnorm (P = 0.003), but not with PAV (P = 0.201). The three plaque burden methods were equally affected by sex. Conclusions: PAV was less affected by patient's body surface area than PV and TAVnorm and may be the preferred method to report coronary atherosclerotic burden.

Vayntraub A, Quinn TJ, Thompson AB, **Chen PY, Gustafson GS, Jawad MS and Dilworth JT** (2020). "Left anterior descending artery avoidance in patients receiving breast irradiation." Medical Dosimetry. ePub Ahead of Print.

[Request Form](#)

*Department of Radiation Oncology*

Purpose: Dose to the left anterior descending artery (LAD) may be significant in patients receiving left-sided irradiation for breast cancer. We investigated if prospective contouring and avoidance of the LAD during treatment planning were associated with lower LAD dose. Methods and Materials: We reviewed dosimetric plans for 323 patients who received left whole breast or chest wall irradiation with or without internal mammary node (IMLN) coverage between 1/2014 and 1/2019 at a single institution. The LAD was contoured prospectively for 155 cases, and techniques were utilized to minimize LAD dose. Dose-volume-histograms from these patients were compared to those of 168 patients for whom the LAD was contoured retrospectively after treatment completion. EQD2 was calculated to account for fractionation differences. Results: Compared to cases where the LAD was contoured retrospectively (n = 126), prospective LAD contouring (n = 124) was associated with lower unadjusted median max and mean LAD doses for 250 patients receiving whole-breast irradiation (WBI) without IMLN coverage: 8.5 Gy vs 5.2 Gy (p < 0.0001) and 3.6 Gy vs 2.7 Gy (p < 0.0001), respectively. EQD2 median max and mean LAD doses were also lower with prospective LAD contouring: 5.2 Gy vs 3.0 Gy (p < 0.0001) and 1.9 Gy vs 1.5 Gy (p < 0.0001), respectively. Compared to cases where the LAD was contoured retrospectively (n = 42), prospective LAD contouring (n = 31) was associated with lower max LAD doses for 73 patients with IMLN coverage: 20.4 Gy vs 14.3 Gy (p = 0.042). There was a nonsignificant reduction in median mean LAD dose: 6.2 Gy vs 6.1 Gy (p = 0.33). LAD doses were reduced while maintaining IMLN coverage (mean V90%(Rx) >90%). Conclusions: Prospective contouring and avoidance of the LAD were associated with lower max and mean LAD doses in patients receiving WBI and with lower max LAD doses in patients receiving IMLN treatment. Further reduction in LAD dose may require stricter optimization weighting or compromise in IMLN coverage.

Vitug S, **Ravi V** and Thangathurai D (2020). "Sedation with ketamine and fentanyl combination improves patient outcomes in intensive care units." SN Comprehensive Clinical Medicine. ePub Ahead of Print.

[Full Text](#)

*OUWB Medical Student Author*

Psychological manifestations such as depression and suicidal ideation are commonly caused by poorly controlled pain, anxiety, and sleep deprivation in intensive care unit (ICU) patients. We are concerned that previous analgesic and sedative techniques administered as single-medication approaches are outdated and inadequate. It is imperative that ICU practitioners are knowledgeable in multimodal approaches to pain and

sedation in high acuity settings. We have shown that appropriate combinations of ketamine and fentanyl are effective, and if further supplementation is needed, we utilize additional pharmacological agents in low doses and regional techniques that ultimately lower the overall opioid consumption. We acknowledge that a variety of medication supplementations tailored to the patient's clinical needs and nature of surgery improves a patient's outcome in ICU and overall quality of life.

Vollstedt AJ, Han E, Nguyen L, Tennyson L, Beck D and **Sirls L** (2020). "Placement of mid-urethral mesh slings at the time of vaginal prolapse repair does not affect post-operative sexual function or orgasm." [International Urogynecology Journal](#). ePub Ahead of Print.

[Full Text](#)

*Department of Urology*

**Introduction and Hypothesis:** Because of the relationship between the clitoral neurovascular supply and the urethra, the dissection for placement of mid-urethral slings (MUS) may negatively impact orgasmic function. We aimed to analyze the role of MUS in orgasmic and overall sexual function in patients undergoing prolapse surgery. **Methods:** A single institution retrospective review was performed on 157 patients undergoing prolapse surgery with and without MUS from 2008 to 2014. Pelvic Organ Prolapse Incontinence Sexual Questionnaires (PISQ-12) scores at baseline, 6, and 12 months post-operatively were compared. The difference in overall mean post-operative PISQ-12 scores at 6 and 12 months in those undergoing POP with or without MUS placement was assessed using Wilcoxon rank tests. **Results:** Of 157 women who underwent prolapse surgery, 81 (52%) had concomitant MUS. Mean baseline PISQ-12 scores were 32 in both groups ( $p = 0.98$ ). Post-operative PISQ-12 scores between the two groups did not differ at 6 ( $p = 0.96$ ) or 12 months ( $p = 0.65$ ). Within the MUS group, mean overall PISQ-12 scores improved at 6 ( $p = 0.05$ ) and 12 months ( $p < 0.01$ ). Mean overall PISQ-12 scores did not improve in patients who did not have slings placed at 6 ( $p = 0.10$ ) or 12 months ( $p = 0.15$ ). Orgasm frequency and intensity did not differ between the two groups at 6 ( $p = 0.39$ ,  $p = 0.91$ , respectively) or 12 months ( $p = 0.11$ ,  $p = 0.44$ , respectively). **Conclusion:** MUS at the time of prolapse repair did not affect orgasmic or overall sexual function. PISQ-12 scores improved after prolapse surgery with concomitant MUS placement. Our findings may help counsel patients regarding the risk of MUS placement affecting sexual function.

**Wasserman JA** and Navin MC (2020). "The irrelevance of origins: Dementia, advance directives, and the capacity for preferences." [American Journal of Bioethics](#) 20(8): 98-100.

[Full Text](#)

*Department of Foundational Medical Studies (OU)*

**Weiner AJ, Weiner Y** and Weiner A (2020). "Corneal parameters following tube shunt implantation through the ciliary sulcus." [Ophthalmology. Glaucoma](#). ePub Ahead of Print.

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*OUWB Medical Student Author*

**Purpose:** To monitor bilateral corneal parameters following unilateral Baerveldt 350 tube shunt implantation through the ciliary sulcus. **Participants:** Patients from one private glaucoma practice with severe uncontrolled glaucoma treated with sulcus tube shunt implantation in one pseudophakic eye. **Design:** Retrospective interventional case series. **Methods:** Specular microscopy data were collected before and following unilateral sulcus tube shunt implantation from the surgical and the glaucomatous fellow eyes. **Main Outcome Measures:** Central corneal endothelial cell density (CECD), coefficient of variation (CV) and percent of hexagonal cells (%Hex), central corneal thickness (CCT), intra-ocular pressure (IOP), IOP-lowering medications (IOPmeds), visual acuity and complications. **Results:** Forty six patients (age, mean (SD): 69.9 (4.6), range: 20-88 years, male: 41.3%) were identified. Following surgery, IOP and the number of IOPmeds decreased significantly by 42.3% ( $p < .0001$ ) and 32.1% ( $p < .0001$ ), respectively in the surgical eye group. Preoperative CECD measured 1,807 (172) and 1,825 (172) cells/mm<sup>2</sup> in the surgical and fellow eyes, respectively ( $p = 0.92$ ), and compared to baseline it decreased by 8.6% ( $p = 0.17$ ) and 3.1% ( $p = 0.65$ ), respectively by 24 months. Preoperative CV, %Hex and CCT were similar in both groups and remained stable. All corneal parameters remained unchanged in a subgroup of 15 patients with low preoperative CECD (1,273 (99) cells/mm<sup>2</sup>). Best corrected visual acuity remained stable in both groups. Hyphema occurred in 23.9% of the surgical eyes and resolved with no intervention. We found no sight-threatening complications or

corneal failures during follow up. Conclusions: Tube shunt implantation through the ciliary sulcus in pseudophakic eyes appears relatively safe to the corneal endothelium demonstrating a small and nonsignificant decline in central corneal endothelial cell density compared to baseline and to their glaucomatous fellow eyes. There were no significant disruption to corneal endothelial cell morphology, increased corneal thickness or corneal failures during the 24-month follow-up period. A prospective head-to-head comparison to assess the effects of the various methods of tube shunt implantation on the corneal endothelium is needed.

**Weiner AJ, Weiner Y** and Weiner A (2020). "Intraocular pressure after cataract surgery combined with ab interno trabeculectomy versus trabecular micro-bypass stent: An intrasubject same-surgeon comparison." Journal of Glaucoma 29(9): 773-782.

[Full Text](#)

*Department of Ophthalmology*

Precis: Combining Trabectome or iStent with phacoemulsification equally reduces intraocular pressure (IOP) and IOP-lowering medication burden during a 24-month follow-up, with a possible advantage to the Trabectome in the early postoperative period. Purpose: Intrasubject same-surgeon comparison between phacoemulsification combined with Trabectome (Phaco/Trabectome) versus one first-generation iStent (Phaco/iStent). Settings: Private glaucoma and cataract practice. Design: This is a retrospective interventional case series. Methods: Data collected at 3 to 4 and 20 to 24 hours and up to 30 months following Phaco/Trabectome in 1 eye and Phaco/iStent in the contralateral eye in patients with bilateral visually-significant cataract and open-angle glaucoma. Evaluations included IOP, intraocular pressure-lowering medications (IOPmeds), visual acuity, and complications. Results: Forty-five patients (90 eyes) were identified (age 76.5, 57 to 95 y). At 3 to 4 hours, IOP was above baseline in 12 and 13 eyes following Phaco/Trabectome and Phaco/iStent, respectively, but the degree of IOP elevation was smaller ( $P=0.048$ ) following Phaco/Trabectome: 4.3 mm Hg, 2.0 to 6.6 mm Hg (95% confidence interval) versus Phaco/iStent: 8.7 mm Hg, 3.8 to 13.6 mm Hg. At 20 to 24 hours, compared with baseline, IOP was significantly lower after Phaco/Trabectome ( $P=0.004$ ) but not after Phaco/iStent ( $P=0.14$ ) although the rate of hyphema was higher following Phaco/Trabectome (12/45 vs. 2/45 eyes,  $P=0.007$ ). IOP reduction from baseline at 3 to 4 hours was significantly larger ( $P=0.020$ ) in the 21 eyes with hyphema: -3.9, -6.4 to -1.4 versus the 69 eyes without hyphema: -0.3, -2.0 to +1.4. At 1, 6, 12, and 24 months, IOP and number of IOPmeds were similar and significantly lower compared with baseline following either procedure. No complications were encountered in either group. Conclusions: Combined phacoemulsification with either Trabectome or first-generation iStent similarly lowers IOP and IOPmeds burden at 1, 6, 12, and 24 months following surgery. The Trabectome may have an advantage in lowering IOP faster and lessening the degree of IOP elevations in the early postoperative period.

Wilkin GP, Poitras S, Clohisy J, Belzile E, **Zaltz I**, Grammatopoulos G, Melkus G, Rakhra K, Ramsay T, Thavorn K and Beaulé PE (2020). "Periacetabular osteotomy with or without arthroscopic management in patients with hip dysplasia: Study protocol for a multicenter randomized controlled trial." Trials 21(1): 725.

[Full Text](#)

*Department of Orthopaedic Surgery*

Background: Hip dysplasia is one of the most common causes of hip arthritis. Its incidence is estimated to be between 3.6 and 12.8% (Canadian Institute for Health Information, Hip and knee replacements in Canada, 2017-2018: Canadian joint replacement registry annual report, 2019; Jacobsen and Sonne-Holm, *Rheumatology* 44:211-8, 2004). The Periacetabular Osteotomy (PAO) has been used successfully for over 30 years (Gosvig et al., *J Bone Joint Surg Am* 92:1162-9, 2010), but some patients continue to exhibit symptoms post-surgery (Wyles et al., *Clin Orthop Relat Res* 475:336-50, 2017). A hip arthroscopy, performed using a small camera, allows surgeons to address torn cartilage inside the hip joint. Although both procedures are considered standard of care treatment options, it is unknown whether the addition of hip arthroscopy improves patient outcomes compared to a PAO alone. To delay or prevent future joint replacement surgeries, joint preservation surgery is recommended for eligible patients. While previous studies found an added cost to perform hip arthroscopies, the cost-effectiveness to Canadian Health care system is not known. Methods: Patients randomized to the experimental group will undergo central compartment hip arthroscopy prior to completion of the PAO. Patients randomized to the control group will

undergo isolated PAO. Patient-reported quality of life will be the primary outcome used for comparison between the two treatment groups as measured by The International Hip Outcome Tool (iHOT-33) (Saber Hosnijeh et al., *Arthritis Rheum* 69:86-93, 2017). Secondary outcomes will include the four-square step test and sit-to-stand (validated in patients with pre-arthritis hip pain) and hip-specific symptoms and impairment using the HOOS; global health assessment will be compared using the PROMIS Global 10 Score; health status will be assessed using the EQ-5D-5L and EQ VAS questionnaires (Ganz et al., *Clin Orthop Relat Res* 466:264-72, 2008) pre- and post-operatively. In addition, operative time, hospital length of stay, adverse events, and health services utilization will be collected. A sub-group of patients (26 in each group) will receive a T1rho MRI before and after surgery to study changes in cartilage quality over time. A cost-utility analysis will be performed to compare costs and quality-adjusted life years (QALYs) associated with the intervention. Discussion: We hypothesize that (1) concomitant hip arthroscopy at the time of PAO to address central compartment pathology will result in clinically important improvements in patient-reported outcome measures (PROMs) versus PAO alone, that (2) additional costs associated with hip arthroscopy will be offset by greater clinical improvements in this group, and that (3) combined hip arthroscopy and PAO will prove to be a cost-effective procedure. Trial Registration: ClinicalTrials.gov NCT03481010 . Registered on 6 March 2020. Protocol version: version 3.

**Wilson GD**, Mehta MP, Welsh JS, Chakravarti A, Rogers CL and **Fontanesi J** (2020). "Investigating low-dose thoracic radiation as a treatment for COVID-19 patients to prevent respiratory failure." *Radiation Research* 194(1): 1-8.

[Full Text](#)

*Department of Neurosurgery*

*Department of Surgery*

Won KB, **Lee BK**, Park HB, Heo R, Lee SE, Rizvi A, Lin FY, Kumar A, Hadamitzky M, Kim YJ, Sung JM, Conte E, Andreini D, Pontone G, Budoff MJ, Gottlieb I, Chun EJ, Cademartiri F, Maffei E, Marques H, De Araújo Gonçalves P, Leipsic JA, Shin S, Choi JH, Virmani R, Samady H, **Chinnaiyan K**, **Raff GL**, Stone PH, Berman DS, Narula J, Shaw LJ, Bax JJ, Min JK and Chang HJ (2020). "Quantitative assessment of coronary plaque volume change related to triglyceride glucose index: The Progression of Atherosclerotic Plaque Determined by Computed Tomographic Angiography IMaging (PARADIGM) registry." *Cardiovascular Diabetology* 19(1): 113.

[Full Text](#)

*Department of Radiation Oncology*

Background: The association between triglyceride glucose (TyG) index and coronary atherosclerotic change remains unclear. We aimed to evaluate the association between TyG index and coronary plaque progression (PP) using serial coronary computed tomography angiography (CCTA). Methods: A total of 1143 subjects (aged  $60.7 \pm 9.3$  years, 54.6% male) who underwent serial CCTA with available data on TyG index and diabetic status were analyzed from The Progression of Atherosclerotic Plaque Determined by Computed Tomographic Angiography IMaging (PARADIGM) registry. PP was defined as plaque volume (PV) (mm<sup>3</sup>) at follow-up minus PV at index > 0. Annual change of PV (mm<sup>3</sup>/year) was defined as PV change divided by inter-scan period. Rapid PP was defined as the progression of percent atheroma volume (PV divided by vessel volume multiplied by 100)  $\geq 1.0\%/year$ . Results: The median inter-scan period was 3.2 (range 2.6-4.4) years. All participants were stratified into three groups based on TyG index tertiles. The overall incidence of PP was 77.3%. Baseline total PV (group I [lowest]: 30.8 (0.0-117.7), group II: 47.2 (6.2-160.4), and group III [highest]: 57.5 (8.4-154.3);  $P < 0.001$ ) and the annual change of total PV (group I: 5.7 (0.0-20.2), group II: 7.6 (0.5-23.5), and group III: 9.4 (1.4-27.7);  $P = 0.010$ ) were different among all groups. The risk of PP (odds ratio [OR] 1.648; 95% confidence interval [CI] 1.167-2.327;  $P = 0.005$ ) and rapid PP (OR 1.777; 95% CI 1.288-2.451;  $P < 0.001$ ) was increased in group III compared to that in group I. TyG index had a positive and significant association with an increased risk of PP and rapid PP after adjusting for confounding factors. Conclusion: TyG index is an independent predictive marker for the progression of coronary atherosclerosis. Clinical registration ClinicalTrials.gov NCT02803411.

Wren JD, Bai Y, Qin ZS, **Yan D** and **Homayouni R** (2020). "Proceedings of the 2019 MidSouth Computational Biology and Bioinformatics Society (MCBIOS) conference." *BMC Bioinformatics* 21(Suppl 4): 254.

[Full Text](#)

*Department of Radiation Oncology*

*Department of Foundational Medical Studies (OU)*

Wright JO, Ho A, Kalma J, Koueiter D, Esterle J, **Marcantonio D, Wiater JM and Wiater B** (2019). "Uncemented reverse total shoulder arthroplasty as initial treatment for comminuted proximal humerus fractures." Journal of Orthopaedic Trauma 33(7): e263-e269.

[Full Text](#)

*Department of Diagnostic Radiology and Molecular Imaging*

*Department of Orthopaedic Surgery*

Objectives: To determine whether uncemented implants would provide similar outcomes while avoiding the complications associated with cement in the treatment of elderly patients with proximal humerus fractures (PHFs) with primary reverse total shoulder arthroplasty (RTSA). Design: Case series. Setting: A single Level I trauma center. Patients/Participants: A prospectively obtained cohort of 30 patients who underwent uncemented RTSA as initial treatment for a comminuted PHF: 4 male, 26 female; average age  $71 \pm 11$  years. Intervention: Uncemented RTSA. Main Outcome Measures: (1) Radiographic analysis, (2) postoperative clinical range of motion, and (3) functional outcome scores: the American Shoulder and Elbow Surgeons Shoulder score and the Simple Shoulder Test score. Results: Radiographic analysis showed 97% achieved stable humeral stem fixation and 70% had healing of the tuberosities in anatomical position. Average range of motion was  $130 \pm 31$  degrees of forward flexion,  $32 \pm 18$  degrees of external rotation, and internal rotation to the midlumbar spine. Average American Shoulder and Elbow Surgeons Shoulder score was  $82.0 \pm 13.5$  (with an average pain rating of  $0.8 \pm 1.3$ ), and average Simple Shoulder Test score was  $69.4\% \pm 19.1\%$ . Conclusions: Our data show that treatment of comminuted PHFs in elderly patients with uncemented RTSA can consistently produce good clinical outcomes with a low rate of complications and suggest that cement may not be necessary for RTSA in the trauma setting. Level of Evidence: Therapeutic Level IV. See Instructions for Authors for a complete description of levels of evidence.

**Yilmaz A, Ugur Z, Bisgin H, Akyol S, Bahado-Singh R, Wilson G, Imam K, Maddens ME and Graham SF** (2020).

"Targeted metabolic profiling of urine highlights a potential biomarker panel for the diagnosis of Alzheimer's Disease and mild cognitive impairment: A pilot study." Metabolites 10(9): 357.

[Full Text](#)

*Department of Internal Medicine*

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The lack of sensitive and specific biomarkers for the early detection of mild cognitive impairment (MCI) and Alzheimer's disease (AD) is a major hurdle to improving patient management. A targeted, quantitative metabolomics approach using both  $^1\text{H}$  NMR and mass spectrometry was employed to investigate the performance of urine metabolites as potential biomarkers for MCI and AD. Correlation-based feature selection (CFS) and least absolute shrinkage and selection operator (LASSO) methods were used to develop biomarker panels tested using support vector machine (SVM) and logistic regression models for diagnosis of each disease state. Metabolic changes were investigated to identify which biochemical pathways were perturbed as a direct result of MCI and AD in urine. Using SVM, we developed a model with 94% sensitivity, 78% specificity, and 78% AUC to distinguish healthy controls from AD sufferers. Using logistic regression, we developed a model with 85% sensitivity, 86% specificity, and an AUC of 82% for AD diagnosis as compared to cognitively healthy controls. Further, we identified 11 urinary metabolites that were significantly altered to include glucose, guanidinoacetate, urocanate, hippuric acid, cytosine, 2- and 3-hydroxyisovalerate, 2-ketoisovalerate, tryptophan, trimethylamine N oxide, and malonate in AD patients, which are also capable of diagnosing MCI, with a sensitivity value of 76%, specificity of 75%, and accuracy of 81% as compared to healthy controls. This pilot study suggests that urine metabolomics may be useful for developing a test capable of diagnosing and distinguishing MCI and AD from cognitively healthy controls.