OAKLAND UNIVERSITY WILLIAM BEAUMONT SCHOOL OF MEDICINE
PUBLICATION LIST
January - March 2020

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Abbas AE (2020). "Prosthesis-patient mismatch following transcatheter aortic valve replacement." JACC-Cardiovascular Interventions 13(1): 138.
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Department of Internal Medicine

Abbas AE, Mando R, **Hanzel GS**, **Shannon F**, **Gallagher M**, Kassas S, Al-Azizi K, Christensen J, Szerlip M, Potluri S, Harrington K and Mack M (2020). "Immediate post-TAVR simultaenous echocardiographic and invasive mean gradients in balloon vs. self-expanding valves: A multi-center retrospective study." Journal of the American College of Cardiology 75(11): 1490.
Full Text
Department of Internal Medicine
Department of Surgery

Background: Discordance between Echocardiographic (ECHO) and invasive (CATH) post-TAVR mean gradient (MG) has been reported. We sought to compare immediate post TAVR ECHO and CATH MG obtained simultaneously in balloon expanding (BEV) vs. self expanding valves (SEV) in a multicenter study. Methods: Post-TAVR ECHO and CATH MG were collected simultaneously and compared using Mann Whitney analysis in patients with aortic stenosis (AS) in BEV vs. SEV from 3 different institutions. Results: 366 patients were included in the study, 95/366 (26%) received a SEV and 271 (74%) received a BEV. ECHO/CATH discordance was present in both BEV and SEV to the same degree. No difference was noted in CATH and ECHO MGs between valve types (Figure 1). Conclusion: In a multicenter study, all valves regardless of type demonstrate significant ECHO/CATH discordance post-TAVR. There is no difference between CATH or ECHO MG between BEV and SEV immediately after TAVR.

Ades PA, Balady GJ, Berra K, **Franklin BA**, Froelicher V, Hamm LF, Kaminsky LA and Williams MA (2020). "The Journal of Cardiopulmonary Rehabilitation and Prevention at 40 years and its role in the evolution of cardiac rehabilitation." Journal of Cardiopulmonary Rehabilitation and Prevention 40(1): 2-8.
Full Text
Department of Internal Medicine

The maturing of a clinical discipline necessitates the ability to document scientific advancements and state-of-the-art reviews with a focus on clinical practice. Such was the case for the field of cardiac rehabilitation in 1981. Whereas a growing body of literature was demonstrating benefits of exercise in cardiac patients with regard to clinical, psychologic, and quality-of-life outcomes,1,2 there were still concerns about the safety of exercise and whether it could be widely adapted in clinical care. Since this was a time period when searches of online databases such as PubMed had not yet been established (began in 1996), there was a great value of concentrating much of the cardiac rehabilitation literature in a single journal. This commentary describes the conceptualization and implementation of the Journal of Cardiopulmonary Rehabilitation and Prevention from 1981 to the present and its acceptance as the official journal of the American Association of Cardiovascular and Pulmonary Rehabilitation and later the Canadian Association of Cardiac Rehabilitation. The commentary also highlights the journal's inclusion in Index Medicus in 1995, its receipt of an impact factor from International Scientific Indexing in 2007, and its publication of many important scientific statements, often in collaboration with major scientific organizations such as the American Heart Association and the American College of Cardiology.

Ahmed N, Mauad VAQ, Gomez-Rojas O, Sushea A, Castro-Tejada G, Michel J, Linares JM, Salles LP, Santos LC, Shan M, Nassir R, Montanez-Valverde R, Fabiano R, Danyi S, Hosseyni SH, Anand S, Ahmad U, Casteleins WA, Sanchez AT, Fouad A, Jacome A, Paiva M, Ruiz AGS, Grochowski RA, Toyama M, Nagi H, Sarvodelli MZ and **Halalau A** (2020). "The impact of rehabilitation-oriented virtual reality device in patients with ischemic stroke in the early subacute recovery phase: Study protocol for a phase III, single-blinded, randomized, controlled clinical trial." Journal of Central Nervous System Disease 12: 1-11.
Full Text
Department of Internal Medicine

Background and Rationale: Stroke is considered the most common cause of adult disability. Intensive rehabilitation protocols outperform nonintensive counterparts. The subacute stroke phase represents a potential window to recovery. Virtual reality (VR) has been shown to provide a more stimulating environment, allowing for increased patient compliance. However, the quality of current literature comparing VR with standard therapies is limited. Our aim is to measure the impact of VR versus standard therapy on the recovery of the upper limb motor function in patients with stroke in the early subacute recovery phase. Method: This is a randomized, controlled trial that will assign 262 patients to tailor-made standard rehabilitation (TMSR) or TMSR plus immersive VR device. The trial will be conducted in an urban rehabilitation clinic in the United States with expertise in the management of poststroke patients. Patients will be 18 to 70 years of age and in the early subacute period (30-90 days post ischemic stroke). The primary outcome will be the change of Fugl-Meyer Assessment-Upper Extremity (FMA-UE) score, measured at baseline and 13 weeks after randomization. The secondary outcome will be the change in the UK Functional Independence Measure and Functional Assessment Measure (UK FIM-FAM) score at the same time points. Discussion: If the use of VR in the rehabilitation of patients with stroke proves to have a significant impact on their motor recovery, it will constitute an extremely important step into decreasing the functional impairment associated with stroke and the related health care expense burden.

Al'Arefilb SJ, Maliakal G, Singh G, van Rosendael AR, Ma XY, Xu ZR, Alawamlh OA, Lee B, Pandey M, Achenbach S, Al-Mallah MH, Andreini D, Bax JJ, Berman DS, Budoff MJ, Cademartiri F, Canister TQ, Chang HJ, **Chinnaiyan K**, Chow BJW, Cury RC, DeLago A, Feuchtner G, Hadamitzky M, Hausleiter J, Kaufmann PA, Kim YJ, Leipsic JA, Maffei E, Marques H, Goncalves PD, Pontone G, **Raff GL**, Rubinshtein R, Villines TC, Gransar H, Lu Y, Jones EC, Pena JM, Lin FY, Min JK and Shaw LJ (2020). "Machine learning of clinical variables and coronary artery calcium scoring for the prediction of obstructive coronary artery disease on coronary computed tomography angiography: Analysis from the CONFIRM registry." European Heart Journal 41(3): 359-367.
Full Text
Department of Internal Medicine

Aims: Symptom-based pretest probability scores that estimate the likelihood of obstructive coronary artery disease (CAD) in stable chest pain have moderate accuracy. We sought to develop a machine [earning (ML) model,utilizing clinical factors and the coronary artery calcium score (CACS), to predict the presence of obstructive CAD on coronary computed tomography angiography (CCTA). Methods and Results: The study screened 35 281 participants enrolled in the CONFIRM registry, who underwent >= 64 detector row CCTA

evaluation because of either suspected or previously established CAD. A boosted ensemble algorithm (XGBoost) was used, with data split into a training set (80%) on which 10-fold cross-validation was done and a test set (20%). Performance was assessed of the (1) ML model (using 25 clinical and demographic features), (2) ML + CACS, (3) CAD consortium clinical score, (4) CAD consortium clinical score + CACS, and (5) updated Diamond-Forrester (UDF) score. The study population comprised of 13 054 patients, of whom 2380 (18.2%) had obstructive CAD (>= 50% stenosis). Machine learning with CACS produced the best performance [area under the curve (AUC) of 0.881] compared with ML alone (AUC of 0.773), CAD consortium clinical score (AUC of 0.734), and with CACS (AUC of 0.866) and UDF (AUC of 0.682), P < 0.05 for all comparisons. CACS, age, and gender were the highest ranking features. Conclusion: A ML model incorporating clinical features in addition to CACS can accurately estimate the pretest likelihood of obstructive CAD on CCTA. In clinical practice, the utilization of such an approach could improve risk stratification and help guide downstream management.

Alhousseini A, Romero R, Benshalom-Tirosh N, Gudicha D, Pacora P, Tirosh D, Kabiri D, Yeo L, Thachil J, Hsu CD, Hassan SS and Erez O (2020). "Nonovert disseminated intravascular coagulation (DIC) in pregnancy: A new scoring system for the identification of patients at risk for obstetrical hemorrhage requiring blood product transfusion." Journal of Maternal-Fetal & Neonatal Medicine Feb 3: 1-16.
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Department of Obstetrics & Gynecology

Background: Nonovert disseminated intravascular coagulation (DIC) is a subclinical hemostatic dysfunction that has not yet reached the decompensation stage. The detection of pregnant patients at this stage may assist in the identification of those who will develop severe obstetrical hemorrhage, as it is one of the leading causes for preventable maternal mortality. Currently, nonovert DIC is diagnosed by a scoring system based on nonpregnant patients, originally generated by the International Society on Thrombosis and Hemostasis (ISTH), which does not address the physiologic changes of the hemostatic system during pregnancy. Objectives: (1) To develop a pregnancy-specific nonovert DIC score, (2) to determine the diagnostic performance of this score in detecting women at risk for obstetrical hemorrhage requiring blood product transfusion, and (3) to compare it to the existing ISTH nonovert DIC score. Study Design: This retrospective study has longitudinal and cross-sectional components and includes three steps: (1) characterization of the longitudinal changes in the components of modified ISTH nonovert DIC scores, including these parameters - fibrinogen, antithrombin III, protein C, prothrombin time (PT), platelets, thrombin-antithrombin (TAT) complex, and D-dimer - during gestation in a group of normal pregnancies (n = 50); (2) development of a pregnancy-specific nonovert DIC score in a cross-sectional design of high-risk (n = 152) and control (n = 50) pregnancies, based on the predictive performance of each analyte for the detection of women at risk for obstetrical hemorrhage requiring blood product transfusion and a logistic regression model; and (3) comparison between the diagnostic performance of the pregnancy-specific nonovert DIC score and the modified ISTH nonovert DIC score to detect, upon admission, women who are at increased risk for subsequent development of obstetrical hemorrhage requiring blood product transfusion. Results: (1) The study cohort included 202 patients, of which 21 (10%) had obstetrical hemorrhage that required blood product transfusion and were considered to have nonovert DIC; (2) using the nonpregnant ISTH nonovert DIC score, 92% of the patients had a D-dimer concentration above the 0.5 mg/L threshold, and only 2% were identified to have a low fibrinogen concentration (<100 mg/dL); thus, this scoring system was unable to identify any of the patients with nonovert DIC based on the suggested cutoff of a score of >/=5; (3) the parameters included in the pregnancy-specific nonovert DIC score were selected based on their contribution to the performance of the model for the prediction of women at risk for obstetrical hemorrhage requiring blood product transfusion; as a result, we excluded the PT difference parameter from the score and the TAT complex concentration was added; and (4) a pregnancy-specific nonovert DIC score of >/=3 had a sensitivity of 71.4% and a specificity of 77.9% to identify patients at risk for obstetrical hemorrhage requiring blood product transfusion. Conclusion: We propose (1) a pregnancy-specific nonovert DIC score adjusted for the physiologic changes in the hemostatic system during gestation; and (2) that the pregnancy-specific nonovert DIC score can be a useful tool for the identification of patients at risk for obstetrical hemorrhage requiring blood product transfusion.

Almahariq MF, **Maywood MJ**, Levitin RB, Squires BS, **Jawad MS**, **Chen PY**, **Gustafson GS** and **Dilworth JT** (2020).

"Mapping of metastatic level I axillary lymph nodes in patients with newly diagnosed breast cancer." International Journal of Radiation Oncology, Biology, Physics 106(4): 811-820.
Full Text
Department of Radiation Oncology
OUWB Medical Student Author

Purpose: We examined the distribution of pretreatment nodal metastases to the level I axilla (Ax-L1) to assess the appropriateness of current breast atlases and provide guidelines in relationship to easily identifiable anatomic landmarks for accurate delineation of this lymph node (LN) basin. Methods and Materials: Patients with newly diagnosed breast cancer and biopsy-proven metastatic Ax-L1 LNs were identified. We related the location of each LN to its most adjacent rib and its distance from the bottom of the humeral head, axillary vessels, and a line connecting the anterior aspects of the pectoralis and latissimus dorsi muscles (P-L line). LNs were mapped onto a representative planning computed tomography scan, and their distribution was used to validate the current Radiation Therapy Oncology Group, European Society for Radiotherapy and Oncology, and Radiotherapy Comparative Effectiveness breast atlases. Furthermore, we examined metastases to a subregion encompassing the superolateral Ax-L1, irradiation of which correlates highly with lymphedema. Results: We identified 106 eligible patients with 107 biopsied LNs. All LNs fell between the second and fifth ribs (mean, 3.8 ± 0.56). Mean distance from the inferior aspect of the humeral head was 4.3 ± 1.6 cm (range, 0.3-8.4). Mean distance from the inferior aspect of the axillary vessels was 2.9 ± 1.5 cm (range, -0.6 to 5.4). Mean distance from the P-L line was 0.01 ± 1.9 cm (range, -2.2 to 2.4); negative and positive values denote medial or lateral to the P-L line. A Radiation Therapy Oncology Group-compliant Ax-L1 consensus contour, created from contours by 4 attending breast radiation oncologists, partially or fully missed 45% of mapped LNs. European Society for Radiotherapy and Oncology- and Radiotherapy Comparative Effectiveness-compliant Ax-L1 similarly missed 46% and 34% of mapped LNs, respectively. LNs were most frequently missed in the lateral direction. The superolateral Ax-L1 encompassed 9.3% of the mapped LNs. Conclusions: A significant percentage of at-risk Ax-L1 tissue falls outside current contouring atlases. We propose expansion of the recommended Ax-L1 borders, most notably in the lateral direction.

Almahariq MF, Quinn TJ, Siddiqui Z, **Jawad MS**, **Chen PY**, **Gustafson GS** and **Dilworth JT** (2020). "Breast conserving therapy is associated with improved overall survival compared to mastectomy in early-stage, lymph node-negative breast cancer." Radiotherapy and Oncology 142: 186-194.
Full Text
Department of Radiation Oncology

Background and Purpose: Recent retrospective studies suggest improved overall survival (OS) with breast conserving therapy (BCT), including breast conserving surgery and adjuvant whole breast radiotherapy, compared to mastectomy in the modern era. The patient subset most likely to benefit from BCT remains unclear, and the role of Oncotype DX Recurrence Score (RS) in this context is unknown. We compared BCT to mastectomy in early-stage, node-negative breast cancer. We further explored outcomes after stratification by RS and age. Materials and Methods: We performed a matched-cohort analysis of National Cancer Database (NCDB) patients with pT1-2, pN0, cM0 breast cancer treated between 2006 and 2014 with BCT or mastectomy. Patients were matched for all available baseline characteristics using propensity scores with inverse probability of treatment weighting (IPTW) with stabilized weights. Results: We identified 144,263 eligible patients treated with BCT and 87,379 patients treated with mastectomy. After IPTW-matching, OS was higher with BCT compared to mastectomy: 5-year OS of 94.4% vs. 91.8% (P < 0.001) and 7-year OS of 90% vs. 85.2% (P < 0.001). Doubly robust multivariable analysis showed an association between BCT and improved OS (HR 0.66, 95% CI, 0.64-0.69, P < 0.001). In a subset analysis, BCT was associated with improved OS in patients with RS >25, but not patients with RS <= 25. When stratified by age, only patients >50 years had improved OS with BCT. Conclusion: BCT is associated with improved OS compared to mastectomy in women with early-stage, node-negative breast cancer. The improvement in OS with BCT appears to be most pronounced in patients with high RS and >50 years of age. Prospective validation of these findings is required.

Almahariq MF, Quinn TJ, Siddiqui ZA, Thompson AB, **Jawad MS**, **Chen PY**, **Gustafson GS** and **Dilworth JT** (2020). "Post-mastectomy radiotherapy is associated with improved overall survival in T3N0 patients who do not receive chemotherapy." Radiotherapy and Oncology 145: 229-237.

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Department of Radiation Oncology

Background and Purpose: There is limited retrospective evidence addressing the utility of post-mastectomy radiotherapy (PMRT) in patients with T3N0 breast cancer. We performed a retrospective analysis of the National Cancer Database (NCDB) comparing overall survival (OS) in T3N0 patients treated with mastectomy alone (MTX) or with PMRT. Materials and Methods: We performed a matched-cohort analysis of NCDB breast cancer patients with pT3N0 disease who did not receive NAC, or cT3N0 patients who received NAC treated between 2006 and 2014. Patients were matched for all available baseline characteristics using propensity scores with inverse probability of treatment weighting (IPTW) with stabilized weights. Results: We identified 13,901 eligible patients. In the pT3N0 cohort, median follow-up was 47 months for the MTX group and 50 months for the PMRT group. In the cT3N0 cohort, median follow-up was 44 months for the MTX group and 46 months for the PMRT group. OS was higher in pT3N0 patients treated with PMRT compared to MTX: 7-year OS of 74% vs. 65% ($P < 0.001$). Doubly robust multivariable analysis showed an association between PMRT and improved OS (HR 0.78, 95% CI 0.68-0.89, $P < 0.001$). There was no benefit to PMRT in patients who received adjuvant chemotherapy (AC). In the NAC cohort, PMRT did not change OS, with 7-year OS of 78% with MTX and 79% with PMRT. There was a trend of improved OS with PMRT in patients with residual disease in the breast and lymph nodes (HR 0.70, 95% CI 0.46-1.07). Conclusion: PMRT improves OS in patients with pT3N0 disease, but the benefit appears limited to those who do not receive AC. PMRT does not improve OS in patients with cT3N0 disease who receive NAC, but there might be a benefit in patients with a poor response to chemotherapy. However, longer follow-up may be needed to make a definitive conclusion about the benefit of PMRT in patients who receive chemotherapy.

Alslaim HS, **Banooni AB**, Shaltaf A and **Novotny NM** (2020). "Tracheoesophageal fistula in the developing world: Are we ready for thoracoscopic repair?" Pediatric Surgery International 30: 649-654.

Full Text

Department of Surgery

Department of Anesthesiology

Purpose: Tracheoesophageal fistula (TEF) is a bellwether for a country's ability to care for sick newborns. We aim to review the existing literature from low- and middle-income countries in regard to management of those newborns and the possible approaches to improve their outcomes. Methods: A review of the existing English literature was conducted with the aim of assessing challenges faced by providers in LMIC in terms of diagnostic, preoperative, operative and post-operative care for TEF patients. We also review the limited literature for performing thoracoscopic repair in the developing world context and suggest methods for introduction of advanced thoracoscopic procedures including techniques for providing anesthesia to these challenging babies. Results: While outcomes related to technique from LMIC are comparable to the developed world, rates of secondary complications like sepsis and pneumonia are higher. In many areas, repairs are conducted in a staged fashion with minimal utilization of thoracoscopic approach. The paucity of resources creates strain on intraoperative and post-operative management. Conclusion: Clearly, not all developing world contexts are ready to attempt thoracoscopic repair but we outline suggestions for assessing the existing capabilities and a stepwise gradual implementation of advanced thoracoscopy when appropriate.

Anusim N, Ionescu F, Afolayan-Oloye O and **Gaikazian SS** (2020). "Diffuse large B-cell lymphoma of the vagina in pregnancy." BMJ Case Reports 13(1): 1-3.

Full Text

Department of Internal Medicine

A 28-year-old primigravida was evaluated for complaints of difficulty urinating and pelvic pain of 6-weeks duration. She denied fever, night sweats, weight loss or fatigue. Pelvic ultrasonography revealed a single fetal pole with cardiac activity and a 7cm mass in the anterior vagina which encased the urethra. The diagnosis of diffuse large B-cell lymphoma germinal centre type was made on analysis of biopsied pelvic mass. Whole body MRI revealed the disease was limited to the vagina. The patient received six cycles of Rituximab-cyclophosphamide, doxorubicin, vincristine and prednisone with significant improvement in her symptoms. Serial ultrasounds over the subsequent months showed appropriate development of the fetus. Whole body MRI after treatment showed decreased size and decreased signal of the primary pelvic mass compatible with

favourable treatment response. Challenges in the management of this rare presentation of lymphoma are discussed.

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. ePub Ahead of Print.
Request Form
Department of Internal Medicine

A 63-year-old woman was seen with hematemesis, melena, acute decline in hemoglobin level (from 13.9 to 10.9 g/dL), profound tachycardia (122 beats per minute, irregularly irregular pulse), and blood pressure of 140/72 mm Hg 1 month after pulmonary vein isolation and catheter ablation (performed for sotalol-refractory paroxysmal atrial fibrillation) with the use of extremely high ablative energy because of complex electrophysiologic anatomy with failure to convert to sinus rhythm. The patient was administered long-term dabigatran (she was allergic to warfarin) for atrial fibrillation.

Assar S, Mando R, Gaines R, **Hanzel GS**, **Shannon F**, **Hanson I**, **Lau W**, **Almany S**, **Safian RD**, **Kerner N**, **Gallagher M**, Vivacqua A and **Abbas AE** (2020). "The effect of flow and gradient on the acceleration and ejection times and their ratio in patients with severe aortic stenosis." Journal of the American College of Cardiology 75(11): 1602.
Full Text
Department of Internal Medicine
Department of Surgery
Department of Anesthesiology

Background: Accurate assessment of aortic stenosis (AS) severity is essential in management of the disease. Prior studies have demonstrated that ejection dynamics, particularly the ratio of acceleration time (AT) to ejection time (ET) can be used to assess severity. The aim of this study was to evaluate the effect of flow and gradient on AT, ET and AT/ET in patients with severe aortic stenosis. Methods: We retrospectively studied patients who underwent TAVR for severe AS from 10/14 to 8/18. Patients were divided into cohorts; low flow (LF) vs. normal flow (NF) based on stroke volume index (SVI) < or ≥ 35 ml/m2, and low gradient (LG) vs. high gradient (HG) based on mean gradient (MG) < or ≥ 40 mmHg. Mann-Whitney U test and Wilcoxon signed-rank test were used to compare AT, ET and AT/ET ratio within the cohorts. Results: 211 patients were included (age 83 ± 8 years, 45% women). In LF patients, AT/ET was higher (0.364 ±.007), than NF patients (0.307 ± 0.007). AT decreased and ET increased in LF vs. NF. In LG patients, AT/ET was higher (0.354 ±.008) than HG (0.331 ± 0.06). AT was similar and ET was higher in HG vs. LG patients. Patients with LF/LG had the highest AT/ET, while NF/HG had the lowest AT/ET. (Figure 1) Conclusion: AT, ET, and AT/ET depend on both flow and gradient. Different cutoffs should be used according to the hemodynamic state in patients with AS.

Bahado-Singh RO, Turkoglu O, **Yilmaz A**, Kumar P, Zeb A, Konda S, Sherman E, Kirma J, Allos M, Odibo A, Maulik D and **Graham SF** (2020). "Metabolomic identification of placental alterations in fetal growth restriction." Journal of Maternal-Fetal and Neonatal Medicine. ePub Ahead of Print.
Request Form
Department of Obstetrics & Gynecology

Introduction: Fetal growth restriction (FGR), viz., birth weight <10th percentile is a common pregnancy complication which increases the risk of adverse fetal and newborn outcomes. The placenta is the key organ for fetal growth as it controls oxygen and nutrient availability. This study aims to elucidate the mechanisms of and identify putative placental biomarkers for FGR using high-resolution metabolomics. Methods: Placenta samples from 19 FGR cases and 30 controls were analyzed using proton magnetic resonance (1H NMR) spectroscopy and direct flow injection mass spectrometry with reverse-phase liquid-chromatography mass spectrometry (DI-LC-MS/MS). Significant concentration differences (p-value <.05) in 179 of the 220 metabolites were measured. Results: Of the 179 metabolites, 176 (98.3%) had reduced placental levels in FGR cases. The best performing metabolite model: 3-hydroxybutyrate, glycine and PCaaC42:0 achieved an AUC (95% CI) = 0.912 (0.814–1.000) with a sensitivity of 86.7% and specificity of 84.2% for FGR detection. Metabolite set enrichment analysis (MSEA) revealed significant (p <.05) perturbation of multiple placental metabolite pathways including urea metabolism, ammonia recycling, porphyrin metabolism, bile acid biosynthesis, galactose metabolism and perturbed protein biosynthesis. Conclusion: The placental metabolic

pathway analysis revealed abnormalities that are consistent with fetal hepatic dysfunction in FGR. Near global reduction of metabolite concentrations was found in the placenta from FGR cases and metabolites demonstrated excellent diagnostic accuracy for FGR detection.

Bahado-Singh RO, Vishweswaraiah S, Aydas B, **Yilmaz A**, Saiyed NM, Mishra NK, Guda C and **Radhakrishna U** (2020). "Precision cardiovascular medicine: Artificial intelligence and epigenetics for the pathogenesis and prediction of coarctation in neonates." Journal of Maternal-Fetal & Neonatal Medicine. ePub Ahead of Print.
Request Form
Department of Obstetrics & Gynecology

Background: Advances in omics and computational Artificial Intelligence (AI) have been said to be key to meeting the objectives of precision cardiovascular medicine. The focus of precision medicine includes a better assessment of disease risk and understanding of disease mechanisms. Our objective was to determine whether significant epigenetic changes occur in isolated, non-syndromic CoA. Further, we evaluated the AI analysis of DNA methylation for the prediction of CoA. Methods: Genome-wide DNA methylation analysis of newborn blood DNA was performed in 24 isolated, non-syndromic CoA cases and 16 controls using the Illumina HumanMethylation450 BeadChip arrays. Cytosine nucleotide (CpG) methylation changes in CoA in each of 450,000 CpG loci were determined. Ingenuity pathway analysis (IPA) was performed to identify molecular and disease pathways that were epigenetically dysregulated. Using methylation data, six artificial intelligence (AI) platforms including deep learning (DL) was used for CoA detection. Results: We identified significant (FDR p-value <= .05) methylation changes in 65 different CpG sites located in 75 genes in CoA subjects. DL achieved an AUC (95% CI) = 0.97 (0.80-1) with 95% sensitivity and 98% specificity. Gene ontology (GO) analysis yielded epigenetic alterations in important cardiovascular developmental genes and biological processes: abnormal morphology of cardiovascular system, left ventricular dysfunction, heart conduction disorder, thrombus formation, and coronary artery disease. Conclusion: In an exploratory study we report the use of AI and epigenomics to achieve important objectives of precision cardiovascular medicine. Accurate prediction of CoA was achieved using a newborn blood spot. Further, we provided evidence of a significant epigenetic etiology in isolated CoA development.

Bahado-Singh RO, Vishweswaraiah S, Er A, Aydas B, Turkoglu O, Taskin BD, Duman M, **Yilmaz D** and **Radhakrishna U** (2020). "Artificial Intelligence and the detection of pediatric concussion using epigenomic analysis." Brain Research 1726: 146510.
Full Text
Department of Obstetrics & Gynecology

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

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. ePub Ahead of Print.

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.

Balinski AM, **Karabon P**, **Pathangey G** and Abbas AE (2020). "Transcatheter aortic valve replacement temporal trends: Procedural volume impact on length of stay and readmissions." Journal of the American College of Cardiology 75(11): 1268.

Full Text

OUWB Medical Student Author

Department of Medical Education

Department of Internal Medicine

Background: Transcatheter aortic valve replacement (TAVR) is an alternative to surgery in patients with severe aortic stenosis. Procedural volume impacts mortality but little is known of its effect on length of stay (LOS) and readmissions. We examined the impact of TAVR procedural volume on LOS and hospital readmission rate from 2012 to 2016. Methods: 102,059 TAVR cases were identified in the 2012-2016 Nationwide Readmissions Database (NRD) and evaluated for any 30-day all-cause hospital readmissions. We defined annual hospital TAVR procedural volume as high-volume (≥ 100 cases/year), medium-volume (50-99 cases/year), and low-volume (< 50 cases/year). Numbers were discharge-weighted and the NRD survey design was considered. Rao-Scott chi-square tests, t-tests, and logistic regression were used. Results: From 2012 to 2016, mean TAVR procedural volume increased (229 cases to 300 cases; P = < 0.0001), but LOS (9.34 days to 5.35 days; P = < 0.0001) and 30-day readmissions (19.12% to 16.32%) decreased. Readmitted TAVR patient mortality was 4.72%. Readmission rate declined for high-volume (17.50% to 15.52%), medium-volume (20.36% to 15.57%), and low-volume (19.60% to 15.55%) hospitals (Fig. 1). Readmissions were lower in hospitals with ≥ 100 cases/year versus those with < 100 cases/year (15.13% vs 17.71%; P = < 0.0001). Conclusion: TAVR procedural volume was inversely associated with both average LOS and readmission rate from 2012 to 2016. Improved readmissions were associated with ≥ 100 TAVR cases/year.

Bastola S, Ojbindra K, Khanal S and **Halalau A** (2020). "Hepatitis-associated aplastic anemia from workout supplement: Rare but potentially fatal entity." SAGE Open Medical Case Reports 8: 2050313X20901937.
Full Text
Department of Internal Medicine

Hepatitis-associated aplastic anemia (HAAA) is a rare clinical syndrome characterized by bone marrow failure 1-3 months after development of hepatitis. Untreated, hepatitis-associated aplastic anemia has poor outcome and the mainstay of treatment remains either bone marrow transplant or immunosuppressive therapy. A previously healthy 21-year-old man presented with a 1-week history of right upper quadrant pain and jaundice. Admission labs revealed mixed hyperbilirubinemia and elevated transaminases ranging in 2000s IU/dl. Extensive workup for etiologies of acute hepatitis including viruses, autoimmune, toxins etc. were negative. He admitted to taking "Dust V2," a workout supplement, for 4 months prior to the presentation. His liver function tests started to improve after conservative treatment. Two months after his discharge, he was found to have severe pancytopenia on routine labs. Bone marrow biopsy revealed hypocellular marrow consistent with aplastic anemia. Extensive workup for etiologies of aplastic anemia were negative. On literature review, none of the components of the supplement were found to cause aplastic anemia. A diagnosis of hepatitis-associated aplastic anemia was made as there was a lag time before development of anemia. His counts failed to improve despite treatment with filgrastim and he was referred for hematopoietic cell transplant.

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

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

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. ePub Ahead of Print.
Request Form
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.

Boyanton BL, **Hanna MM**, **Hafez-Khayyata S** and **Robinson-Dunn B** (2020). "Fatal postpartum infection." Infectious Diseases in Clinical Practice 28(1): 53-54.
Request Form
Department of Internal Medicine
Department of Pathology

Brockman RM, Taylor JM, Segars LW, Selke V and **Taylor TAH** (2020). "Student perceptions of online and in-person microbiology laboratory experiences in undergraduate medical education." Medical Education Online 25(1): 1710324.
Full Text
Department of Foundational Medical Studies (OU)

Background: Universities are facing increased budget constraints, often resulting in reduced funds to support microbiology laboratories. Online mock laboratory activities are often instituted as a cost-effective alternative to traditional wet labs for medical students. Objective: The purpose of this study was to examine students' perceptions of online and in-person microbiology lab learning experiences. Design: We investigated undergraduate medical student perception of the in-person and online microbiology lab experience; 164 first-year medical students participated in newly designed online labs, while 83 second-year medical students continued to use in-person labs. An online survey was administered to collect student opinions of the lab experience. Results: In terms of student self-reported learning styles, those students who attended the lab in person were more likely to report a tactile learning style (33% vs 16%) while those students who learned the material online reported a visual learning style preference (77% vs 61%; n = 264). Students felt that the online microbiology lab was more convenient for their schedules when compared to the in-person lab. A greater proportion of online students (12%) felt that they encountered brand-new material on the final quiz than in-person students (1%; n = 245). Even so, 43% of the online educated students and 37% of the in-person educated students perceived their assigned lab experiences to be the optimal lab design, and over 89% of both groups reported a desire for at least some in-person instruction in a wet-laboratory environment. Conclusions: Our findings suggest that, while students are strongly supportive of digital online lab activities, the overwhelming majority of students still report a desire for a blend of online and in-person, hands-on laboratory activities. These findings will further research directed towards student perception of the lab experience and aid in the adaptation of microbiology curriculums to accommodate both student and university needs.

Campbell D and **Ditkoff J** (2020). "Evaluating hospital readmissions through the perspective of the returning emergency department patient." Quality Management in Health Care 29(1): 15-19.
Full Text
Department of Emergency Medicine

Background and Objective: Hospital readmissions have garnered attention over the last few years. The reasons are myriad, including penalties from the Centers for Medicare & Medicaid Services, as well as acknowledgment from hospitals that readmissions highlight failures in the treatment spectrum. The purpose of this project was to investigate patients' perspective of why they return to the emergency department (ED) within 30 days of discharge from the inpatient setting. Methods: A descriptive qualitative study was conducted in an attempt to elucidate causes of readmissions in our patient population. Detailed interviews of 80 patients who returned to the ED within 30 days of discharge were completed to determine patients' health status upon discharge, ability to obtain resources, and health status that prompted return for care.

Results: Of the 80 patients who returned, 64 were admitted to the hospital. The median time from discharge to return was 13.4 days. Pain was the most common reason for return to the ED. Of the 80 patients, only 19 followed up with a physician prior to return. Conclusions: The data show that once patients return to the ED after discharge, it is very likely they will be admitted to the hospital. An intervention prior to the return to the ED is imperative.

Cappell MS (2020). "Two case reports of novel syndrome of bizarre performance of gastrointestinal endoscopy due to toxic encephalopathy of endoscopists among 181767 endoscopies in a 13-year-university hospital review: Endoscopists, first do no harm!" World Journal of Gastroenterology 26(9): 984-991.
Full Text
Department of Internal Medicine

Background: Although deficient procedures performed by impaired physicians have been reported for many specialists, such as surgeons and anesthesiologists, systematic literature review failed to reveal any reported cases of deficient endoscopies performed by gastroenterologists due to toxic encephalopathy. Yet gastroenterologists, like any individual, can rarely suffer acute-changes-in-mental-status from medical disorders, and these disorders may first manifest while performing gastrointestinal endoscopy because endoscopy comprises so much of their workday. Case Summaries: Among 181767 endoscopies performed by gastroenterologists at William-Beaumont-Hospital at Royal-Oak, two endoscopies were performed by normally highly qualified endoscopists who manifested bizarre endoscopic interpretation and technique during these endoscopies due to toxic encephalopathy. Case-1-endoscopist repeatedly insisted that gastric polyps were colonic polyps, and absurdly "pressed" endoscopic steering dials to "take" endoscopic photographs; Case-2-endoscopist repeatedly insisted that had intubated duodenum when intubating antrum, and wildly turned steering dials and bumped endoscopic tip forcefully against antral wall. Endoscopy nurses recognized endoscopists as impaired and informed endoscopy-unit-nurse-manager. She called Chief-of-Gastroenterology who advised endoscopists to terminate their esophagogastroduodenoscopies (fulfilling ethical imperative of "physician, first-do-no-harm"), and go to emergency room for medical evaluation. Both endoscopists complied. In-hospital-work-up revealed toxic encephalopathy in both from: case-1-urosepsis and left-ureteral-impacted-nephrolithiasis; and case-2-dehydration and accidental ingestion of suspected illicit drug given by unidentified stranger. Endoscopists rapidly recovered with medical therapy. Conclusion: This rare syndrome (0.0011% of endoscopies) may manifest abruptly as bizarre endoscopic interpretation and technique due to impairment of endoscopists by toxic encephalopathy. Recommended management (followed in both cases): 1-recognize incident as medical emergency demanding immediate action to prevent iatrogenic patient injury; 2- inform Chief-of-Gastroenterology; and 3-immediately intervene to abort endoscopy to protect patient. Syndromic features require further study.

Cappell MS, Stavropoulos SN and Friedel D (2020). "Updated systematic review of achalasia, with a focus on POEM therapy." Digestive Diseases & Sciences 65(1): 38-65.
Full Text
Department of Internal Medicine

Aim: To systematically review clinical presentation, diagnosis, and therapy of achalasia, focusing on recent developments in high-resolution esophageal manometry (HREM) for diagnosis and peroral endoscopic myotomy (POEM) for therapy. Methods: Systematic review of achalasia using computerized literature search via PubMed and Ovid of articles published since 2005 with keywords ("achalasia") AND ("high resolution" or "HREM" or "peroral endoscopic myotomy" or "POEM"). Two authors independently performed literature searches and incorporated articles into this review by consensus according to prospectively determined criteria. Results: Achalasia is an uncommon esophageal motility disorder, usually manifested by dysphagia to solids and liquids, and sometimes manifested by chest pain, regurgitation, and weight loss. Symptoms often suggest more common disorders, such as gastroesophageal reflux disease (GERD), thus often delaying diagnosis. Achalasia is a predominantly idiopathic chronic disease. Diagnosis is typically suggested by barium swallow showing esophageal dilation; absent distal esophageal peristalsis; smoothly tapered narrowing ("bird's beak") at esophagogastric junction; and delayed passage of contrast into stomach. Diagnostic findings at high-resolution esophageal manometry (HREM) include: distal esophageal aperistalsis and integrated relaxation pressure (trough LES pressure during 4 s) > 15 mmHg. Achalasia is classified by HREM into: type 1 classic; type 2 compartmentalized high pressure in esophageal body, and type 3 spastic.

This classification impacts therapeutic decisions. Esophagogastroduodenoscopy is required before therapy to assess esophagus and esophagogastric junction and to exclude distal esophageal malignancy. POEM is a revolutionizing achalasia therapy. POEM creates a myotomy via interventional endoscopy. Numerous studies demonstrate that POEM produces comparable, if not superior, results compared to standard laparoscopic Heller myotomy (LHM), as determined by LES pressure, dysphagia frequency, Eckardt score, hospital length of stay, therapy durability, and incidence of GERD. Other therapies, including botulinum toxin injection and pneumatic dilation, have moderately less efficacy and much less durability than POEM. Conclusion: This comprehensive review suggests that POEM is equivalent or perhaps superior to LHM for achalasia in terms of cost efficiency, hospital length of stay, and relief of dysphagia, with comparable side effects. The data are, however, not conclusive due to sparse long-term follow-up and lack of randomized comparative clinical trials. POEM therapy is currently limited by a shortage of trained endoscopists.

Chancellor MB, Bartolone SN, **Lamb LE**, Ward E, **Zwaans BMM** and **Diokno A** (2020). "Underactive bladder: Review of progress and impact from the International CURE-UAB Initiative." International Neuro-Urology Journal 24(1): 3-11.
Full Text
Department of Urology

There is a significant need for research and understanding of underactive bladder (UAB). The International Congress of Urologic Research and Education on Aging UnderActive Bladder (CURE-UAB) was organized by Doctors Michael Chancellor and Ananias Diokno in order to address these concerns. CURE-UAB was supported, in part, by the US National Institute of Aging and National Institute of Diabetes Digestive and Kidney. Since 2014, there have been 5 successful CURE-UAB congresses. They have brought together diverse stakeholders in the UAB field to identify areas of major scientific challenge and initiated a call to action among the medical community. In this review, we will highlight current and novel treatments under development for UAB and the progress and impact from the CURE-UAB initiative.

Cheah C, **Hussein IH**, El Othmani A, **Rizvi SA**, Sayeed Z and El-Othmani MM (2020). "Assessing preoperative risk factors with sex disparities in total joint arthroplasty patients and financial outcomes from the National Inpatient Sample Database." The Journal of the American Academy of Orthopaedic Surgeons. ePub Ahead of Print.
Request Form
OUWB Medical Student Author
Department of Foundational Medical Studies (OU)

Introduction: Disparities in the healthcare system imply potential risks for vulnerable groups whose needs are not appropriately met. Total joint arthroplasty (TJA) is successful in treating end-stage arthritis, resulting in increased demand for the procedure, however remains underused in both sexes, especially in women. Although multiple studies assessed the differences in postoperative morbidities between sexes, there remains a lack in understanding patients' preoperative clinical profile and nonclinical demographics. The aim of this study is to provide a population-based epidemiologic assessment of preoperative risk factors and sex disparities and assess differences in outcomes following TJA. Methods: The National Inpatient Sample database from 2006 to 2011 was analyzed. Patients who underwent primary total knee and hip arthroplasty were identified and stratified into two cohorts of male and female, and demographic data and comorbidities were collected. Postoperative complications, length of stay, total charges, and discharge destination were measured for matched cohorts. Results: Female patients present for TJAs at an older average age, are less likely to present with AIDS, alcohol abuse, coagulopathy, congestive heart failure, drug abuse, liver disease, peripheral vascular disease, and renal failure, and are more likely to present with anemia, autoimmune disorders, chronic obstructive pulmonary disease, depression, obesity, and valvular disease. Postoperatively, the average length of stay for female patients was markedly higher (3.52 versus 3.39) and a lower percentage went home (59% versus 73%). Overall, female patients experience greater odds of any complication while in-patient. Discussion: This study highlighted sex differences in areas that could account for the underuse of the procedure in both sexes, with women affected to a greater extent. Understanding these factors will help address the unmet needs of both sexes after TJA by encouraging future studies and provider education to ensure that all patients are able to access the necessary procedures for pain relief and functional improvement.

Chen B, **Kanaan C**, **Jaiyesimi I**, Ezekwudo D and **Swor R** (2020). "Clinical characteristics of patients with cancer

presenting to the emergency department and their use of Emergency Medical Service transport." Prehospital Emergency Care. ePub Ahead of Print.
Request Form
Department of Internal Medicine
OUWB Medical Student Author

Objectives: Although life-threatening emergencies for cancer patients are relatively rare, cancer patients often seek care in the emergency department. The use of emergency medical service (EMS) by these patients is not well studied. The aim of this study was to investigate the characteristics of cancer patients who present to the emergency department (ED) for care, and; compare characteristics of patients transported by EMS versus those transported by private vehicle. Methods: Our retrospective cohort study was conducted in an EMS system with 21,070 annual transports and an academic ED with 129,263 annual visits. Our study consisted of patients with a new diagnosis of cancer between January 1 and July 1, 2015 who subsequently presented to the ED between January 1, 2015 and July 1, 2017. Study variables included patient demographics, mode of ED arrival, cancer type and treatment, patient clinical characteristics and disposition. To describe differences in patient characteristics of EMS vs. private vehicle transport, we report variable frequencies and stratified them by mode of transport. Results: Of the 2,727 patients with a new diagnosis of cancer, 1,303 (47.8%) presented to the ED with a total of 3,590 visits in 30 months. EMS transported 22% of cancer patients to the ED versus 78% transported by private vehicle. Thus, cancer patients would make up approximately 1.5% (781/52,675) of all EMS transports during the study period. For those transported by EMS, the most common chief complaints were respiratory distress (16.0%), pain (15.4%), and neurological symptoms (12.6%). Patients with cancer of the lung/respiratory tract (21.5%), upper GI (12.4%), and CNS (11.0%) were most frequently transported by EMS. Older age, presence of CNS cancer, presentation with neurological or cardiovascular complaints, and higher acuity were significantly associated with EMS transport to ED, while gender and pain severity were not. Patients transported by EMS were more likely to be hospitalized and for greater than 2 days ($p < 0.0001$). Conclusions: Cancer patients frequently seek emergency care after initial diagnosis, most commonly present for symptom relief, and are often admitted. Patients transported by EMS are more likely to be admitted and for longer periods of time.

Chen CJ, Kearns KN, Ding D, Kano H, Mathieu D, Kondziolka D, Feliciano C, Rodriguez-Mercado R, **Grills IS**, Barnett GH, Dade Lunsford L and Sheehan JP (2020). "Stereotactic radiosurgery for arteriovenous malformations of the basal ganglia and thalamus: An international multicenter study." Journal of Neurosurgery 132(1): 122-131.
Request Form
Department of Radiation Oncology

Objective: Arteriovenous malformations (AVMs) of the basal ganglia (BG) and thalamus are associated with elevated risks of both hemorrhage if left untreated and neurological morbidity after resection. Therefore, stereotactic radiosurgery (SRS) has become a mainstay in the management of these lesions, although its safety and efficacy remain incompletely understood. The aim of this retrospective multicenter cohort study was to evaluate the outcomes of SRS for BG and thalamic AVMs and determine predictors of successful endpoints and adverse radiation effects. Methods: The authors retrospectively reviewed data on patients with BG or thalamic AVMs who had undergone SRS at eight institutions participating in the International Gamma Knife Research Foundation (IGKRF) from 1987 to 2014. Favorable outcome was defined as AVM obliteration, no post-SRS hemorrhage, and no permanently symptomatic radiation-induced changes (RICs). Multivariable models were developed to identify independent predictors of outcome. Results: The study cohort comprised 363 patients with BG or thalamic AVMs. The mean AVM volume and SRS margin dose were 3.8 cm3 and 20.7 Gy, respectively. The mean follow-up duration was 86.5 months. Favorable outcome was achieved in 58.5% of patients, including obliteration in 64.8%, with rates of post-SRS hemorrhage and permanent RIC in 11.3% and 5.6% of patients, respectively. Independent predictors of favorable outcome were no prior AVM embolization ($p = 0.011$), a higher margin dose ($p = 0.008$), and fewer isocenters ($p = 0.044$). Conclusions: SRS is the preferred intervention for the majority of BG and thalamic AVMs. Patients with morphologically compact AVMs that have not been previously embolized are more likely to have a favorable outcome, which may be related to the use of a higher margin dose.

Chernyaysky A, **Patel KG** and Grando SA (2020). "Mechanisms of synergy of autoantibodies to M3 muscarinic acetylcholine receptor and secretory pathway Ca2+/Mn2+-ATPase isoform 1 in patients with non-desmoglein

pemphigus vulgaris." International Immunopharmacology 80: 106149.
Request Form
OUWB Medical Student Author

Pemphigus vulgaris (PV) is a potentially lethal mucocutaneous blistering disease characterized by IgG auto antibodies (AuAbs) binding to epidermal keratinocytes and inducing a devastating blistering disease affecting oral and/or esophageal surfaces and, sometimes, also the skin. Anti-keratinocyte AuAbs developed by the desmoglein (Dsg) 1/3 AuAb-negative acute PV patients are pathogenic, as they induced acantholysis and epidermal split in the experimental models of PV in vitro and in vivo. These PV patients have various combinations of AuAbs to keratinocyte muscarinic acetylcholine receptor subtype M3 (M3AR), the secretory pathway Ca2+/Mn2+-ATPase isoform 1 (SPCA1), and desmocollin 3 whose relative concentrations correlate with the disease activity. In this study, we identified new molecular mechanisms of the synergistic cooperation of AuAbs to M3AR and SPCA1 in inducing acantholysis in the anti-Dsg 1/3 AuAb-negative PV patients. Anti-M3AR AuAb was found to play an important role in determining the level of intraepidermal split just above the basal cells, caspase to mediate early pro-apoptotic events triggered by anti-SPCA1 AuAb, and the neonatal Fc receptor (FcRn) to contribute to the pathobiological actions of both anti-M3AR and anti-SPCA1 AuAbs. Altogether, these novel results support our original hypothesis that pemphigus acantholysis is a complex disease process (also known as apoptolysis) initiated by AuAbs directed against different keratinocyte proteins that play important roles in supporting cell viability and regulating vital cell functions.

Chesnut R, Aguilera S, Buki A, Bulger E, Citerio G, Cooper DJ, Arrastia RD, Diringer M, Figaji A, Gao G, Geocadin R, Ghajar J, Harris O, Hoffer A, Hutchinson P, Joseph M, Kitagawa R, Manley G, Mayer S, Menon DK, Meyfroidt G, **Michael DB**, Oddo M, Okonkwo D, Patel M, Robertson C, Rosenfeld JV, Rubiano AM, Sahuquillo J, Servadei F, Shutter L, Stein D, Stocchetti N, Taccone FS, Timmons S, Tsai E, Ullman JS, Vespa P, Videtta W, Wright DW, Zammit C and Hawryluk GWJ (2020). "A management algorithm for adult patients with both brain oxygen and intracranial pressure monitoring: the Seattle International Severe Traumatic Brain Injury Consensus Conference (SIBICC)." Intensive Care Medicine. ePub Ahead of Print.
Full Text
Department of Neurosurgery

Background: Current guidelines for the treatment of adult severe traumatic brain injury (sTBI) consist of high-quality evidence reports, but they are no longer accompanied by management protocols, as these require expert opinion to bridge the gap between published evidence and patient care. We aimed to establish a modern sTBI protocol for adult patients with both intracranial pressure (ICP) and brain oxygen monitors in place. Methods: Our consensus working group consisted of 42 experienced and actively practicing sTBI opinion leaders from six continents. Having previously established a protocol for the treatment of patients with ICP monitoring alone, we addressed patients who have a brain oxygen monitor in addition to an ICP monitor. The management protocols were developed through a Delphi-method-based consensus approach and were finalized at an in-person meeting. Results: We established three distinct treatment protocols, each with three tiers whereby higher tiers involve therapies with higher risk. One protocol addresses the management of ICP elevation when brain oxygenation is normal. A second addresses management of brain hypoxia with normal ICP. The third protocol addresses the situation when both intracranial hypertension and brain hypoxia are present. The panel considered issues pertaining to blood transfusion and ventilator management when designing the different algorithms. Conclusions: These protocols are intended to assist clinicians in the management of patients with both ICP and brain oxygen monitors but they do not reflect either a standard-of-care or a substitute for thoughtful individualized management. These protocols should be used in conjunction with recommendations for basic care, management of critical neuroworsening and weaning treatment recently published in conjunction with the Seattle International Brain Injury Consensus Conference.

Chinnaiyan KM, **Safian RD**, **Gallagher ML**, George J, **Dixon SR**, **Bilolikar AN**, **Abbas AE**, **Shoukfeh M**, **Brodsky M**, Stewart J, Cami E, **Forst D**, **Timmis S**, Crile J and **Raff GL** (2020). "Clinical use of CT-derived fractional flow reserve in the emergency department." JACC - Cardiovascular Imaging 13(2): 452-461.
Request Form
Department of Internal Medicine

Objectives: This study sought to examine the feasibility, safety, clinical outcomes, and costs associated with

computed tomography-derived fractional flow reserve (FFRCT) in acute chest pain (ACP) patients in a coronary computed tomography angiography (CTA)-based triage program. Background: FFRCT is useful in determining lesion-specific ischemia in patients with stable ischemic heart disease, but its utility in ACP has not been studied. Methods: ACP patients with no known coronary artery disease undergoing coronary CTA and coronary CTA with FFRCT were studied. FFRCT <= 0.80 was considered positive for hemodynamicalty significant stenosis. Results: Among 555 patients, 297 underwent coronary CTA and FFRCT (196 negative, 101 positive), whereas 258 had coronary CTA only. The rejection rate for FFRCT was 1.6%. At 90 days, there was no difference in major adverse cardiac events (including death, nonfatal myocardial infarction, and unexpected revascularization after the index visit) between the coronary CTA and FFRCT groups (4.3% vs. 2.7%; p = 0.310). Diagnostic failure, defined as discordance between the coronary CTA or FFRCT results with invasive findings, did not differ between the groups (1.9% vs. 1.68%; p = NS). No deaths or myocardial infarction occurred with negative FFRCT when revascularization was deferred. Negative FFRCT was associated with higher nonobstructive disease on invasive coronary angiography (56.5%) than positive FFRCT (8.0%) and coronary CTA (22.9%) (p < 0.001). There was no difference in overall costs between the coronary CTA and FFRCT groups ($8,582 vs. $8,048; p = 0.550). Conclusions: In ACP, FFRCT is feasible, with no difference in major adverse cardiac events and costs compared with coronary CTA alone. Deferral of revascularization is safe with negative FFRCT, which is associated with higher nonobstructive disease on invasive angiography.

Choi JW, van Rosendael AR, Bax AM, van den Hoogen IJ, Gianni U, Baskaran L, Andreini D, De Cecco CN, Earls J, Ferencik M, Hecht H, Leipsic JA, Maurovich-Horvat P, Nicol E, Pontone G, Raman S, Schoenhagen P, Arbab-Zadeh A, Choi AD, Feuchtner G, Weir-McCall J, **Chinnaiyan K**, Whelton S, Min JK, Villines TC and Al'Aref SJ (2020). "The Journal of Cardiovascular Computed Tomography year in review – 2019." Journal of Cardiovascular Computed Tomography. ePub Ahead of Print.
Full Text
Department of Internal Medicine

The purpose of this review is to summarize the work published by the Journal of Cardiovascular Computed Tomography (JCCT) for the year 2019, highlighting original research and new guidelines.

Creagh S, **Macknis J** and **Zhang P** (2020). "A re-evaluation: Acute Kidney Injury (AKI) patterns are similar in human autopsy kidneys and rat kidneys despite differences in renal tubule structure." Laboratory Investigation 100(SUPPL 1): 6.
Request Form
Department of Pathology

Daley E and **Zaltz I** (2020). "Proximal femoral osteotomy," In Beaulé PE (ed). Hip Dysplasia: Understanding and Treating Instability of the Native Hip. Cham: Springer International Publishing. pp**:** 155-164.
Full Text
Department of Orthopaedic Surgery

The proximal femoral osteotomy is a valuable adjunct to the treatment of native hip instability and dysplasia. The indications for an osteotomy are diverse and may include correction of upper femoral deformity, improvement of articular congruity often in conjunction with acetabular procedures, reduction of risk of avascular necrosis in high-grade dysplasia, correction of gait abnormalities, and management of early-onset arthritis in young patients. Appropriate preoperative planning requires consideration of multiple factors including proximal femoral deformity in the sagittal, coronal, and frontal planes as well as the overall mechanical axis of the limb. Proper planning will optimize patient outcomes and minimize complications, including alteration in limb alignment, generation of limb length discrepancy, and creation of deformities that will potentially compromise subsequent surgical intervention, especially total hip arthroplasty. Finally, the choice of fixation, including blade plate, proximal femoral locking plate, and intramedullary nails, should be guided by surgical experience and comfort as well as the ability to restore biomechanics using any selected device.

Dallaghan GLB, **Ledford CH**, Ander D, Spollen J, Smith S, Graziano S and Cox SM (2020). "Evolving roles of clerkship directors: Have expectations changed?" Medical Education Online 25(1).
Full Text

Department of Foundational Medical Studies (OU)

Background: Physician educators directing medical student programs face increasingly more complex challenges to ensure students receive appropriate preparation to care for patients. The Alliance for Clinical Education (ACE) defined expectations of and for clerkship directors in 2003. Since then, much has changed in medical education and health care. Methods: ACE conducted a panel discussion at the 2016 Association of American Medical Colleges Learn Serve Lead conference, soliciting input on these expectations and the changing roles of clerkship directors. Using workshops as a cross-sectional study design, participants reacted to roles and responsibilities of clerkship directors identified in the literature using an audience response system and completing worksheets. Results: The participants represented different disciplines of medicine and ranged from clerkship directors to deans of curriculum. Essential clerkship director qualifications identified by participants included: enthusiasm, experience teaching, and clinical expertise. Essential tasks included grading and assessment and attention to accreditation standards. Participants felt clerkship directors need adequate resources, including budget oversight, full-time clerkship support, and dedicated time to be the clerkship director. To whom clerkship directors report was mixed. Clerkship directors look to their chair for career advice, and they also report to the dean to ensure educational standards are being met. Expectations to meet accreditation standards and provide exemplary educational experiences can be difficult to achieve if clerkship directors' time and resources are limited. Conclusions: Participant responses indicated the need for a strong partnership between department chairs and the dean's office so that clerkship directors can fulfill their responsibilities. Our results indicate a need to ensure clerkship directors have the time and resources necessary to manage clinical medical student education in an increasingly complex health care environment. Further studies need to be conducted to obtain more precise data on the true amount of time they are given to do that role.

Damiani G, Grossi E, Berti E, Conic RRZ, **Radhakrishna U**, Pacifico A, Bragazzi NL, Piccinno R and Linder D (2020). "Artificial neural networks allow response prediction in squamous cell carcinoma of the scalp treated with radiotherapy." Journal of the European Academy of Dermatology and Venereology. ePub Ahead of Print.
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Department of Obstetrics & Gynecology

Background: Epithelial neoplasms of the scalp account for approximately 2% of all skin cancers and for about 10-20% of the tumours affecting the head and neck area. Radiotherapy is suggested for localized cutaneous squamous cell carcinomas (cSCC) without lymph node involvement, multiple or extensive lesions, for patients refusing surgery, for patients with a poor general medical status, as adjuvant for incompletely excised lesions and/or as a palliative treatment. To date, prognostic risk factors in scalp cSCC patients are poorly characterized. Objective: To identify patterns of patients with higher risk of postradiotherapy recurrence. Methods: A retrospective observational study was performed on scalp cSCC patients with histological diagnosis who underwent conventional radiotherapy (50-120 kV) (between 1996 and 2008, follow-up from 1 to 140 months, median 14 months). Out of the 79 enrolled patients, 22 (27.8%) had previously undergone a surgery. Two months after radiotherapy, 66 (83.5%) patients achieved a complete remission, 6 (7.6%) a partial remission, whereas 2 (2.5%) proved non-responsive to the treatment and 5 cases were lost to follow-up. Demographical and clinical data were preliminarily analysed with classical descriptive statistics and with principal component analysis. All data were then re-evaluated with a machine learning-based approach using a 4th generation artificial neural networks (ANNs)-based algorithm. Results: Artificial neural networks analysis revealed four scalp cSCC profiles among radiotherapy responsive patients, not previously described: namely, (i) stage T2 cSCC type, aged 70-80 years; (ii) frontal cSCC type, aged <70 years; (iii) non-recurrent nodular or nodulo-ulcerated, stage T3 cSCC type, of the vertex and treated with >60 Grays (Gy); and (iv) flat, occipital, stage T1 cSCC type, treated with 50-59 Gy. The model uncovering these four predictive profiles displayed 85.7% sensitivity, 97.6% specificity and 91.7% overall accuracy. Conclusions: Patient profiling/phenotyping with machine learning may be a new, helpful method to stratify patients with scalp cSCCs who may benefit from a RT-treatment.

Daram NR, Jordan KL, Dadi PK, Berry L and Jacobson DA (2020). "Glucagon-like peptide 1 shows glucose dependence in regulating islet hormone secretion." Metabolism-Clinical and Experimental 104: 154069.
Request Form

OUWB Medical Student Author

Dess RT, Sun YL, Muenz DG, Paximadis PA, Dominello MM, **Grills IS**, Kestin LL, Movsas B, Masi KJ, Matuszak MM, Radawski JD, Moran JM, Pierce LJ, Hayman JA, Schipper MJ, Jolly S and Michigan Radiation Oncology Q (2020). "Cardiac dose in locally advanced lung cancer: Results from a statewide consortium." Practical Radiation Oncology 10(1): E27-E36.
Full Text
Department of Radiation Oncology

Purpose: The heart has been identified as a potential significant organ at risk in patients with locally advanced non-small cell lung cancer treated with radiation. Practice patterns and radiation dose delivered to the heart in routine practice in academic and community settings are unknown. Methods and Materials: Between 2012 and 2017, 746 patients with stage III non-small cell lung cancer were treated with radiation within the statewide Michigan Radiation Oncology Quality Consortium (MROQC). Cardiac radiation dose was characterized, including mean and those exceeding historical or recently proposed Radiation Therapy Oncology Group and NRG Oncology constraints. Sites were surveyed to determine dose constraints used in practice. Patient-, anatomic-, and treatment-related associations with cardiac dose were analyzed using multivariable regression analysis and inverse probability weighting. Results: Thirty-eight percent of patients had a left-sided primary, and 80% had N2 or N3 disease. Median prescription was 60 Gy (interquartile range, 60-66 Gy). Twenty-two percent of patients were prescribed 60 Gy in 2012, which increased to 62% by 2017 (P < .001). Median mean heart dose was 12 Gy (interquartile range, 5-19 Gy). The volume receiving 30 Gy (V30 Gy) exceeded 50% in 5% of patients, and V40 Gy was >35% in 3% of cases. No heart dose constraint was uniformly applied. Intensity modulated radiation therapy (IMRT) usage increased from 33% in 2012 to 86% in 2017 (P < .001) and was significantly associated with more complex cases (larger planning target volume, higher stage, and preexisting cardiac disease). In multivariable regression analysis, IMRT was associated with a lower percent of the heart receiving V30 Gy (absolute reduction = 3.0%; 95% confidence interval, 0.5%-5.4%) and V50 Gy (absolute reduction = 3.6%; 95% confidence interval, 2.4%-4.8%) but not mean dose. In inverse probability weighting analysis, IMRT was associated with 29% to 48% relative reduction in percent of the heart receiving V40-V60 Gy without increasing lung or esophageal dose or compromising planning target volume coverage. Conclusions: Within MROQC, historical cardiac constraints were met in most cases, yet 1 in 4 patients received a mean heart dose exceeding 20 Gy. Future work is required to standardize heart dose constraints and to develop treatment approaches that allow for constraints to be met without compromising other planning goals.

Dokter J, Tennyson LE, Nguyen L, Han E and **Sirls LT** (2020). "The clinical rate of antibiotic change following empiric treatment for suspected urinary tract infections." International Urology and Nephrology 52(3): 431-436.
Full Text
OUWB Medical Student Author
Department of Urology

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

Douglas JK, Callahan RE, Hothem ZA, Cousineau CS, Kawak S, Thibodeau BJ, Bergeron S, **Li W**, **Peeples CE** and

Wasvary HJ (2020). "Genomic variation as a marker of response to neoadjuvant therapy in locally advanced rectal cancer." Molecular & Cellular Oncology. ePub Ahead of Print.
Request Form
Department of Surgery
Department of Pathology

There is variation in the responsiveness of locally advanced rectal cancer to neoadjuvant chemoradiation, from complete response to total resistance. This study compared genetic variation in rectal cancer patients who had a complete response to chemoradiation versus poor response, using tumor tissue samples sequenced with genomics analysis software. Rectal cancer patients treated with chemoradiation and proctectomy June 2006-March 2017 were grouped based on response to chemoradiation: those with no residual tumor after surgery (CR, complete responders, AJCC-CPR tumor grade 0, n = 8), and those with poor response (PR, AJCC-CPR tumor grade two or three on surgical resection, n = 8). We identified 195 variants in 83 genes in tissue specimens implicated in colorectal cancer biopathways. PR patients showed mutations in four genes not mutated in complete responders: KDM6A, ABL1, DAXX-ZBTB22, and KRAS. Ten genes were mutated only in the CR group, including ARID1A, PMS2, JAK1, CREBBP, MTOR, RB1, PRKAR1A, FBXW7, ATM C11orf65, and KMT2D, with specific discriminating variants noted in DMNT3A, KDM6A, MTOR, APC, and TP53. Although conclusions may be limited by small sample size in this pilot study, we identified multiple genetic variations in tumor DNA from rectal cancer patients who are poor responders to neoadjuvant chemoradiation, compared to complete responders.

Ducatman BS, Ducatman AM, Crawford JM, Laposata M and Sanfilippo F (2020). "The value proposition for pathologists: A population health approach." Academic Pathology 7: 2374289519898857.
Full Text
Department of Foundational Medical Studies (OU)

The transition to a value-based payment system offers pathologists the opportunity to play an increased role in population health by improving outcomes and safety as well as reducing costs. Although laboratory testing itself accounts for a small portion of health-care spending, laboratory data have significant downstream effects in patient management as well as diagnosis. Pathologists currently are heavily engaged in precision medicine, use of laboratory and pathology test results (including autopsy data) to reduce diagnostic errors, and play leading roles in diagnostic management teams. Additionally, pathologists can use aggregate laboratory data to monitor the health of populations and improve health-care outcomes for both individual patients and populations. For the profession to thrive, pathologists will need to focus on extending their roles outside the laboratory beyond the traditional role in the analytic phase of testing. This should include leadership in ensuring correct ordering and interpretation of laboratory testing and leadership in population health programs. Pathologists in training will need to learn key concepts in informatics and data analytics, health-care economics, public health, implementation science, and health systems science. While these changes may reduce reimbursement for the traditional activities of pathologists, new opportunities arise for value creation and new compensation models. This report reviews these opportunities for pathologist leadership in utilization management, precision medicine, reducing diagnostic errors, and improving health-care outcomes.

Edhi AI, Gjeorgjievski M, **Kulesza G** and **Cappell MS** (2020). "Esophagopericardial fistula from thermal injury after local abnormal ventricular activity arrhythmia ablation therapy: Endoscopic findings and therapy." Gastrointestinal Endoscopy 91(3): 709-711.
Request Form
Department of Internal Medicine

Edhi AI, Hakim S, **Shams C**, Bedi D, **Amin M** and **Cappell MS** (2020). "Clarithromycin-associated acute liver failure leading to fatal, massive upper gastrointestinal hemorrhage from profound coagulopathy: Case report and systematic literature review." Case Reports in Hepatology 2020: 2135239.
Full Text
Department of Surgery
Department of Internal Medicine
OUWB Medical Student Author

While erythromycin has caused numerous cases of acute liver failure (ALF), clarithromycin, a similar macrolide antibiotic, has caused only six reported cases of ALF. A new case of clarithromycin-associated ALF is reported with hepatic histopathology and exclusion of other etiologies by extensive workup, and the syndrome of clarithromycin-associated ALF is better characterized by systematic review. A 60-year-old nonalcoholic man, with normal baseline liver function tests, was admitted with diffuse abdominal pain and AST = 499 U/L and ALT = 539 U/L, six days after completing a 7-day course of clarithromycin 500 mg twice daily for suspected upper respiratory infection. AST and ALT each rose to about 1,000 U/L on day-2 of admission, and rose to >/=6,000 U/L on day-3, with development of severe hepatic encephalopathy and severe coagulopathy. Planned liver biopsy was cancelled due to coagulopathies. Extensive evaluation for infectious, immunologic, and metabolic causes of liver disease was negative. Abdominal computerized tomography and abdominal ultrasound with Doppler were unremarkable. The patient developed massive, acute upper gastrointestinal bleeding associated with coagulopathies. Esophagogastroduodenoscopy was planned after massive blood product transfusions, but the patient rapidly expired from hemorrhagic shock. Autopsy revealed a golden-brown heavy liver with massive hepatic necrosis and sinusoidal congestion. Rise of AST/ALT to about 1,000 U/L each was temporally incompatible with shock liver because this rise preceded the hemorrhagic shock, but the subsequent AST/ALT rise to >/=6,000 U/L each may have had a component of shock liver. The six previously reported cases were limited by failure to exclude hepatitis E (4), lack of liver biopsy (2), and uninterpretable liver biopsy (1) and by confounding potential etiologies including disulfiram, israpidine, or recent acetaminophen use (3), clarithromycin overdose (1), active alcohol use (1), and severe heart failure (1). Review of 6 previously reported and current case of clarithromycin-associated ALF revealed that patients had AST and ALT values in the thousands. Five patients died and 2 survived.

Edwards CT, Alslaim HS, Alebbini MM, **Evbuomwan M**, **Chan JC**, Hamouri S and **Novotny NM** (2020). "Contrasting esophageal coin removal in countries with different sized coins in circulation." International Journal of Pediatric Otorhinolaryngology 129: 109775.
Full Text
Department of Surgery
OUWB Medical Student Author

Farshad S, **Halalau A**, Townsend W and Schiopu E (2020). "Utility of Coronary Calcium Scoring (CCS) in Connective Tissue Disorders (CTDs) for the evaluation of subclinical coronary atherosclerosis: A systematic review." ACR Open Rheumatology 2(2): 84-91.
Full Text
Department of Internal Medicine

Objective: To assess the current state of knowledge for the utility of coronary calcium scoring (CCS) in connective tissue disorders (CTDs) as it relates to the presence and quantification of coronary atherosclerosis. Methods: Following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, a literature search via PubMed, Embase, Scopus, Web of Science Core Collection, CINAHL, and Cochrane Database of Systematic Review retrieved 1019 studies (since database inception on May 7, 2018) from which 121 manuscripts were eligible for review. Inclusion criteria consisted of studies that investigated CCS in adults with respective CTDs. Studies were excluded if a complete manuscript was not written in English or was a case report. Results: Thirty-one studies were included (27 with healthy age-/gender-matched control group for comparison and 4 without). CTDs analyzed in articles with control group: 11 rheumatoid arthritis (RA), 14 systemic lupus erythematosus (SLE), 4 systemic sclerosis (SSc), 1 idiopathic inflammatory myopathies (IIM), 1 Takayasu arteritis, and 1 psoriasis. Nine out of 11 RA studies, 12 out of 14 SLE studies, and 2 out of 4 SSc studies showed statistically significant increased CCS when compared with the control group. CTDs analyzed in studies without control group: two Kawasaki disease, one juvenile idiopathic arthritis (JIA), and one antiphospholipid syndrome (APS) article, which demonstrated increased coronary arterial calcium burden, however, without statistically significant data. Conclusion: CTDs, especially SLE and RA, are associated with higher CCS compared with the control group, indicating increased risk of coronary atherosclerosis. Our search did not elicit sufficient publications or statistically significant results in many other CTDs.

Fellous TG, Redpath AN, Fleischer MM, Gandhi S, Hartner SE, Newton MD, Francois M, Wong SP, Gowers KHC, Fahs

AM, Possley DR, Bonnet D, Urquhart P, Nicolaou A, **Baker KC** and Rankin SM (2020). "Pharmacological tools to mobilise mesenchymal stromal cells into the blood promote bone formation after surgery." NPJ Regenerative Medicine 5: 3.
Full Text
Department of Orthopaedic Surgery

Therapeutic approaches requiring the intravenous injection of autologous or allogeneic mesenchymal stromal cells (MSCs) are currently being evaluated for treatment of a range of diseases, including orthopaedic injuries. An alternative approach would be to mobilise endogenous MSCs into the blood, thereby reducing costs and obviating regulatory and technical hurdles associated with development of cell therapies. However, pharmacological tools for MSC mobilisation are currently lacking. Here we show that beta3 adrenergic agonists (beta3AR) in combination with a CXCR4 antagonist, AMD3100/Plerixafor, can mobilise MSCs into the blood in mice and rats. Mechanistically we show that reversal of the CXCL12 gradient across the bone marrow endothelium and local generation of endocannabinoids may both play a role in this process. Using a spine fusion model we provide evidence that this pharmacological strategy for MSC mobilisation enhances bone formation.

Fortin PT and Beaman DN (2020). "Revision of nonunion and malunion: Ankle arthrodesis," In Berkowitz MJ, Clare MP, Fortin PT, Schon LC and Sanders RW (ed). Revision Surgery of the Foot and Ankle: Surgical Strategies and Techniques. Cham: Springer International Publishing. pp**:** 313-334.
Full Text
Department of Orthopaedic Surgery

The causes of failed ankle arthrodesis are numerous. Failure can be defined in multiple ways including nonunion, bone loss, avascular bone, infection, wound breakdown, and continued pain. Successful boney fusion does not always translate to clinical success. Prominent implants, adjacent joint overload, subfibular impingement, limb malalignment, foot deformity, and chronic pain are additional reasons for clinical failure in the setting of radiographic union.

Friedman P, **Yilmaz A**, Ugur Z, Jafar F, **Whitten A**, Turkoglu O, **Graham S** and **Singh RB** (2020). "Maternal urine metabolomics and the prediction of fetal non-syndromic congenital heart defect (CHD)." American Journal of Obstetrics and Gynecology 222(1): S79.
Full Text
Department of Obstetrics & Gynecology

Fritz CG, **Bojrab DI, II**, Lin KF, **Schutt CA**, **Babu SC** and **Hong RS** (2020). "Surgical explantation of bone-anchored hearing devices: A 10-year single institution review." Otolaryngology - Head and Neck Surgery 162(1): 95-101.
Request Form
OUWB Medical Student Author
Department of Surgery

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

Gandhi SD, Fahs AM, Wahlmeier ST, Louie P, Possley DR, **Khalil JG** and **Park DK** (2020). "Radiographic fusion rates following a stand-alone interbody cage versus an anterior plate construct for adjacent segment disease after anterior cervical discectomy and fusion." Spine. ePub Ahead of Print.
Full Text
Department of Orthopaedic Surgery

Study Design: Case-Control. Objective: To evaluate fusion rates and compare a stand-alone cage construct with an anterior-plate construct in the setting revision ACDF for adjacent segment disease. Summary of Background Data: Anterior cervical discectomy and fusion is considered the gold standard of surgical treatment for cervical myelopathy and radiculopathy. One common consequence is adjacent segment disease. Treatment of adjacent segment disease is complicated by the prior surgical implants which may make application of an additional anterior cervical plate difficult. Stand-alone cage constructs obviate the need for removal or revision of prior implants in the setting of adjacent segment disease. Methods: All patients undergoing surgery for adjacent segment disease in a 2 year period were identified and separated into groups based on implant construct. A control group of patients undergoing primary, single level ACDF were selected from during the same 2 year period. Demographic variables, fusion rate and reoperation rate were compared between groups. Continuous variables were compared using Student's t-test, fusion and revision rates were compared using Pearson chi-square test. Results: Patients undergoing primary ACDF had lower age and ASA score as well as shorter operative time. Fusion rate was higher for primary ACDF compared to all patients who underwent ACDF for adjacent segment disease (95% vs 74%). When compared to primary ACDF, patients with a stand-alone cage construct had significantly lower fusion rate and (69% vs 95%) and higher re-operation rate (14% vs 0%). There were no significant differences in anterior plate construct versus stand-alone cage construct in terms of fusion and re-operation. Conclusions: Symptomatic adjacent segment disease can be managed surgically with either revision anterior plating or a stand-alone cage constructs, although our results raise questions regarding a difference in fusion rates that requires further investigation.

Gandhi SD, Wahlmeier ST, Louie P, Sauber R, **Tooley TR**, **Baker KC** and **Park DK** (2020). "Effect of local retropharyngeal steroids on fusion rate after anterior cervical discectomy and fusion." Spine Journal 20(2): 261-265.
Full Text
Department of Orthopaedic Surgery
OUWB Medical Student Author

Background Context: Anterior cervical discectomy and fusion (ACDF) is considered the gold standard surgical intervention for cervical myelopathy and radiculopathy. Obtaining a solid fusion is an important goal of ACDF, and doing so has correlated with favorable clinical outcomes. A common complication after surgery is postoperative dysphagia. Multiple techniques have been utilized in attempt to prevent and treat dysphagia, including use of retropharygeal steroids. Purpose: To examine the effects of retropharyngeal steroids on fusion rate in ACDF. Study Design: Case control. Methods: Forty-two patients who received local retropharyngeal steroids during ACDF surgery were the sample patient population. The control group consisted of matched cases based on number of spinal levels treated and age at approximately 1:2 case to control ratio. Data were collected on demographic variables, as well as operative and postoperative courses. Radiographic data were collected and fusion determined by <2 mm motion on flexion/extension views and bridging bone. Data were compared between case and control populations. Continuous variables were compared using Student's t test and nominal/ordinal values were compared using Z-test. Fusion status was assessed using Pearson chi-squared test. Results: A total of 121 patients were reviewed based on matching status and sufficient follow-up. The case and control groups were successfully matched based on age, spinal levels treated, and smoking status. The case group had an overall fusion rate of 64.7%, whereas the control group had a fusion rate of 91%. When analyzed at each level of attempted fusion, the case group had a fusion rate of 81% compared to 93% in the control group. There was a single patient in the case group that developed esophageal rupture and retropharygeal abscess requiring surgical intervention with irrigation, debridement and repair at 8 months after index operation. Conclusions: The use of retropharyngeal steroids to mitigate postoperative dysphagia is associated with a decreased rate of radiographic fusion in ACDF surgery.

Garber AJ, Handelsman Y, **Grunberger G**, Einhorn D, Abrahamson MJ, Barzilay JI, Blonde L, Bush MA, DeFronzo RA, Garber JR, Garvey WT, Hirsch IB, Jellinger PS, McGill JB, Mechanick JI, Perreault L, Rosenblit PD, Samson S and Umpierrez GE (2020). "Consensus statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the comprehensive type 2 diabetes management algorithim - 2020 executive summary." Endocrine Practice 26(1): 107-139.
Full Text
Department of Internal Medicine

Gebhard C, Maredziak M, Messerli M, Buechel RR, Lin F, Gransar H, Achenbach S, Al-Mallah MH, Andreini D, Bax JJ, Berman DS, Budoff MJ, Cademartiri F, Callister TQ, Chang HJ, **Chinnaiyan K**, Chow BJW, Cury RC, DeLago A, Feuchtner G, Hadamitzky M, Hausleiter J, Kim YJ, Leipsic J, Maffei E, Marques H, Gonçalves PA, Pontone G, Raff GL, Rubinshtein R, Shaw LJ, Villines TC, Lu Y, Jones EC, Peña JM, Min JK and Kaufmann PA (2020). "Increased long-term mortality in women with high left ventricular ejection fraction: Data from the CONFIRM (COronary CT Angiography EvaluatioN For Clinical Outcomes: An InteRnational Multicenter) long-term registry." European Heart Journal of Cardiovascular Imaging 21(4): 363-374.
Full Text
Department of Internal Medicine

Aims: There are significant sex-specific differences in left ventricular ejection fraction (LVEF), with a higher LVEF being observed in women. We sought to assess the clinical relevance of an increased LVEF in women and men. Methods and Results: A total of 4632 patients from the CONFIRM (COronary CT Angiography EvaluatioN For Clinical Outcomes: An InteRnational Multicenter) registry (44.8% women; mean age 58.7 ± 13.2 years in men and 59.5 ± 13.3 years in women, P = 0.05), in whom LVEF was measured by cardiac computed tomography, were categorized according to LVEF (low <55%, normal 55-65%, and high >65%). The prevalence of high LVEF was similar in both sexes (33.5% in women and 32.5% in men, P = 0.46). After 6 years of follow-up, no difference in mortality was observed in patients with high LVEF in the overall cohort (P = 0.41). When data were stratified by sex, women with high LVEF died more often from any cause as compared to women with normal LVEF (8.6% vs. 7.1%, log rank P = 0.032), while an opposite trend was observed in men (5.8% vs. 6.8% in normal LVEF, log rank P = 0.89). Accordingly, a first order interaction term of male sex and high LVEF was significant (hazard ratios 0.63, 95% confidence intervals 0.41-0.98, P = 0.043) in a Cox regression model of all-cause mortality adjusted for age, cardiovascular risk factors, and severity of coronary artery disease (CAD). Conclusion: Increased LVEF is highly prevalent in patients referred for evaluation of CAD and is associated with an increased risk of death in women, but not in men. Differentiating between normal and hyperdynamic left ventricles might improve risk stratification in women with CAD.

Ginsburg KB, Schwabe JR, Cochrane JA, Tapper A, **Burks F** and Rambhatla A (2020). "Low serum albumin correlates with adverse events following surgery for male urinary incontinence: Analysis of the American College of Surgeons National Surgical Quality Improvement Project." Urology 137: 178-182.
Full Text
Department of Urology

Objective: To investigate the incidence and risk factors associated with artificial urinary sphincter (AUS) and male urethral sling placement (MUS), revision, and removal.Methods: We identified CPT codes of patients undergoing AUS and sling placement, revision, and removal in the American College of Surgeons National Surgery Quality Improvement Program database. Bivariate analysis was used to compare preoperative parameters against adverse events of interest (Length of stay (LOS) >1, readmission, reoperation, other postoperative complications, and death). Variables that were significant or neared significance (P <.1) in the univariate analysis were entered into multivariable logistic regression models. Multivariable models were used to estimate the probability of adverse events.Results: About 2792 patients underwent surgical treatment for stress urinary incontinence in the American College of Surgeons National Surgery Quality Improvement Program database from 2008 to 2016. Increased length of stay was the most common adverse event (12.7%), followed by other postoperative complications (4.9%), readmission (4%), reoperation (2.3%), and death (0.3%). We noted an association between perioperative adverse events and preoperative hypoalbuminemia. Patients with preoperative hypoalbuminemia compared with patients with normal preoperative serum albumin had an increase predicted probability of LOS >1 day (42% vs 10%), readmission (10% vs 4%), reoperation (6% vs 2%), other postoperative complications (18% vs 4%) after adjusting for other

factors.Conclusion: Surgical treatment for stress urinary incontinence is well tolerated with acceptable levels of perioperative adverse events. Low serum albumin (<3.5 ng/dL) was associated with perioperative adverse events. These data may affect preoperative decision making and direct future quality improve efforts at the highest risk patients to help minimize perioperative morbidity and mortality.

Gite J, Milko E, Brady L and Baker SK (2020). "Phenotypic convergence in Charcot-Marie-Tooth 2Y with novel VCP mutation." Neuromuscular Disorders 30(3): 232-235.
Full Text
OUWB Medical Student Author

Charcot-Marie-Tooth (CMT) disease, a hereditary motor and sensory neuropathy, has subtypes with varied inheritance patterns and phenotypic presentation. Subtypes additionally vary by genetic variants in a number of genes. Pathogenic variants in the VCP gene have newly been associated with CMT type 2. We present a family with CMT type 2 with a novel heterozygous VCP variant and phenotypic variability between the proband, his brother, and father.

Goldstein JA (2020). "Cardiac tamponade in the interventional era: A paradigm shift in etiology and outcomes." Catheterization and Cardiovascular Interventions 95(3): 387-388.
Request Form
Department of Internal Medicine

Goldstein JA and Kern MJ (2020). "Hemodynamics of constrictive pericarditis and restrictive cardiomyopathy." Catheterization and Cardiovascular Interventions. ePub Ahead of Print.
Request Form
Department of Internal Medicine

Constrictive pericarditis (CP) and restrictive cardiomyopathy (RCM) are indolent disabling diseases of diastolic function. The two conditions share common pathophysiologic features, resulting in similar and overlapping clinical presentations, echocardiographic findings, and hemodynamic characteristics. However, their clinical course differs, as CP is surgically curable whereas RCM is a chronic condition managed medically. Separating these two entities is based on delineation of anatomic and physiologic derangements employing multimodality hemodynamic interrogation by advanced imaging techniques (Echo–Doppler, CT, and especially MRI) combined with sophisticated invasive hemodynamics.

Grunberger G (2020). "Continuous glucose monitoring: Musing on our progress in memory of Dr Andrew Jay Drexler." Journal of Diabetes. ePub Ahead of Print.
Full Text
Department of Internal Medicine

Grunberger G, Rosenfeld CR, Bode BW, Abbott SD, Nikkel C, Shi L and Strange P (2020). "Effectiveness of V-Go® for patients with type 2 diabetes in a real-world setting: A prospective observational study." Drugs Real World Outcomes 7(1): 31-40.
Full Text
Department of Internal Medicine

Background: V-Go is a wearable, patch-like, 24-h insulin delivery device that delivers both a continuous preset basal rate and on-demand bolus dosing. The aim of this study was to observe glycemic control, insulin dosing, and hypoglycemia risk in patients switched to V-Go in a real-world setting. The primary objective was to compare change in mean hemoglobin A1c (HbA1c) from baseline to the end of V-Go use. Methods: This prospective, open-label, multicenter study recruited patients with type 2 diabetes (T2D) and suboptimal glycemic control (HbA1c ≥ 7%) across 28 centers. Efficacy analyses were conducted for all patients with a post-baseline HbA1c and results stratified based on prior antihyperglycemic medication therapies. Insulin dosing was at the discretion of the health care provider and the protocol did not mandate glycemic targets. Treatment satisfaction surveys were utilized to gain patient feedback on the use of V-Go. Results: One hundred eighty-eight patients were enrolled in the study, among whom 140 patients had a valid post-baseline HbA1c and were included in the primary efficacy analysis. Use of V-Go resulted in a change of − 0.64%; (P = 0.003) in HbA1c from baseline, and in those prescribed insulin, the total daily dose

of insulin was decreased by 12 units/day (P < 0.0001). Twenty-two patients (12%) reported hypoglycemic events (≤ 70 mg/dL), with an event rate of 1.51 events/patient/year. Conclusion: In a T2D population with suboptimal HbA1c, initiating V-Go therapy in a real-world setting significantly improved glycemic control and led to significant insulin dose reductions. ClinicalTrial.gov registry identifier: NCT01326598.

Gualdoni J, Meka SG and **Bozyk PD** (2020). "Principles of nutrition in the critically ill patient," In Hyzy RC and McSparron J (ed). Evidence-Based Critical Care: A Case Study Approach. Cham: Springer International Publishing. pp**:** 545-550.
Full Text
Department of Internal Medicine

Nutrition in the critically ill patient is an important but often overlooked entity. After resuscitation, enteric feeds should be initiated as soon as technically feasible. Enteral nutrition (EN) has immunologic, anti-infectious, and functional benefits. Parenteral nutrition (PN) should only be considered in patients who do not have a functional gastrointestinal tract and have pre-existing protein-calorie malnutrition prior to the acute illness. Enteric feeds should not be withheld for gastric residuals or decreased bowel sounds. If a patient cannot tolerate full nutrition, a trophic feeding strategy may be used. Caloric and micronutrient goals still need further research as patients have differing individualized requirements based on their pre-illness nutritional status and illness severity scoring. Obese patients are often malnourished and should be treated the same as normal- or under-weight patients.

Gupta A, **Macknis J** and **Zhang P** (2020). "Immunohistochemistry panels to help understand differentiation and maturation of mesonephros and metanephros." Laboratory Investigation 100(SUPPL 1): 1735.
Request Form
Department of Pathology

Gupta A, **Menoch M**, **Levasseur K** and **Gonzalez IE** (2020). "Screening Pediatric Patients in New-Onset Syncope (SPINS) Study." Clinical Pediatrics 59(2): 127-133.
Request Form
Department of Emergency Medicine
Department of Pediatrics

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

Hafron JM (2020). "Practicing in a prostate cancer "revolution": Applying key insights from the PROCEED real-world registry to clinical practice." Urology Times 48(3): 48.
Full Text
Department of Urology

The article discusses the application of insights on immunotherapy from the PROCEED Registry (2011-2017) in 2020. It states that men with metastatic castration-resistant prostrate cancer (mCRPC) who were treated

with PROVENGE when their prostrate-specific antigen (PSA) levels were low have extended their lives a median of nearly four years. Also noted is the PROCEED registry findings' help in the clinical decisions of urologists with advanced prostrate cancer patients.

Hakim S, **Aneese AM**, Edhi A, **Shams C**, Purohit T, **Cannon ME** and **Cappell MS** (2020). "A statistically significant reduction in length of stay and hospital costs with equivalent quality of care metrics for ERCPs performed during the weekend versus postponed to weekdays: A 6-year study of 533 ERCPs at four teaching hospitals." Digestive Diseases and Sciences. ePub Ahead of Print.
Full Text
OUWB Medical Student Author
Department of Internal Medicine

Background: Endoscopic retrograde cholangiopancreatography (ERCP) is a diagnostic/therapeutic endoscopic procedure for numerous pancreaticobiliary diseases. Data regarding performing ERCP on weekend (WE; Saturday/Sunday) versus postponing ERCP to first two available weekdays (WD; Monday/Tuesday) are scarce. ERCP requires costly resources including specialized nurses, endoscopy room equipped with fluoroscopy, anesthesia services, and highly trained therapeutic endoscopists. Hospitals frequently do not have these resources readily available during WE, leading to postponing ERCPs to WD. AIMS: This study analyzes the effect of performing ERCP on WE versus postponement to WD on hospital efficiency, and on patient safety/outcomes. Methods: A computerized search of electronic medical records, January 2011-December 2016, at four Beaumont Hospitals retrospectively identified all gastroenterology consults performed on Friday or Saturday before 12:00 noon, which resulted in ERCP performed for any indication on WE versus postponing ERCP to WD. Length of stay (LOS), hospital costs, hospital charges, and hospital reimbursements were compared between both groups, as were quality of care measures. Results: Among 5196 patients undergoing ERCPs, 533 patients were identified, including 315 patients in the WE group and 218 patients in the WD group. Comparing WE versus WD groups, median LOS was shorter (4.5 days vs. 6.9 days, $p < 0.0001$); median hospital costs were less ($9208 vs. $11,657, $p < 0.0001$); and median hospital charges were less ($28,026 vs. $37,899, $p < 0.0001$). Median hospital reimbursements were not significantly different in WE versus WD groups ($10,277 vs. $10,362, $p = 0.65$). Median hospital charges were lower than median hospital reimbursements (net profit) in WE but not in WD. WE versus WD had no significant differences in morbidity, mortality, </= 30-day readmission rates, need for repeat ERCP </= 30 days, or post-ERCP complications. LIMITATIONS: This is a retrospective study. Conclusions: Performing ERCPs during weekends significantly reduced LOS, hospital costs, and hospital charges compared to postponing ERCP to WD and resulted in net hospital profits, without impairing quality of medical care.

Han D, Kolli KK, Al'Aref SJ, Baskaran L, van Rosendael AR, Gransar H, Andreini D, 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, Virmani R, Samady H, Stone P, Narula J, Berman DS, Bax JJ, Shaw LJ, Lin FY, Min JK and Chang HJ (2020). "Machine learning framework to identify individuals at risk of rapid progression of coronary atherosclerosis: From the PARADIGM registry." Journal of the American Heart Association 9(5): e013958.
Full Text
Department of Internal Medicine

Background: Rapid coronary plaque progression (RPP) is associated with incident cardiovascular events. To date, no method exists for the identification of individuals at risk of RPP at a single point in time. This study integrated coronary computed tomography angiography-determined qualitative and quantitative plaque features within a machine learning (ML) framework to determine its performance for predicting RPP. Methods and Results: Qualitative and quantitative coronary computed tomography angiography plaque characterization was performed in 1083 patients who underwent serial coronary computed tomography angiography from the PARADIGM (Progression of Atherosclerotic Plaque Determined by Computed Tomographic Angiography Imaging) registry. RPP was defined as an annual progression of percentage atheroma volume ≥1.0%. We employed the following ML models: model 1, clinical variables; model 2, model 1 plus qualitative plaque features; model 3, model 2 plus quantitative plaque features. ML models were compared with the atherosclerotic cardiovascular disease risk score, Duke coronary artery disease score, and a logistic regression statistical model. 224 patients (21%) were identified as RPP. Feature selection in ML

identifies that quantitative computed tomography variables were higher-ranking features, followed by qualitative computed tomography variables and clinical/laboratory variables. ML model 3 exhibited the highest discriminatory performance to identify individuals who would experience RPP when compared with atherosclerotic cardiovascular disease risk score, the other ML models, and the statistical model (area under the receiver operating characteristic curve in ML model 3, 0.83 [95% CI 0.78-0.89], versus atherosclerotic cardiovascular disease risk score, 0.60 [0.52-0.67]; Duke coronary artery disease score, 0.74 [0.68-0.79]; ML model 1, 0.62 [0.55-0.69]; ML model 2, 0.73 [0.67-0.80]; all P<0.001; statistical model, 0.81 [0.75-0.87], P=0.128). Conclusions: Based on a ML framework, quantitative atherosclerosis characterization has been shown to be the most important feature when compared with clinical, laboratory, and qualitative measures in identifying patients at risk of RPP.

Han E, Killinger KA, Turner KM, **Gilleran J**, Tenney D and **Peters KM** (2020). "Small fiber polyneuropathy in Hunner lesion and non-Hunner lesion interstitial cystitis/bladder pain syndrome." Female Pelvic Medicine & Reconstructive Surgery. ePub Ahead of Print.
Request Form
Department of Urology

Objective: This study aimed to determine whether small fiber polyneuropathy (SFPN) diagnosis differs between Hunner lesion interstitial cystitis/bladder pain syndrome (HL IC/BPS) and non-Hunner lesion IC/BPS (NHL IC/BPS). Methods: This was a pilot study of 20 women with IC/BPS. Results from baseline questionnaires, such as Genitourinary Pain Index, Interstitial Cystitis Symptom Index/Interstitial Cystitis Problem Index (ICSI/ICPI), Patient Health Questionnaire-2, were collected.Two punch biopsies were performed on each patient: distal leg and thigh. The samples were evaluated for intraepidermal nerve fiber density. One intraepidermal nerve fiber density less than the fifth percentile, regardless of site, indicated a positive SPFN diagnosis. Results: Twenty patients were enrolled; 10 HL IC/BPS and 10 NHL IC/BPS. The HL IC/BPS group was found to be significantly older than the NHL IC/BPS group (63 vs 48 years, P = 0.007). No significant differences were found in employment or relationship statuses, or in levels of education or comorbidities between the 2 groups.Sixty percent (6/10) of patients had SFPN in the NHL IC/BPS group compared with 40% (4/10) in the HL IC/BPS group. No significant differences were seen in SFPN positivity (P = 0.3) or Genitourinary Pain Index, Patient Health Questionnaire-2, or Interstitial Cystitis Symptom Index/Interstitial Cystitis Problem Index scores between the NHL and HL IC/BPS groups. Conclusions: Similar to previously published studies, 60% of NHL IC/BPS patients in this cohort were positive for SFPN compared with only 40% of the HL IC/BPS patients. Larger studies may be needed to realize the full impact of SFPN in IC/BPS.

Hanna A, Imam Z, Odish F and **Dalal B** (2020). "Multiple liver abscesses caused by Streptococcus intermedius bacteremia in the setting of a routine dental cleaning." BMJ Case Reports 13(2): e233097.
Full Text
Department of Internal Medicine

Streptococcus intermedius is a Gram-positive cocci, normally found in the oral cavity and gastrointestinal tract. It has been associated with deep-seated purulent abscesses commonly in the brain or liver in immunocompromised patients. Here, we discuss the case of a 21-year-old immunocompetent patient that presented with septic shock in the setting of multiple pyogenic liver abscesses with positive blood cultures for S. intermedius. The patient had a dental cleaning 3 months prior to admission. The abscesses resolved with ultrasound guided drainage and antibiotic therapy.

Hanna NH, Schneider BJ, Temin S, Baker S, Brahmer J, Ellis PM, Gaspar LE, Haddad RY, Hesketh PJ, Jain D, **Jaiyesimi I**, Johnson DH, Leighl NB, Phillips T, Riely GJ, Robinson AG, Rosell R, Schiller JH, Singh N, Spigel DR, Stabler JO, Tashbar J and Masters G (2020). "Therapy for stage IV non-small-cell lung cancer without driver alterations: ASCO and OH (CCO) joint guideline update." Journal of Clinical Oncology: JCO1903022.
Full Text
Department of Internal Medicine

Purpose: The aim of this work is to provide evidence-based recommendations updating the 2017 ASCO guideline on systemic therapy for patients with stage IV non-small-cell lung cancer (NSCLC) without driver alterations. A guideline update for patients with stage IV NSCLC with driver alterations will be published

separately. Methods: The American Society of Clinical Oncology and Ontario Health (Cancer Care Ontario) NSCLC Expert Panel made updated recommendations based on a systematic review of randomized controlled trials from December 2015 to 2019. Results: This guideline update reflects changes in evidence since the previous guideline update. Five randomized controlled trials provide the evidence base. Additional literature suggested by the Expert Panel is discussed. Recommendations: Recommendations apply to patients without driver alterations in epidermal growth factor receptor or ALK. For patients with high programmed death ligand 1 (PD-L1) expression (tumor proportion score [TPS] ≥ 50%) and non-squamous cell carcinoma (non-SCC), the Expert Panel recommends single-agent pembrolizumab. Additional treatment options include pembrolizumab/carboplatin/pemetrexed, atezolizumab/carboplatin/paclitaxel/bevacizumab, or atezolizumab/carboplatin/nab-paclitaxel. For most patients with non-SCC and either negative (0%) or low positive (1% to 49%) PD-L1, the Expert Panel recommends pembrolizumab/carboplatin/pemetrexed. Additional options are atezolizumab/carboplatin/nab-paclitaxel, atezolizumab/carboplatin/paclitaxel/bevacizumab, platinum-based two-drug combination chemotherapy, or non-platinum-based two-drug therapy. Single-agent pembrolizumab is an option for low positive PD-L1. For patients with high PD-L1 expression (TPS ≥ 50%) and SCC, the Expert Panel recommends single-agent pembrolizumab. An additional treatment option is pembrolizumab/carboplatin/(paclitaxel or nab-paclitaxel). For most patients with SCC and either negative (0%) or low positive PD-L1 (TPS 1% to 49%), the Expert Panel recommends pembrolizumab/carboplatin/(paclitaxel or nab-paclitaxel) or chemotherapy. Single-agent pembrolizumab is an option in select cases of low positive PD-L1. Recommendations are conditional on the basis of histology, PD-L1 status, and/or the presence or absence of contraindications. Additional information is available at www.asco.org/lung-cancer-guidelines.

Hansen TWR, **Maisels MJ**, 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(2): 180-193.
Full Text
Department of Pediatrics

A breakthrough discovery 60 years ago by Cremer et al. has since changed the way we treat infants with hyperbilirubinemia and saved the lives of millions from death and disabilities. "Photobiology" has evolved by inquiry of diverse light sources: fluorescent tubes (wavelength range of 400–520 nm; halogen spotlights that emit circular footprints of light; fiberoptic pads/blankets (mostly, 400–550 nm range) that can be placed in direct contact with skin; and the current narrow-band blue light-emitting diode (LED) light (450–470 nm), which overlaps the peak absorption wavelength (458 nm) for bilirubin photoisomerization. Excessive bombardment with photons has raised concerns for oxidative stress in very low birthweight versus term infants treated aggressively with phototherapy. Increased emphasis on prescribing phototherapy as a "drug" that is dosed cautiously and judiciously is needed. In this historical review, we chronicled the basic to the neurotoxic components of severe neonatal hyperbilirubinemia and the use of standardized interventions.

Heitzer AM, Piercy JC, Peters BN, Mattes AM, **Klarr JM**, Batton B, Ofen N and Raz S (2020). "Cumulative antenatal risk and kindergarten readiness in preterm-born preschoolers." Journal of Abnormal Child Psychology 48(1): 1-12.
Full Text
Department of Pediatrics

A suboptimal intrauterine environment is thought to increase the probability of deviation from the typical neurodevelopmental trajectory, potentially contributing to the etiology of learning disorders. Yet the cumulative influence of individual antenatal risk factors on emergent learning skills has not been sufficiently examined. We sought to determine whether antenatal complications, in aggregate, are a source of variability in preschoolers' kindergarten readiness, and whether specific classes of antenatal risk play a prominent role. We recruited 160 preschoolers (85 girls; ages 3-4 years), born </=33(6)/7 weeks' gestation, and reviewed their hospitalization records. Kindergarten readiness skills were assessed with standardized intellectual, oral-language, prewriting, and prenumeracy tasks. Cumulative antenatal risk was operationalized as the sum of complications identified out of nine common risks. These were also grouped into four classes in follow-up analyses: complications associated with intra-amniotic infection, placental insufficiency, endocrine dysfunction, and uteroplacental bleeding. Linear mixed model analyses, adjusting for sociodemographic and medical background characteristics (socioeconomic status, sex, gestational age, and sum of perinatal

complications) revealed an inverse relationship between the sum of antenatal complications and performance in three domains: intelligence, language, and prenumeracy (p = 0.003, 0.002, 0.005, respectively). Each of the four classes of antenatal risk accounted for little variance, yet together they explained 10.5%, 9.8%, and 8.4% of the variance in the cognitive, literacy, and numeracy readiness domains, respectively. We conclude that an increase in the co-occurrence of antenatal complications is moderately linked to poorer kindergarten readiness skills even after statistical adjustment for perinatal risk.

Hinckel BB, Pratte EL, Baumann CA, Gowd AK, Farr J, Liu JN, Yanke AB, Chahla J and Sherman SL (2020). "Patellofemoral cartilage restoration: A systematic review and meta-analysis of clinical outcomes." American Journal of Sports Medicine. ePub Ahead of Print.
Full Text
Department of Orthopaedic Surgery

Background: Many surgical options for treating patellofemoral (PF) cartilage lesions are available but with limited evidence comparing their results. Purpose: To determine and compare outcomes of PF cartilage restoration techniques. Study Design: Systematic review and meta-analysis. Methods: PRISMA (Preferred Reporting Items for Systematic Meta-Analyses) guidelines were followed by utilizing the PubMed, EMBASE, and Cochrane Library databases. Inclusion criteria were clinical studies in the English language, patient-reported outcomes after PF cartilage restoration surgery, and >12 months' follow-up. Quality assessment was performed with the Coleman Methodology Score. Techniques were grouped as osteochondral allograft transplantation (OCA), osteochondral autograft transfer (OAT), chondrocyte cell–based therapy, bone marrow–based therapy, and scaffolds. Results: A total of 59 articles were included. The mean Coleman Methodology Score was 71.8. There were 1937 lesions (1077 patellar, 390 trochlear, and 172 bipolar; 298 unspecified). The frequency of the procedures was as follows, in descending order: chondrocyte cell–based therapy (65.7%), bone marrow–based therapy (17.2%), OAT (8%), OCA (6.6%), and scaffolds (2.2%). When compared with the overall pooled lesion size (3.9 cm2; 95% CI, 3.5-4.3 cm2), scaffold (2.2 cm2; 95% CI, 1.8-2.5 cm2) and OAT (1.5 cm2; 95% CI, 1.1-1.9 cm2) lesions were smaller (P <.001), while chondrocyte cell–based therapy lesions were larger (4.7 cm2; 95% CI, 4.1-5.3 cm2; P =.039). Overall, the instability pool was 11.9%, and the anatomic risk factors pool was 32.1%. Statistically significant improvement was observed on at least 1 patient-reported outcome in chondrocyte cell–based therapy (83%), OAT (78%), OCA (71%), bone marrow–based therapy (64%), and scaffolds (50%). There were no significant differences between any group and the overall pooled change in International Knee Documentation Committee score (30.2; 95% CI, 27.4-32.9) and Lysholm score (25.2; 95% CI, 16.9-33.5). There were no significant differences between any group and the overall pooled rate in minor complication rate (7.6%; 95% CI, 4.7%-11.9%) and major complication rate (8.3%; 95% CI, 5.7%-12.0%); however, OCA had a significantly greater failure rate (22.7%; 95% CI, 14.6%-33.4%) as compared with the overall rate (6.8%; 95% CI, 4.7%-9.5%). Conclusion: PF cartilage restoration leads to improved clinical outcomes, with low rates of minor and major complications. There was no difference among techniques; however, failures were higher with OCA.

Hobson G, Bates J and **Sherbert D** (2020). "Breast implant-associated anaplastic large cell lymphoma affecting a neosubpectoral pocket." Cureus 12(3).
Full Text
Department of Surgery

The complications associated with breast implants are under perpetual scrutiny to maximize patient safety. In this era of plastic surgery, a new concern being addressed is breast implant-associated anaplastic large cell lymphoma (BIA-ALCL). Patients with BIA-ALCL most commonly present several years after implant placement with a periprosthetic fluid collection. The body of literature and reports of BIA-ALCL continues to grow with additional nuances in proposed causes as well as management. Most recently, this has led to a recall of breast implants manufactured utilizing a specific texturing. We describe here the time course, diagnosis, and management of BIA-ALCL in a 52-year-old patient who underwent submuscular implant-based reconstruction and subsequent revision of that reconstruction with the creation of a neosubpectoral pocket. The patient was managed in accordance with current guidelines under the supervision of a multidisciplinary team. In our review of the literature, several case reports, case series, and guideline publications were identified. Current guidelines for management are based on the staging of BIA-ALCL at diagnosis and span from only surgical with implant removal, excision of the lymphoma, and excision of the surrounding fibrous

capsule to addition of chemotherapeutic regimens or radiation for distant and locally advanced disease.

Jae SY, Kurl S, Bunsawat K, **Franklin BA**, Choo J, Kunutsor SK, Kauhanen J and Laukkanen JA (2020). "Impact of cardiorespiratory fitness on survival in men with low socioeconomic status." European Journal of Preventive Cardiology. ePub Ahead of Print.
Full Text
Department of Internal Medicine

Aims: Although both low socioeconomic status (SES) and poor cardiorespiratory fitness (CRF) are associated with increased chronic disease and heightened mortality, it remains unclear whether moderate-to-high levels of CRF are associated with survival benefits in low SES populations. This study evaluated the hypothesis that SES and CRF predict all-cause mortality and cardiovascular disease mortality and that moderate-to-high levels of CRF may attenuate the association between low SES and increased mortality. Methods: This study included 2368 men, who were followed in the Kuopio Ischaemic Heart Disease Study cohort. CRF was directly measured by peak oxygen uptake during progressive exercise testing. SES was characterized using self-reported questionnaires. Results: During a 25-year median follow-up, 1116 all-cause mortality and 512 cardiovascular disease mortality events occurred. After adjusting for potential confounders, men with low SES were at increased risks for all-cause mortality (hazard ratio 1.49, 95% confidence interval: 1.30–1.71) and cardiovascular disease mortality (hazard ratio1.38, 1.13–1.69). Higher levels of CRF were associated with lower risks of all-cause mortality (hazard ratio 0.54, 0.45–0.64) and cardiovascular disease mortality (hazard ratio 0.53, 0.40–0.69). In joint associations of SES and CRF with mortality, low SES-unfit had significantly higher risks of all-cause mortality (hazard ratio 2.15, 1.78–2.59) and cardiovascular disease mortality (hazard ratio 1.95, 1.48-2.57), but low SES-fit was not associated with a heightened risk of cardiovascular disease mortality (hazard ratio 1.09, 0.80-1.48) as compared with their high SES-fit counterparts. Conclusion: Both SES and CRF were independently associated with subsequent mortality; however, moderate-to-high levels of CRF were not associated with an excess risk of cardiovascular disease mortality in men with low SES.

Jindal V, Khoury J, Gupta R and **Jaiyesimi I** (2020). "Current status of chimeric antigen receptor T-cell therapy in multiple myeloma." American Journal of Clinical Oncology. ePub Ahead of Print.
Full Text
Department of Internal Medicine

Multiple myeloma (MM) is an incurable malignancy of plasma cells. Recently multiple new therapeutic options have been introduced which was able to improve overall survival but ultimately patient become refractory specifically in patients with poor cytogenetics. Therefore, novel therapeutic options like immunotherapy are needed to improve outcomes. Chimeric antigen receptor (CAR) T-cell therapy is immunotherapy in which T cell are genetically engineered against a tumor-specific antigen and transfused back to the patient to mount major histocompatibility complex-independent cancer-specific immune response. The success of CAR T-cell therapy in lymphoid malignancies encouraged its development in MM. Most of the clinical studies target B-cell maturation antigen in relapsed refractory MM and relapse is the major issue. In this article, we will present the basics of CAR T-cell therapy, the most recent clinical and preclinical data, and we will discuss the future therapeutic realm of CAR T cells in MM.

Johnson PC, Le M, **Sims MD** and **Bozyk PD** (2020). "Diagnosis and management of Clostridium Difficile Infection (CDI)," In Hyzy RC and McSparron J (ed). Evidence-Based Critical Care: A Case Study Approach. Cham: Springer International Publishing. pp**:** 539-543.
Full Text
Department of Internal Medicine

Infection due to Clostridium difficile is a prevalent cause of morbidity and mortality in the intensive care unit. Appropriate diagnosis and treatment of CDI remains challenging in the face of new methods of detection and emerging management strategies. We describe CDI symptoms, epidemiology, diagnosis, medical therapy, and surgical interventions for treatment. A review of upcoming modalities of therapy is additionally detailed.

Jung D (2020). "Gender-based harassment of emergency medicine trainees: What faculty educators need to know." AEM Education and Training 4(1): 77-80.

Full Text

Department of Emergency Medicine

There is increased interest in workplace harassment as reports of improper workplace conduct have surfaced among multiple industries and governments. Accounts of sexual misconduct in academic medical centers also highlight the need for further education and training for faculty educators. The purpose of this paper is to provide faculty educators with the tools to recognize and respond to gender-based harassment of medical trainees. More specifically, we will review existing literature, the definition of gender-based harassment, federal laws, institutional reporting protocols, and retaliation toward reporters of harassing behavior.

Keihani S, Rogers DM, Putbrese BE, Anderson RE, Stoddard GJ, Nirula R, Luo-Owen X, Mukherjee K, Morris BJ, Majercik S, Piotrowski J, Dodgion CM, Schwartz I, Elliott SP, DeSoucy ES, Zakaluzny S, Sherwood BG, Erickson BA, Baradaran N, Breyer BN, Fick CN, Smith BP, Okafor BU, Askari R, Miller BD, Santucci RA, Carrick MM, Allen L, Norwood S, Hewitt T, **Burks FN**, Heilbrun ME, Gross JA and Myers JB (2020). "The American Association for the Surgery of Trauma renal injury grading scale: Implications of the 2018 revisions for injury reclassification and predicting bleeding interventions." Journal of Trauma and Acute Care Surgery 88(3): 357-365.

Full Text

Department of Urology

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

Kerndt CC, **Balinski AM** and Papukhyan HV (2020). "Giant pericardial lipoma inducing cardiac tamponade and new onset atrial flutter." Case Reports in Cardiology 2020: 6937126.

Full Text

OUWB Medical Student Author

Although pericardial lipomas are both rare and benign, rapid or excessive growth can induce potentially fatal conditions such as pericarditis, arrhythmia, and cardiac tamponade. This case illustrates an example where a 65-year-old with atypical chest tightness unveiled a 10 x 15 cm anterior pericardial mass with circumferential effusion and progressive deterioration to cardiac tamponade. Initial transthoracic echocardiogram imaging was technically difficult in this patient due to habitus and body mass, which failed to illustrate underlying effusion. Recurrent bouts of refractory supraventricular tachycardia prompted further investigation of this patient's presentation with transesophageal echocardiogram, which showed evidence of an echogenic mass with cardiac tamponade. An urgent pericardial window and pericardial lipectomy immediately relieved this hemodynamically compromising condition. Subsequent atrial flutter resulted with the removal of the anterior fat pad during surgery, complicating recovery.

Kim DH, Hwang RW, Lee GH, Joshi R, **Baker KC**, Arnold P, Sasso R, **Park D** and **Fischgrund J** (2020). "Potential significance of facet joint fusion or posteromedial fusion observed on CT imaging following attempted posterolateral

or posterior interbody fusion." Spine Journal 20(3): 337-343.
Full Text
Department of Orthopaedic Surgery

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

Kim SK, Idler J, Turkoglu O, Talbot C, Friedman P, **Whitten A** and Bronsteen R (2020). "Increased risk of spontaneous miscarriage in angular pregnancy diagnosed by first trimester ultrasound." American Journal of Obstetrics & Gynecology 222(1): S366-S367.
Full Text
Department of Obstetrics & Gynecology

Klement RJ, Sonke JJ, Allgauer M, Andratschke N, Appold S, Belderbos J, Belka C, Dieckmann K, Eich HT, Flentje M, **Grills I**, Eble M, Hope A, Grosu AL, Semrau S, Sweeney RA, Horner-Rieber J, Werner-Wasik M, Engenhart-Cabillic R, Ye H and Guckenberger M (2020). "Estimation of the alpha/beta ratio of non-small cell lung cancer treated with stereotactic body radiotherapy." Radiotherapy and Oncology 142: 210-216.
Full Text
Department of Radiation Oncology

Background: High-dose hypofractionated radiotherapy should theoretically result in a deviation from the typical linear-quadratic shape of the cell survival curve beyond a certain threshold dose, yet no evidence for this hypothesis has so far been found in clinical data of stereotactic body radiotherapy treatment (SBRT) for early-stage non-small cell lung cancer (NSCLC). A pragmatic explanation is a larger alpha/beta ratio than the conventionally assumed 10 Gy. We here attempted an estimation of the alpha/beta ratio for NSCLC treated with SBRT using individual patient data. Materials and methods: We combined two large retrospective datasets, yielding 1294 SBRTs (<= 10 fractions) of early stage NSCLC. Cox proportional hazards regression, a logistic tumor control probability model and a biologically motivated Bayesian cure rate model were used to estimate the alpha/beta ratio based on the observed number of local recurrences and accounting for tumor size. Results: A total of 109 local progressions were observed after a median of 17.7 months (range 0.60-76.3

months). Cox regression, logistic regression of 3 year tumor control probability and the cure rate model yielded best-fit estimates of alpha/beta = 12.8 Gy, 14.9 Gy and 12-16 Gy (depending on the prior for alpha/beta), respectively, although with large uncertainties that did not rule out the conventional alpha/beta = 10 Gy. Conclusions: Clinicians can continue to use the simple LQ formalism to compare different SBRT treatment schedules for NSCLC. While alpha/beta = 10 Gy is not ruled out by our data, larger values in the range 12-16 Gy are more probable, consistent with recent meta-regression analyses.

Kochanny SE, Worden FP, Adkins DR, Lim DW, Bauman JE, Wagner SA, **Brisson RJ**, Karrison TG, Stadler WM, Vokes EE and Seiwert TY (2020). "A randomized phase 2 network trial of tivantinib plus cetuximab versus cetuximab in patients with recurrent/metastatic head and neck squamous cell carcinoma." Cancer. ePub Ahead of Print.
Full Text
OUWB Medical Student Author

Background: MET signaling is a well described mechanism of resistance to anti-EGFR therapy, and MET overexpression is common in head and neck squamous cell carcinomas (HNSCCs). In the current trial, the authors compared the oral MET inhibitor tivantinib (ARQ197) in combination with cetuximab (the TC arm) versus a control arm that received cetuximab monotherapy (C) in patients with recurrent/metastatic HNSCC. Methods: In total, 78 evaluable patients with cetuximab-naive, platinum-refractory HNSCC were enrolled, including 40 on the TC arm and 38 on the C arm (stratified by human papillomavirus [HPV] status). Patients received oral tivantinib 360 mg twice daily and intravenous cetuximab 500 mg/m2 once every 2 weeks. The primary outcome was the response rate (according to Response Evaluation Criteria in Solid Tumors, version 1.1), and secondary outcomes included progression-free and overall survival. After patients progressed on the C arm, tivantinib monotherapy was optional. Results: The response rate was 7.5% in the TC arm (N = 3; 1 complete response) and 7.9% in the C arm (N = 3; not significantly different [NS]). The median progression-free survival in both arms was 4 months (NS), and the median overall survival was 8 months (NS). Both treatments were well tolerated, with a trend toward increased hematologic toxicities in the TC arm (12.5% had grade 3 leukopenia). The response rate in 31 HPV-positive/p16-positive patients was 0% in both arms, whereas the response rate in HPV-negative patients was 12.7% (12.5% in the TC arm and 13% in the C arm). Fifteen patients received tivantinib monotherapy, and no responses were observed. Conclusions: Combined tivantinib plus cetuximab does not significantly improve the response rate or survival compared with cetuximab alone but does increase toxicity in an unselected HNSCC population. Cetuximab responses appear to be limited to patients who have HPV-negative HNSCC. MET-aberration–focused trials for HNSCC and the use of higher potency, selective MET inhibitors remain of interest.

Kocher KE, Arora R, Bassin BS, Benjamin LS, Bolton M, **Dennis BJ**, Ham JJ, Krupp SS, **Levasseur KA**, Macy ML, O'Neil BJ, Pribble JM, Sherwin RL, Sroufe NS, Uren BJ and Nypaver MM (2020). "Baseline performance of real-world clinical practice within a Statewide Emergency Medicine Quality Network: The Michigan Emergency Department Improvement Collaborative (MEDIC)." Annals of Emergency Medicine 75(2): 192-205.
Full Text
Department of Emergency Medicine

Study Objective: Large-scale quality and performance measurement across unaffiliated hospitals is an important strategy to drive practice change. The Michigan Emergency Department Improvement Collaborative (MEDIC), established in 2015, has baseline performance data to identify practice variation across 15 diverse emergency departments (EDs) on key emergency care quality indicators.Methods: MEDIC is a unique physician-led partnership supported by a major third-party payer. Member sites contribute electronic health record data and trained abstractors add supplementary data for eligible cases. Quality measures include computed tomography (CT) appropriateness for minor head injury, using the Canadian CT Head Rule for adults and Pediatric Emergency Care Applied Network rules for children; chest radiograph use for children with asthma, bronchiolitis, and croup; and diagnostic yield of CTs for suspected pulmonary embolism. Baseline performance was established with statistical process control charts.Results: From June 1, 2016, to October 31, 2017, the MEDIC registry contained 1,124,227 ED visits, 23.2% for children (<18 years). Overall baseline performance included the following: 40.9% of adult patients with minor head injury (N=11,857) had appropriate CTs (site range 24.3% to 58.6%), 10.3% of pediatric minor head injury cases (N=11,183) exhibited CT overuse (range 5.8% to 16.8%), 38.1% of pediatric patients with a respiratory condition (N=18,190) received a chest radiograph (range 9.0% to 62.1%), and 8.7% of pulmonary embolism

CT results (N=16,205) were positive (range 7.5% to 14.3%).Conclusion: Performance varied greatly, with demonstrated opportunity for improvement. MEDIC provides a robust platform for emergency physician engagement across ED practice settings to improve care and is a model for other states.

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. ePub Ahead of Print.
Full Text
Department of Internal Medicine
Department of Diagnostic Radiology and Molecular Imaging

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.

Koneru H, Pattisapu A and **Bozyk PD** (2020). "Tumor lysis syndrome," In Hyzy RC and McSparron J (ed). Evidence-Based Critical Care: A Case Study Approach. Cham: Springer International Publishing. pp**:** 611-614.
Full Text
Department of Internal Medicine

Tumor lysis syndrome is an oncological emergency. The massive turnover of tumor cells leads to accumulation of electrolytes and uric acid that could lead to renal failure and cardiac arrhythmias. There are clinical and laboratory classifications of tumor lysis syndrome, and several risk stratification models have been proposed. Prevention of tumor lysis syndrome involves intravenous hydration and administration of hypouricemic agents. Rasburicase is preferred over allopurinol in high risk cases. Urinary alkalization in prevention is controversial. Treatment of tumor lysis syndrome includes intensive monitoring of renal function, fluid balance and electrolytes. Neuromuscular irritability manifesting as cardiac arrhythmias and seizures is a significant concern. Prevention of cardiac arrhythmias is done by appropriately managing hyperkalemia and hypocalcemia. Despite aggressive preventive measures, renal failure develops in some patients requiring initiation of renal replacement therapy. Pre-phase treatment with low intensity chemotherapy has been a strategy that is being used frequently in certain forms of cancer to reduce the development of tumor lysis syndrome. Certain aspects of management of tumor lysis syndrome remain controversial.

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. ePub Ahead of Print.
Full Text
Department of Surgery

Kus KJB, Karia PS, Schmults CD and Ruiz ES (2020). "Identification of skin cancer screening visits by using claims data." Journal of the American Academy of Dermatology 82(2): 504-505.
Full Text
OUWB Medical Student Author

Lao KM, **Kanaan H**, **Li W** and **Zhang P** (2020). "Clinical indices for overlapping syndrome (ANCA Associated Crescentic Glomerulonephritis AACGN and Immune Complex Medicated Glomerulopathy) are similar to AACGN only cases." Laboratory Investigation 100(SUPPL 1): 1585.
Request Form
Department of Pathology

Leal A, Andrade R, **Hinckel B**, Tompkins M, Bastos R, Flores P, Samuel F, Espregueira-Mendes J and Arendt E (2020). "Patients with different patellofemoral disorders display a distinct ligament stiffness pattern under instrumented stress testing." Journal of ISAKOS 5(2): 74-79.
Full Text
Department of Orthopaedic Surgery

Objective: Investigate the patellar force-displacement profile (ligament stiffness) of patellofemoral disorders. Methods: Fifty-two knees from 34 consecutive patients (mean 31.6 years and 53% male) were analysed including 24 knees with patellofemoral pain (PFP), 19 with potential patellofemoral instability (PPI) and 9 with objective patellofemoral instability (OPI). Physical examination, patient-reported outcome measures (Kujala and Lysholm Scores), standard radiography and MRI or CT were performed in all patients. Instrumented stress testing (Porto Patella testing device) concomitantly with imaging (MRI or CT) was performed to calculate ligament stiffness. Results: The force-displacement curves in patients with PPI and OPI displayed a similar pattern, which was different from that of the PFP group. Patients with PPI showed higher ligament stiffness (a higher force was required to displace the patella) than the patients in the OPI group. Patients with OPI had a statistically significant shallower trochlear groove and increased lateral tilt. More than half of the PPI and OPI population presented with at least one classic risk factor (patella alta, trochlear dysplasia, increased quadriceps vector, lateral tilt). In the PPI group, at least two risk factors were found in 37% of patients, whereas at least 33% of patients in the OPI group had three risk factors present. None of the patients presented with all four anatomical risk factors. Conclusion: Patients presenting with patellofemoral instability (PPI and OPI) display similar ligament stiffness patterns (force-displacement curve). Patients with PFP and PPI showed higher ligament stiffness as compared with patients with OPI. Level of evidence Level V, case series.

Lee AA, Rao K, Limsrivilai J, Gillilland M, **Malamet B**, Briggs E, Young VB and Higgins PDR (2020). "Temporal gut microbial changes predict recurrent clostridiodes difficile infection in patients with and without ulcerative colitis." Inflammatory Bowel Diseases. ePub Ahead of Print.
Request Form
OUWB Medical Student Author

Background: Ulcerative colitis (UC) carries an increased risk of primary and recurrent Clostridiodes difficile infection (rCDI), and CDI is associated with UC flares. We hypothesized that specific fecal microbial changes associate with UC flare and rCDI. Methods: We conducted a prospective observational cohort study of 57 patients with UC and CDI, CDI only, and UC only. Stool samples were collected at baseline, at the end of antibiotic therapy, and after reconstitution for 16S rRNA sequencing. The primary outcomes were recurrent UC flare and rCDI. Logistic regression and Lasso models were constructed for analysis. Results: There were 21 (45.7%) patients with rCDI, whereas 11 (34.4%) developed UC flare. Patients with rCDI demonstrated significant interindividual (P = 0.008) and intraindividual differences (P = 0.004) in community structure by Jensen-Shannon distance (JSD) compared with non-rCDI. Two cross-validated Lasso regression models predicted risk of rCDI: a baseline model with female gender, hospitalization for UC in the past year, increased Ruminococcaceae and Verrucomicrobia, and decreased Eubacteriaceae, Enterobacteriaceae, Lachnospiraceae, and Veillonellaceae (AuROC, 0.94); and a model 14 days after completion of antibiotics with female gender, increased Shannon diversity, Ruminococcaceae and Enterobacteriaceae, and decreased community richness and Faecalibacterium (AuROC, 0.9). Adding JSD between baseline and post-treatment samples to the latter model improved fit (AuROC, 0.94). A baseline model including UC hospitalization in the past year and increased Bacteroidetes was associated with increased risk for UC flare (AuROC, 0.88). Conclusion: Fecal microbial features at baseline and after therapy predict rCDI risk in patients with and without UC. These results may help risk stratify patients to guide management.

Lee Y, **Banooni A**, Yuki K, Staffa SJ, DiNardo JA and Brown ML (2020). "Incidence and predictors of postoperative nausea and vomiting in children undergoing electrophysiology ablation procedures." Paediatric Anaesthesia 30(2): 147-152.
Full Text
Department of Anesthesiology

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

Levine WN, **Fischgrund JS** and Urrutia EJ (2020). "Guest nation Chile and a new chapter for JAAOS Unplugged®." The Journal of the American Academy of Orthopaedic Surgeons 28(5): 179.
Full Text
Department of Orthopaedic Surgery

Levin-Epstein R, Romero T, Wong JK, Cook K, Dess RT, Spratt DE, Moran BJ, Merrick GS, Tran PT, Demanes DJ, Stish BJ, **Krauss DJ**, Wedde TB, Lilleby W, Stock R, Tward JD, Steinberg ML, Horwitz EM, Tendulkar RD and Kishan AU (2020). "Impact of initial treatment selection on clinical outcomes after biochemical failure in radiorecurrent high-risk prostate cancer." Journal of Clinical Oncology 38(6): 208.
Full Text
Department of Radiation Oncology

Background: Treatment of high risk prostate cancer (HRPCa) with external beam radiotherapy (EBRT) plus brachytherapy (BT) boost (EBRT+BT) has been prospectively associated with lower rates of BCR, albeit potentially with increased toxicity, and retrospectively linked to decreased distant metastasis (DM) and PCa-specific mortality (PCSM) compared to EBRT alone. However, it is unclear whether patients who develop BCR following either approach have similar downstream oncologic outcomes. Methods: We identified 706 out of 3820 men with HRPCa treated at 13 institutions from 1998-2015 with EBRT (n=468/2134) or EBRT+BT (n=238/1686) who developed BCR. We compared rates of DM, PCSM, and all-cause mortality (ACM) after BCR between treatment groups using Fine-Gray competing risk regression. Models were adjusted for age, Gleason grade group, initial PSA (iPSA), clinical T stage, time-dependent use of systemic salvage, and interval to BCR using inverse probability of treatment weighting. Results: Median follow-up was 9.9 years from RT and 4.8 years from BCR. Groups were similar in age, iPSA, presence of >2 HR features, and median interval to BCR (3.3 years). Most men received neoadjuvant/concurrent androgen deprivation therapy (ADT), 92.5% and 91.0% for EBRT and EBRT+BT, respectively, though for a longer duration with EBRT (median 14.7 vs. 9.0 months, p=0.0012). Local and systemic salvage rates were 2.3% and 36.3% after EBRT, and 2.6% and 43.6% after EBRT+BT, respectively. Initial EBRT+BT was associated with significantly lower rates of DM after BCR (HR 0.48, 95% CI 0.36-0.64, p<0.001). Rates of PCSM and ACM did not significantly differ (HR 0.93, 95% CI 0.67-1.30, p=0.93, and HR 0.8, 95% CI 0.6-1.1, p=0.11, respectively). Conclusions: In this large retrospective series of radiorecurrent HRPCa, initial treatment with EBRT+BT was associated with significantly lower rates of DM after BCR compared with EBRT, despite shorter ADT use and a similar median interval to BCR. Local salvage was widely underutilized in both groups. In the absence of salvage for local failure after EBRT, upfront treatment intensification with BT may reduce DM, though not PCSM or ACM, even after development of

BCR.

Lew D, Kashani A, Lo SK and **Jamil LH** (2020). "Efficacy and safety of cap-assisted endoscopic mucosal resection of ileocecal valve polyps." Endoscopy International Open 8(3): E241-E246.
Full Text
Department of Internal Medicine

Background and Study Aims: Standard endoscopic mucosal resection (EMR) of ileocecal valve (ICV) polyps is challenging. Cap-assisted endoscopic mucosal resection (C-EMR) can be performed when polyps are not easily amenable to standard EMR. Current literature is limited regarding its efficacy and safety for ICV polyps. The objectives of this study were to assess the efficacy and safety of C-EMR for ICV polyps. Patients and Methods: A retrospective review was conducted from September 2008 to November 2018 at a tertiary care center. Patients included in the study underwent C-EMR for ICV polyps by a single gastroenterologist (LHJ). Polyps were successfully eradicated if they were removed en-bloc as confirmed by pathology, or had a negative biopsy on follow-up colonoscopy. Outcomes of the procedures were evaluated, including complete adenoma clearance and adverse events. Results: Twenty-one ICV polyps were removed with C-EMR. Median polyp size was 15 mm (range, 5-45). The rate of complete adenoma clearance was 100 %. Procedure-related complications occurred in five patients (24 %): delayed GI bleeding (4.8 %) and deep mucosal resection/visible vessel (14.3 %). Three patients had subsequent surveillance colonoscopies at 8, 56, and 67 months, respectively. The third patient was found to have a 6-mm flat polyp at the edge of the previous polypectomy site. This was treated with C-EMR and repeat colonoscopy 6 months later did not show residual. Conclusion: C-EMR is highly effective in treating ICV polyps with a low complication rate. It is our suggested method in approaching ICV polyps that are difficult to remove via standard freehand snare EMR technique.

Liebmann JM, Barton K, Weinreb RN, Eichenbaum DA, Gupta PK, McCabe CM, **Wolfe JD**, Ahmed I, Sheybani A and Craven ER (2020). "Evolving guidelines for intracameral injection." Journal of Glaucoma 29 Suppl 1: S1-S7.
Full Text
Department of Ophthalmology

Purpose: To review evidence and provide guidelines on intracameral (ICM) injection techniques and monitoring. Materials and Methods: A review of published literature on ICM injection and intravitreal injections formed the basis for roundtable deliberations by an expert panel of ophthalmologists. Results: ICM injection as a way to deliver medications is growing in popularity. However, there is limited published literature and no standard approach to best practices for ICM injections, particularly when not accompanying another surgical procedure. Fortunately, there is long clinical experience with ICM manipulation and a large body of evidence surrounding intravitreal injections that has provided important guidance. The expert panel formulates several concrete guidelines and many suggested techniques to help physicians safely and effectively employ ICM injections. Conclusions: This committee addressed the many considerations surrounding ICM injection of drugs or implants and agree that it is a safe and effective surgical procedure when performed with appropriate training and according to established safe practices.

Liu G, **Li XQ**, **Qin A**, Zheng WL, **Yan D**, Zhang S, **Stevens C**, **Kabolizadeh P** and **Ding XF** (2020). "Improve the dosimetric outcome in bilateral head and neck cancer (HNC) treatment using spot-scanning proton arc (SPArc) therapy: A feasibility study." Radiation Oncology 15(1): 21.
Request Form
Department of Radiation Oncology

Background: To explore the dosimetric improvement, delivery efficiency, and plan robustness for bilateral head and neck cancer (HNC) treatment utilizing a novel proton therapy technique - the spot-scanning proton arc (SPArc) therapy. Methods: We evaluated fourteen bilateral HNC patients retrospectively. Both SPArc and 3-field Intensity Modulated Proton Therapy (IMPT) plans were generated for each patient using the same robust optimization parameters. The prescription doses were 70Gy (relative biological effectiveness (RBE) for CTV_high and 60Gy[RBE] for CTV_low. Clinically significant dosimetric parameters were extracted and compared. Root-mean-square deviation dose (RMSDs) Volume Histogram(RVH) was used to evaluate the plan robustness. Total treatment delivery time was estimated based on the machine parameters. Results: The SPArc plan was able to provide equivalent or better robust target coverage while showed significant

dosimetric improvements over IMPT in most of the organs at risk (OARs). More specifically, it reduced the mean dose of the ipsilateral parotid, contralateral parotid, and oral cavity by 25.8%(p = 0.001), 20.8%(p = 0.001) and 20.3%(p = 0.001) respectively compared to IMPT. This technique reduced D1 (the maximum dose covering 1% volume of a structure) of cord and brain stem by 20.8% (p = 0.009) and 10.7% (p = 0.048), respectively. SPArc also reduced the average integral dose by 17.2%(p = 0.001) and external V3Gy (the volume received 3Gy[RBE]) by 8.3%(p = 0.008) as well. RVH analysis showed that the SPArc plans reduced the dose uncertainties in most OARs compared to IMPT, such as cord: 1.1 +/- 0.4Gy[RBE] vs 0.7 +/- 0.3Gy[RBE](p = 0.001), brain stem: 0.9 +/- 0.7Gy[RBE] vs 0.7 +/- 0.7Gy[RBE](p = 0.019), contralateral parotid: 2.5 +/- 0.5Gy[RBE] vs 2.2 +/- 0.6Gy[RBE](p = 0.022) and ipsilateral parotid: 3.1 +/- 0.7Gy[RBE] vs 2.8 +/- 0.6Gy[RBE](p = 0.004) respectively. The average total estimated treatment delivery time were 283.4 +/- 56.2 s, 469.2 +/- 62.0 s and 1294.9 +/- 106.7 s based on energy-layer-switching-time (ELST) of 0.1 s, 1 s, and 5 s respectively for SPArc plans, compared to the respective values of 328.0 +/- 47.6 s(p = 0.002), 434.1 +/- 52.0 s(p = 0.002), and 901.7 +/- 74.8 s(p = 0.001) for 3-field IMPT plans. The potential clinical benefit of utilizing SPArc will lead to a decrease in the mean probability of salivary flow dysfunction by 31.3%(p = 0.001) compared with IMPT. Conclusions: SPArc could significantly spare OARs while providing a similar or better robust target coverage compared with IMPT in the treatment of bilateral HNC. In the modern proton system with ELST less than 0.5 s, SPArc could potentially be implemented in the routine clinic with a practical, achievable treatment delivery efficiency.

Liu J, Friedman P and Savasan ZA (2020). "Does pulse pressure help to determine the effectiveness of labetalol in severe hypertension?" American Journal of Obstetrics & Gynecology 222(1): S278-S279.
Full Text
Department of Pathology

Loudon N, Loudon J, Gonchigar A, Laage Gaupp F and Minja F (2020). "Implementation of an automated patient follow-up system in a low-resource setting." Journal of Vascular & Interventional Radiology 31: S36-S37.
Full Text
OUWB Medical Student Author

Lu AQ, Prensky JG, Baker PS, Scott IU, **Mahmoud TH** and Todorich B (2020). "Update on medical and surgical management of submacular hemorrhage." Expert Review of Ophthalmology 15(1): 43-57.
Request Form
Department of Ophthalmology

Introduction: Despite consistent use of anti-vascular endothelial growth factor (anti-VEGF), prognosis of large, fovea-involving submacular hemorrhage (SMH) has remained guarded, particularly in patients with neovascular age-related macular degeneration. Areas covered: This review provides an update on management of SMH, with particular focus on the role of anti-VEGF therapy and surgical management of thick, large, and/or subfoveal SMH. A literature search and meta-analysis of studies published from January 2010 to February 2019 was performed to evaluate outcomes of eyes with SMH following management with either medical treatment (i.e. anti-VEGF monotherapy) or a combined surgical approach of pars plana vitrectomy, subretinal tPA with or without subretinal air, pneumatic displacement, and anti-VEGF. The surgical techniques are summarized, with emphasis on novel surgical techniques described in the past decade. Prognostic factors associated with, and potential indications for, choice of management approach were evaluated. Expert commentary: SMH represents a continuing treatment challenge. Anti-VEGF monotherapy is a reasonable approach in patients with small, thin, and localized hemorrhage. Combination vitrectomy, tPA, pneumatic displacement, and anti-VEGF may be effective in managing thick, large SMH in some cases. While no consensus exists on optimal treatment algorithm, choice of medical or surgical therapy should be tailored to each patient.

Luehmann NC, **Pastewski JM**, Cirino JA, **Al-Hadidi A**, **DeMare AM**, Riggs TW, **Novotny NM** and **Akay B** (2020). "Implementation of a pediatric trauma cervical spine clearance pathway." Pediatric Surgery International 36(1): 93-101.
Full Text
OUWB Medical Student Author
Department of Surgery

Purpose: Pediatric cervical spine injuries are rare events. Missed injuries must be weighed against radiation exposure and excess resource utilization in a young population. A universal pediatric cervical spine clearance algorithm does not exist. The study objective is to determine if care improved after the implementation of a standardized cervical spine clearance pathway by evaluating imaging rates, length of stay, speciality consultation, and injury detection. Methods: A multidisciplinary group reviewed relevant literature to develop an algorithm for cervical spine clearance in pediatric trauma patients. We reviewed patient charts 15 months before and after implementation. Categorical comparisons were tested with Chi-square. A p value less than 0.05 was considered statistically significant. Results: The pre- and post-implementation groups were homogenous when comparing demographics, mechanism and severity of injury. Using the cervical spine clearance pathway, patients received fewer plain cervical spine radiographs (34% vs 16%), fewer spine speciality consults (28% vs 13%), and more patients were cleared clinically (44% vs 62%) ($p < 0.05$). There were 2 (1.7%) documented injuries in the pre-implementation group and 3 (3%) documented injuries in the post-implementation group. There were no missed injuries. Conclusions: Use of a standardized pathway allows more patients' cervical spines to be cleared clinically and better utilizes resources without compromising patient care. Level Of Evidence: Level III. Type Of Study: Care Management Study.

Lyapichev KA, Piña-Oviedo S, Medeiros LJ, Evans MG, Liu H, Miranda AR, Hunt KK, Clemens MW, Stewart JM, **Amin MB**, Quesada AE, Chai SM, Di Napoli A, Yoga A, Dave SK, Wistuba II, Wu Y, Bueso-Ramos CE, Schlette EJ, Ferrufino-Schmidt MC, Loghavi S, Khoury JD, Young KH and Miranda RN (2020). "A proposal for pathologic processing of breast implant capsules in patients with suspected breast implant anaplastic large cell lymphoma." Modern Pathology 33(3): 367-379.
Full Text
Department of Pathology

Breast implant anaplastic large cell lymphoma is an entity recently recognized by the World Health Organization. The tumor arises around textured-surface breast implants and is usually confined to the surrounding fibrous capsule. Currently, there are no recommendations for handling and sampling of capsules from patients with suspected breast implant anaplastic large cell lymphoma without a grossly identifiable tumor. We analyzed complete capsulectomies without distinct gross lesions from patients with breast implant anaplastic large cell lymphoma. The gross appearance of the capsules as well as the presence, extent and depth of tumor cells on the luminal side and number of sections involved by lymphoma were determined by review of routine stains and CD30 immunohistochemistry. We then used a mathematical model that included the extent of tumor cells and number of positive sections to calculate the minimum number of sections required to identify 95% of randomly distributed lesions. We identified 50 patients with breast implant anaplastic large cell lymphoma who had complete capsulectomies. The implants were textured in all 32 (100%) cases with available information. Anaplastic large cell lymphoma was found in 44/50 (88%) capsules; no tumor was found in six (12%) patients who had lymphoma cells only in the effusion. The median number of sections reviewed was 20 (range, 2–240), the median percentage of sections involved by tumor was 6% (range, 0–90%), and the median percentage of sections involved by lymphoma was 10% (range, 0–90%). Invasion deep into or through the capsule was identified in 18/50 (36%) patients. In patients with breast implant anaplastic large cell lymphoma without a grossly identifiable tumor we identified a spectrum of involvement and we propose a protocol for handling, sampling and reporting these cases. The number of sections to exclude the presence of lymphoma with more than 95% certainty was supported by a mathematic rationale.

Maisels MJ and Watchko JF (2020). "Improving post-discharge neonatal surveillance for the jaundiced newborn." Acta Paediatrica.
Full Text
Department of Pediatrics

Mando R, Tim D, DeCicco A, **Trivax J** and **Hanson I** (2020). "Master of the masquerade: An atypical presentation of acute aortic dissection." Case Reports in Cardiology 2020: 5743985.
Full Text
Department of Internal Medicine

Acute aortic dissection (AAD) is associated with unacceptably high mortality rate. As such, early diagnosis

and aggressive management are essential in order to avoid life-threatening complications. Herein, we report an atypical presentation of AAD and clinical sequelae.

Markman JD, Rhyne AL, Sasso RC, Patel AA, Hsu WK, **Fischgrund JS**, Edidin AA and Vajkoczy P (2020). "Association between opioid use and patient-reported outcomes in a randomized trial evaluating basivertebral nerve ablation for the relief of chronic low back pain." Clinical Neurosurgery 86(3): 343-347.
Full Text
Department of Orthopaedic Surgery

Background: Chronic low back pain (CLBP) is a primary indication for opioid therapy. Objective: To evaluate the hypothesis that CLBP patients reporting reduced opioid use have superior functional outcomes following basivertebral nerve (BVN) radiofrequency ablation. Methods: This post hoc analysis from a sham-controlled trial examined short-acting opioid use from baseline through 1 yr. Opioid use was stratified into 3 groups by two blinded external reviewers. Two-sample t-tests were used to compare Oswestry Disability Index (ODI) and Visual Analog Scale (VAS) measurements between those patients who increased or decreased their opioid usage compared to baseline. Results: Actively treated patients with decreased opioid use at 12 mo had a mean ODI improvement of 24.9 ± 16.0 (n = 27) compared to 7.3 ± 9.8 (n = 18) for patients reporting increased opioid use (P <. 001). In the sham arm, the improvements in ODI were 17.4 ± 16.1 (n = 19) and 1.2 ± 14.3 (n = 5; P =. 053) for the patients reporting decreased vs increased opioid usage, respectively. Actively treated patients reporting decreased opioid use had a mean improvement in VAS of 3.3 ± 2.5 (n = 27) compared to 0.6 ± 1.8 (n = 18) for patients reporting increased opioid use (P <. 001). In the sham arm, the improvements in VAS were 2.5 ± 2.6 (n = 19) and 1.4 ± 1.9 (n = 5; P =. 374) for patients reporting decreased vs increased opioid use, respectively. Conclusion: Subjects undergoing BVN ablation who decreased opioid use had greater improvement in ODI and VAS scores compared with those reporting increased opioid usage. There is an association between functional benefit from BVN ablation and reduced opioid use.

Marples B and **Wilson GD** (2020). "Predicting outcome using genomic-based liquid biomarkers." International Journal of Radiation Oncology Biology Physics 106(1): 1-4.
Full Text
Department of Radiation Oncology

Martin S, Han E and **Peters KM** (2020). "A novel approach to managing post retropubic vaginal sling pain." Urology 137: 196-199.
Full Text
Department of Urology

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

Martusiewicz A, Khan AZ, Chamberlain AM, Keener JD and Aleem AW (2020). "Outpatient narcotic consumption following total shoulder arthroplasty." JSES International 4(1): 100-104.
Full Text

Department of Orthopaedic Surgery

Introduction: In the setting of the opioid epidemic, physicians continue to scrutinize ways to minimize exposure to narcotic medications. Several studies emphasize improvements in perioperative pain management following total shoulder arthroplasty (TSA). However, there is a paucity of literature describing outpatient narcotic consumption requirements following TSA. Methods: A single-institution, prospective study of patients undergoing primary TSA was performed. Preoperative demographics including exposure to narcotics, smoking history, and alcohol exposure were collected. The primary outcome was measurement of total outpatient narcotic consumption 6 weeks from surgery. Narcotic consumption was verified by counting leftover pills at the final follow-up visit. Results: Overall, 50 patients were enrolled. The median narcotic consumption in the cohort was 193 morphine equivalent units (MEUs), approximately 25 (5-mg) tablets of oxycodone, and the mean consumption was 246 MEUs, approximately 32 (5-mg) tablets. Almost 25% of patients consumed fewer than 10 total tablets, with 10% of patients taking no narcotics at home. Multivariate regression found preoperative narcotic exposure associated with increased consumption of 31 MEUs (P = .004). Older age was found to be protective of narcotic consumption, with increasing age by 1 year associated with 0.75 MEU decrease in consumption (P = .04). Conclusions: Anatomic total shoulder arthroplasty in general provides quick, reliable pain relief and does not require a significant amount of narcotic medication postoperatively. For most patients, it is reasonable to prescribe the equivalent of 25-30 (5-mg) oxycodone tablets following TSA.

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. ePub Ahead of Print.
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 no 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.

Mazumder S, Ma M, Champigny M and **Adeyemo A** (2020). "A case of adult-onset Henocn-Schonlein Purpura triggered by fire ants." Cureus 12(3): e7431.
Full Text

Department of Surgery

Adult-onset IgA vasculitis, also known as Henoch-Schonlein purpura (HSP), is a rare disease that often presents with a non-blanchable, purpuric rash and can simultaneously affect the gastrointestinal, renal and musculoskeletal systems. The etiology of HSP is unknown. It can be triggered by any entity that creates an immunological insult, including medications, infections and vaccines. We describe a unique case of an adult woman who presented with HSP after experiencing multiple insect bites from fire ants and mosquitos while traveling overseas.

McCrery R, Lane F, Benson K, Taylor C, Padron O, Blok B, De Wachter S, Pezzella A, Gruenenfelder J, Pakzad M, Perrouin-Verbe MA, Le Normand L, Van Kerrebroeck P, Mange J, **Peters K**, Kennelly M, Shapiro A, Lee U, Comiter C, Mueller M and Goldman HB (2020). "Treatment of urinary urgency incontinence using a rechargeable SNM system: 6-month results of the ARTISAN-SNM study." Journal of Urology 203(1): 185-191.
Request Form
Department of Urology

Purpose: Sacral neuromodulation is a guideline recommended treatment of urinary dysfunction and fecal incontinence in patients in whom conservative treatments have failed. Historically sacral neuromodulation has been delivered using a nonrechargeable device with an average life span of 4.4 years. Surgery is required to replace the implanted neurostimulator due to battery depletion. Implantation of a long-lived implanted neurostimulator can eliminate the need for replacement surgeries, potentially reducing patient surgical risks and health care costs. The Axonics r-SNM System (TM) is a miniaturized, rechargeable sacral neuromodulation system designed to deliver therapy for at least 15 years. The ARTISAN-SNM(Axonics (R) Sacral Neuromodulation System for Urinary Urgency Incontinence Treatment) study is a pivotal study using rechargeable sacral neuromodulation therapy to treat urinary urgency incontinence. Six-month results are presented. Materials and Methods: A total of 129 eligible patients with urinary urgency incontinence were treated. All participants were implanted with a tined lead and the rechargeable sacral neuromodulation system in a nonstaged procedure. Efficacy data were collected using a 3-day bladder diary, the validated ICIQ-OABqol (International Consultation on Incontinence Questionnaire Overactive Bladder quality of life) questionnaire and a participant satisfaction questionnaire. Therapy responders were identified as participants with a 50% or greater reduction in urinary urgency incontinence episodes compared to baseline. We performed an as-treated analysis in all implanted participants. Results: At 6 months 90% of participants were therapy responders. The mean +/- SE number of urinary urgency incontinence episodes per day was reduced from 5.6 +/- 0.3 at baseline to 1.3 +/- 0.2. Participants experienced a clinically meaningful 34-point improvement on the ICIQ-OABqol questionnaire. There were no serious device related adverse events. Conclusions: The Axonics r-SNM System is safe and effective with 90% of participants experiencing clinically and statistically significant improvements in urinary urgency incontinence symptoms.

McDermott PN (2020). "Photon skyshine from medical linear accelerators." Journal of Applied Clinical Medical Physics 21(3): 108-114.
Full Text
Department of Radiation Oncology

A widely used formula for the prediction of photon skyshine has been shown to be very inaccurate by comparison with numerous measurements. Discrepancies of up to an order of magnitude have been observed. In addition to this, the formula does not predict the observed dependence on field size, nor the fact that skyshine dose rates exhibit a local maximum. A scaling formula is derived here, with a single fitting parameter, which properly accounts for these properties, provides physical insight into the skyshine phenomenon, and is more accurate. The location of the maximum dose rate depends on the ratio of the roof height above isocenter to the distance from the isocenter to the outer surface of the sidewall. For nominal linac room dimensions, the maximum dose occurs at a distance from the outer wall of approximately two times the height of the roof above the isocenter. The skyshine dose rate is proportional to the field area and not Ω1.3 , as predicted by the standard formula, where Ω is the solid angle subtended by the beam. For lightly shielded roofs (concrete thickness less than about 0.5 m), the photon skyshine for 6 MV exceeds that for 18 MV. Evidence is presented that at intermediate distances the skyshine declines as one over the distance and not one over the distance squared. Predictions of skyshine dose rates depend critically on accurate knowledge of the roof transmission factor. If a roof is shielded so as to avoid designation as a "high

radiation area," photon skyshine will be negligible.

McKee C, Beeravolu N, Brown C, **Perez-Cruet M** and Chaudhry GR (2020). "Mesenchymal stem cells transplanted with self-assembling scaffolds differentiated to regenerate nucleus pulposus in an ex vivo model of degenerative disc disease." Applied Materials Today 18: 100474.
Full Text
Department of Neurosurgery

Intervertebral disc (IVD) degeneration is one of the major causes of chronic severe low back pain (LBP). IVD degeneration is characterized by changes in cell populations, and the subsequent loss of extracellular matrix (ECM) of the nucleus pulposus (NP) causing degenerative disc disease (DDD). Current treatments only address symptomatic pain rather than repairing the damaged IVDs. Therefore, there is a need for regenerative therapies that restore native tissue structure, cellularity and mechanical function to treat DDD. However, the development of cell therapeutic approaches is hindered due to the lack of availability of high quality and quantity of cells. Other problems include poor growth and differentiation of transplanted cells, and cell leakage from the site of injection in the damaged IVD. In this study, we investigated a novel strategy by combining biocompatible biomaterials and cell therapy to regenerate NP through in situ differentiation of transplanted cells using an ex vivo rabbit disc model of DDD. Results indicated that hydrogel scaffolds composed of self-assembling polyethylene glycol (PEG) functionalized with acrylate and thiol end groups promoted differentiation of human umbilical cord mesenchymal stem cells (MSCs) into NP-like cells (NPCs) in vitro. Upon transplantation into degenerated IVDs, PEG scaffolds limited leakage and retained the cells in the NP region of IVD transplants. Both the scaffold and the ex vivo disc environment promoted differentiation of MSCs into cell types capable of producing ECM including sulfated glycoaminoglycans at levels higher than when MSCs were injected into IVD explants alone. Transplanted cells using self-assembling scaffolds also expressed chondrogenic markers, SOX9, COL2, and ACAN, as well as putative NP markers, FOXF1, K19, and VIMENTIN both at transcriptional and translational levels as determined by quantitative real-time PCR and immunostaining. Overall, this study demonstrates the potential of MSCs for regeneration of the NP using a combined strategy of biomaterials and cell therapy.

McLean SA, Ressler K, Koenen KC, Neylan T, Germine L, Jovanovic T, Clifford GD, Zeng D, An X, Linnstaedt S, Beaudoin F, House S, Bollen KA, Musey P, Hendry P, Jones CW, Lewandowski C, **Swor R**, Datner E, Mohiuddin K, Stevens JS, Storrow A, Kurz MC, McGrath ME, Fermann GJ, Hudak LA, Gentile N, Chang AM, Peak DA, Pascual JL, Seamon MJ, Sergot P, Peacock WF, Diercks D, Sanchez LD, Rathlev N, Domeier R, Haran JP, Pearson C, Murty VP, Insel TR, Dagum P, Onnela JP, Bruce SE, Gaynes BN, Joormann J, Miller MW, Pietrzak RH, Buysse DJ, Pizzagalli DA, Rauch SL, Harte SE, Young LJ, Barch DM, Lebois LAM, van Rooij SJH, Luna B, Smoller JW, Dougherty RF, Pace TWW, Binder E, Sheridan JF, Elliott JM, Basu A, Fromer M, Parlikar T, Zaslavsky AM and Kessler R (2020). "The AURORA Study: S longitudinal, multimodal library of brain biology and function after traumatic stress exposure." Molecular Psychiatry 25(2): 283-296.
Request Form
Department of Emergency Medicine

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

Miller P, **Xiao A**, Kung V, Sibley R, Higgins J, Kambham N, Charu V, Lenihan C, Talley E, Walavalkar V, Laszik GZ, Arora N, Nast C and Troxell M (2020). "Progression of proliferative glomerulonephritis with monoclonal IgG deposits in pediatric patients." Laboratory Investigation 100(SUPPL 1): 1589-1590.
Request Form
OUWB Medical Student Author

Moore AB, Su E, Weiss RE, Yagapen AN, Malveau SE, Adler DH, **Bastani A**, Baugh CW, Caterino JM, **Clark CL**, Diercks DB, Hollander JE, Nicks BA, Nishijima DK, Shah MN, Stiffler KA, Storrow AB, Wilber ST and Sun BC (2020). "Frequency of abnormal and critical laboratory results in older patients presenting to the emergency department with syncope." Academy Emergency Medicine 27(2): 161-164.
Full Text
Department of Emergency Medicine

Nair GB, Castillo E, Myzuik N, **Grills I**, **Stevens C** and **Guerrero T** (2020). "Differential ventilation pattern on novel functional imaging in a patient with unilateral bronchial obstruction caused by adenoid cystic carcinoma." American Journal of Respiratory & Critical Care Medicine 201(3): e6-e7.
Full Text
Department of Radiation Oncology
Department of Internal Medicine

> The article presents a case study of 50-year-old man who received a new diagnosis of adenoid cystic carcinoma of the left mainstem bronchus. Topics discussed include the patient underwent a four-dimensional computed tomography (4DCT) scan, computation of image processing–based lung ventilation and 4DCT-derived ventilation imaging in a patient with unilateral bronchial obstruction.

Navin MC, **Wasserman JA**, **Jain S**, Baughman KR and Laventhal NT (2020). "When do pediatricians call the ethics consultation service? Impact of clinical experience and formal ethics training." AJOB Empirical Bioethics. ePub Ahead of Print.
Request Form
Department of Foundational Studies (OU)
OUWB Medical Student Author

> Background: Previous research shows that pediatricians inconsistently utilize the ethics consultation service (ECS). Methods: Pediatricians in two suburban, Midwestern academic hospitals were asked to reflect on their ethics training and utilization of ECS via an anonymous, electronic survey distributed in 2017 and 2018, and analyzed in 2018. Participants reported their clinical experience, exposure to formal and informal ethics training, use of formal and informal ethics consultations, and potential barriers to formal consultation. Results: Less experienced pediatricians were more likely to utilize formal ethics consultation and more likely to have formal ethics training. The most commonly reported reasons not to pursue formal ECS consultation were inconvenience and self-reported expertise in pediatric ethics. Conclusions: These results inform ongoing discussions about ethics consultation among pediatricians and the role of formal ethics training in both undergraduate and graduate medical education.

Oska S, Zarbo A and Jahnke MN (2020). "Sleep-related rhythmic movement disorder: A case report of head banging alopecia." Pediatric Dermatology 37(2): 350-351.
Full Text
OUWB Medical Student Author

> We present a case of alopecia associated with sleep-related rhythmic movement disorder (RMD) in an otherwise healthy 2-year-old boy. The alopecic patch he presented with on his scalp coincided with the location of repeated head banging in a video taken by the patient's mother. Alopecia secondary to RMD is an under recognized entity and should be included in the differential diagnosis of pediatric alopecia.

Partiali B, **Oska S**, **Touriel RB**, **Delise A**, **Barbat A** and **Folbe A** (2020). "Gender disparity in speakers at a major academic emergency medicine conference." Emergency Medicine Journal. ePub Ahead of Print.
Full Text

OUWB Medical Student Author
Department of Surgery

Background: Although women make up a substantial portion of the workforce in emergency medicine, they remain under-represented in academia. Methods: This study investigates trends in the representation of female speakers at the American College of Emergency Physicians scientific assembly-the largest academic emergency medicine conference in the world. Publication profiles, speaking duration and gender composition of speakers were collected and compared over a 3-year period. Results: The authors described increased representation of female speakers at the conference from 2016 to 2018, as well as an upward trend in women's actual speaking time. Conclusion: This upward trend in women's representation may translate to more opportunities for female engagement in academic emergency medicine. Despite the increasing representation of women, male speakers outnumbered female speakers all 3 years, demonstrating that a speaker gender gap persists in academic emergency medicine.

Parzen JS, Ye H, **Gustafson G**, **Yan D**, Martinez A, **Chen PY**, Ghilezan M, Sebastian E, Limbacher A and **Krauss DJ** (2020). "Rates of rectal toxicity in patients treated with high dose rate brachytherapy as monotherapy compared to dose-escalated external beam radiation therapy for localized prostate cancer." Radiotherapy and Oncology 147: 123-129.
Request Form
Department of Radiation Oncology

Background: Using a prospectively collected institutional database, we compared rectal toxicity following high dose rate (HDR) brachytherapy as monotherapy relative to dose-escalated external beam radiotherapy (EBRT) for patients with localized prostate cancer. Methods: 2683 patients treated with HDR or EBRT between 1994 and 2017 were included. HDR fractionation was 38 Gy/4 fractions (n = 321), 24 Gy/2 (n = 96), or 27 Gy/2 (n = 128). EBRT patients received a median dose of 75.6 Gy in 1.8 Gy fractions [range 70.2–82.8 Gy], using either 3D conformal or intensity modulated radiotherapy (IMRT). EBRT patients underwent 3D image guidance via an off-line adaptive process. Results: Median follow-up was 7.5 years (7.4 years for EBRT and 7.9 years for HDR). 545 patients (20.3%) received HDR brachytherapy and 2138 (79.7%) EBRT. 69.1% of EBRT patients received IMRT. Compared to EBRT, HDR was associated with decreased rates of acute grade ≥2 diarrhea (0.7% vs. 4.5%, $p < 0.001$), rectal pain/tenesmus (0.6% vs. 7.9%, $p < 0.001$), and rectal bleeding (0% vs. 1.6%, $p = 0.001$). Rates of chronic grade ≥2 rectal bleeding (1.3% vs. 8.7%, $p < 0.001$) and radiation proctitis (0.9% vs. 3.3%, $p = 0.001$) favored HDR over EBRT. Rates of any chronic rectal toxicity grade ≥2 were 2.4% vs. 10.5% ($p < 0.001$) for HDR versus EBRT, respectively. In those treated with IMRT, acute and chronic rates of any grade ≥2 GI toxicity were significantly reduced but remained significantly greater than those treated with HDR. Conclusions: In appropriately selected patients with localized prostate cancer undergoing radiation therapy, HDR brachytherapy as monotherapy is an effective strategy for reducing rectal toxicity.

Pathangey G, **Hanzel GS**, **Shannon F**, **Hanson I**, **Lau W**, **Almany S**, **Safian RD**, **Kerner N**, **Gallagher M**, Vivacqua A and **Abbas AE** (2020). "Left ventricular diastolic function improvement one year after transcatheter aortic valve replacement for severe aortic stenosis." Journal of the American College of Cardiology 75(11): 1256.
Full Text
Department of Internal Medicine
Department of Surgery
OUWB Medical Student Author
Department of Anesthesiology

Background: Long term outcomes in diastolic dysfunction (DD) after transcatheter aortic valve replacement (TAVR) for severe aortic stenosis (AS) remains controversial. The aim of this study is to determine changes in DD in severe AS patients before and 1-year after TAVR. Methods: A retrospective study was conducted for patients who underwent TAVR at Beaumont Hospital (2015-2018). We collected patient demographics, comorbidities, echocardiographic data, and DD grades; we excluded patients with incomplete data. Baseline pre-procedure data were compared with 1-year follow-up. DD parameters of left ventricular ejections fraction (LVEF), E-wave, E/A ratio, E/e' lateral and septal e', left atrial volume index (LAVI), tricuspid regurgitation peak velocity (TR Pk Vel), and aortic mean gradient were obtained. Descriptive statistics, multivariate analysis, and independent T-tests were used. Results: 249 patients were included in the final analysis. At 1-year post-TAVR, there were significant increases in LVEF in Grades 2 and 3, LAVI in Grades 1

and 3, and TR peak velocity in all Grades. Grade 3 demonstrated the most significant improvement in diastolic parameters especially E/A ratio and E velocity. Moreover, there was a significant decrease in the incidence of Grade 2 and 3 with a resultant increase in normal and Grade 1. Conclusion: There were significant improvements in the LVEF, LAVI, diastolic parameters, and diastolic function grading at 1-year. Most improvement was noted in advanced grades of DD.

Peter IM, Deraney RN, Orango O, Philip T, **Rosen B**, Cu-Uvin S and Cu-Uvin S (2020). "Radical hysterectomy for operable early cervical cancer in HIV-positive and HIV-negative women in western Kenya." International Journal of Gynecology & Obstetrics 148(3): 403-404.
Full Text
Department of Obstetrics & Gynecology

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

Porter E, **Fuentes P**, Siddiqui Z, Thompson A, Levitin R, Solis D, Myziuk N and **Guerrero T** (2020). "Hippocampus segmentation on non-contrast CT using deep learning." Medical Physics. ePub Ahead of Print.
Full Text
OUWB Medical Student Author
Department of Radiation Oncology

Accurate segmentation of the hippocampus for hippocampal avoidance whole brain radiotherapy currently requires high resolution 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-CT image registration, and cost. Three-dimensional deep convolutional network models have the potential to automate hippocampal segmentation. In this study, we demonstrate that deep learning models, utilizing 3D convolutional neural networks, can accurately delineate the hippocampus using only high-resolution non-contrast CT images. PURPOSE: To investigate the inter-observer accuracy and reliability of hippocampal segmentation by experts using MRI -fusion and an automated deep learning model using CT alone. 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 x 200 x 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 10-fold validation. From the predicted test set volumes, we calculated the 100% Hausdorff distance (HD). Acceptability was assessed using the RTOG 0933 protocol criteria, contours were considered passing with HD ≤ 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. CONCLUSION: Our proposed AG-3D ResNet's segmentation of the hippocampus from non-contrast CT images alone are comparable to those obtained by participating physicians from the RTOG 0933 Phase II clinical trial.

Probst MA, Gibson T, Weiss RE, Yagapen AN, Malveau SE, Adler DH, **Bastani A**, Baugh CW, Caterino JM, **Clark CL**, Diercks DB, Hollander JE, Nicks BA, Nishijima DK, Shah MN, Stiffler KA, Storrow AB, Wilber ST and Sun BC (2020). "Risk stratification of older adults who present to the emergency department with syncope: The FAINT score." Annals of Emergency Medicine 75(2): 147-158.
Request Form
Department of Emergency Medicine

Study Objective: Older adults with syncope are commonly treated in the emergency department (ED). We seek to derive a novel risk-stratification tool to predict 30-day serious cardiac outcomes. Methods: We performed a prospective, observational study of older adults (>/=60 years) with unexplained syncope or near syncope who presented to 11 EDs in the United States. Patients with a serious diagnosis identified in the ED were excluded. We collected clinical and laboratory data on all patients. Our primary outcome was 30-day all-cause mortality or serious cardiac outcome. Results: We enrolled 3,177 older adults with

unexplained syncope or near syncope between April 2013 and September 2016. Mean age was 73 years (SD 9.0 years). The incidence of the primary outcome was 5.7% (95% confidence interval [CI] 4.9% to 6.5%). Using Bayesian logistic regression, we derived the FAINT score: history of heart failure, history of cardiac arrhythmia, initial abnormal ECG result, elevated pro B-type natriuretic peptide, and elevated high-sensitivity troponin T. A FAINT score of 0 versus greater than or equal to 1 had sensitivity of 96.7% (95% CI 92.9% to 98.8%) and specificity 22.2% (95% CI 20.7% to 23.8%), respectively. The FAINT score tended to be more accurate than unstructured physician judgment: area under the curve 0.704 (95% CI 0.669 to 0.739) versus 0.630 (95% CI 0.589 to 0.670). Conclusion: Among older adults with syncope or near syncope of potential cardiac cause, a FAINT score of zero had a reasonably high sensitivity for excluding death and serious cardiac outcomes at 30 days. If externally validated, this tool could improve resource use for this common condition.

Qu Z (2020). "Challenges for data extraction from narrative pathology reports." Archives of Pathology and Laboratory Medicine 144(3): 273.
Full Text
Department of Pathology

Quinn TJ and **Kabolizadeh P** (2020). "Racial disparity of stage III rectal cancer among young adults: A combined NCDB/SEER analysis." Journal of Clinical Oncology 38(4): 85.
Full Text
Department of Radiation Oncology

Background: With the advent of screening colonoscopy in 1997, there has been an overall decreasing incidence in rectal cancer. Recently, the ACS updated guidelines to started screening patients at 45 years old. The purpose of this study was to further investigate incidence and overall survival trends for rectal cancer among young white and African-American (AA) patients using the SEER and NCDB databases. Methods: Rectal cancer incidence trends in SEER-9/SEER-18 were analyzed for patients < 50 years old. Treatment and survival outcomes were also evaluated using the NCDB (2004-2014). White and AA patients were matched using propensity score analysis and inverse probability of treatment weighting (IPTW). Baseline characteristics were compared with Pearson Chi Square, before and after matching. Univariate and multivariable analyses were performed with Kaplan- Meier and Cox proportional hazard modeling, incorporating the IPTW-adjusted population. Results: 6,144 (SEER) and 17,819 (NCDB) young, white or AA patients were identified. There was an overall increase in incidence of stage III (APC 5.57, P < 0.05) and IV (APC 4.66, P < 0.05) rectal cancer among young white patients. For the entire population, there was improved overall survival for white patients compared to AA patients, even after adjusting for confounding factors. Subset analysis of both the SEER and NCDB databases revealed that the largest disparity was between AAn and white rectal cancer patients, is among the Stage III subset with HR of 1.6 (P < 0.001) and HR of 1.4 (P < 0.001), respectively. Conclusions: There is an alarming increase in younger patients being diagnosed with rectal cancer. Specifically, there appears to be more locally advanced rectal cancer among younger patients and a racial disparity favoring whites for survival outcomes was identified. This research further supports the utility of earlier screening and to identify the factors involved in this rise in rectal cancer incidence.

Quinn TJ, Rajagopalan MS, Gill B, Mehdiabadi SM and **Kabolizadeh P** (2020). "Patterns of care and outcomes for adjuvant treatment of pT3N0 rectal cancer using the National Cancer Database." Journal of Gastrointestinal Oncology 11(1): 1-12.
Full Text
Department of Radiation Oncology

Background: The standard of care in locally advanced rectal cancer is preoperative chemoradiation followed by surgical resection. However, the optimal treatment paradigm is currently controversial for patients with pathological T3N0 (pT3N0) in the era of total mesorectal excision (TME). Given the paucity of data, we conducted an analysis using the National Cancer Database (NCDB) to identify patterns of care and outcomes. Methods: We utilized the NCDB to identify 7,836 non-metastatic, pT3N0 rectal cancer patients who did not receive neoadjuvant therapy from 2004-2014. Univariate and multivariable analysis for factors affecting treatment selection were completed using logistic regression. Overall survival (OS) analyses were completed using Cox regression modeling, incorporating propensity scores with inverse probability of

treatment weighting (IPTW) and conditional landmark analysis. Results: There was a significant improvement in OS in patients receiving adjuvant chemotherapy (P<0.01) or radiotherapy (RT) with chemotherapy (P<0.01) vs. observation alone. There was no significant difference between RT vs. observation (P=0.54) and chemotherapy vs. chemotherapy with RT cohorts (P=0.15). Multivariable analysis showed age, gender, race, insurance status, income, Charlson-Deyo Comorbidity Condition (CDCC) score, facility location, grade, surgical margin, RT, and chemotherapy to be statistically significant predictors of OS. After correcting for indication and immortal time biases, chemotherapy, with or without RT, improved OS compared with observation [hazard ratio (HR) 0.48, P<0.001]. This benefit was maintained in the margin negative cohort. Conclusions: Practice patterns vary in the management of pT3N0 rectal cancer patients. This analysis suggests that the use of adjuvant therapy, particularly adjuvant chemotherapy with or without RT, appears to improve OS.

Radhakrishna U, **Singh RB**, Taylor RW, Vishweswaraiah S, Aydas B, Szymanska M, **Wharton K** and **Yilmaz A** (2020). "Artificial Intelligence accurately predicts outcomes in Preterm PROM." American Journal of Obstetrics and Gynecology 222(1): S393-S394.
Full Text
Department of Obstetrics & Gynecology

Rosen T, Liu SW, **Cameron-Comasco L**, Clark S, Mulcare MR, Biese K, Magidson PD, Tyler KR, Melady D, Thatphet P, Wongtangman T, Elder NM, Stern ME and the Academy of Geriatric Emergency M (2020). "Geriatric emergency medicine fellowships: Current state of specialized training for emergency physicians in optimizing care for older adults." AEM Education and Training 4(S1): S122-S129.
Full Text
Department of Emergency Medicine

Improving emergency department (ED) care for older adults is a critical issue in emergency medicine. Institutions throughout the United States and Canada have recognized the growing need for a workforce of emergency physician (EP) leaders focused on clinical innovation, education, and research and have developed specialized fellowship training in geriatric emergency medicine (GEM). We describe here the overview, structure, and curricula of these fellowships as well as successes and challenges they have encountered. Seven GEM fellowships are active in the United States and Canada, with five offering postresidency training only, one offering fellowship training during residency only, and one offering both. The backbone of the curriculum for all fellowships is the achievement of core competencies in various aspects of GEM, and each includes clinical rotations, teaching, and a research project. Evaluation strategies and feedback have allowed for significant curricular changes as well as customization of the fellowship experience for individual fellows. Key successes include an improved collaborative relationship with geriatrics faculty that has led to additional initiatives and projects and former fellows already becoming regional and national leaders in GEM. The most critical challenges have been ensuring adequate funding and recruiting new fellows each year who are interested in this clinical area. We believe that interest in GEM fellowships will grow and that opportunities exist to combine GEM fellowship training with a focus in research, administration, or health policy to create unique new types of highly impactful specialized training. Future research may include exploring former fellows' postfellowship experiences, careers, accomplishments, and contributions to GEM to better understand the impact of GEM fellowships.

Rusilko PJ, Fuller TW and **Burks F** (2020). "Surgical reconstruction of buried penis," In Martins FE, Kulkarni SB and Köhler TS (ed). Textbook of Male Genitourethral Reconstruction. Cham: Springer International Publishing. pp**:** 737-749.
Full Text
Department of Urology

Entrapment of the phallus because of morbid obesity, post-circumcision cicatrix formation, genital skin loss, trauma, or genital lymphedema in the adult patient is referred to collectively as acquired buried penis or concealed penis. It is a morbid condition due to sexual dysfunction, lower urinary tract symptoms, local skin excoriation, and associated depression. Increasingly, there is a recognition that adult acquired buried penis is associated with lichen sclerosus and urethral stricture disease. Surgical management is complex and complications include penile reburying, wound breakdown, and unsatisfactory cosmetic and functional outcomes are not uncommon. Preoperative evaluation and optimization is paramount as patients with

buried penis very often have comorbidities associated with obesity that affect wound healing. Despite the challenges and frequent complications, patients report significant improvements in quality of life in both urinary and sexual domains with contemporary surgical treatment. Almost universally, patients also report they would undergo surgery again when queried.

Saban RJ, **Berns MM**, **Al-Hakim MM** and **Patino GA** (2020). "Hydrocephalus as the presenting symptom of sarcoidosis: A case report and review of literature." Clinical Case Reports 8(2): 363-368.
Full Text
OUWB Medical Student Author
Department of Neurology
Department of Foundational Medical Studies (OU)

Hydrocephalus is rare in sarcoidosis, especially as the presenting symptom. Neurosarcoidosis as a cause of unexplained communicating hydrocephalus should be considered in cases of abnormal cerebrospinal fluid (CSF) and negative infectious and tumoral studies.

Sandler KA, Cook RR, Ciezki JP, Ross AE, Pomerantz MM, Nguyen PL, Shaikh T, Tran PT, Stock RG, Merrick GS, Demanes DJ, Spratt DE, Abu-Isa EI, Wedde TB, Lilleby W, **Krauss DJ**, Shaw GK, Alam R, Reddy CA, Song DY, Klein EA, Stephenson AJ, Tosoian JJ, Hegde JV, Yoo SM, Fiano R, D'Amico AV, Nickols NG, Aronson WJ, Sadeghi A, Greco SC, Deville C, Jr., McNutt T, DeWeese TL, Reiter RE, Said JW, Steinberg ML, Horwitz EM, Kupelian PA, King CR and Kishan AU (2020). "Prostate-only versus whole-pelvis radiation with or without a brachytherapy boost for Gleason Grade Group 5 prostate cancer: A retrospective analysis." European Urology 77(1): 3-10.
Request Form
Department of Radiation Oncology

Background: The role of elective whole-pelvis radiotherapy (WPRT) remains controversial. Few studies have investigated it in Gleason grade group (GG) 5 prostate cancer (PCa), known to have a high risk of nodal metastases. Objective: To assess the impact of WPRT on patients with GG 5 PCa treated with external-beam radiotherapy (EBRT) or EBRT with a brachytherapy boost (EBRT+BT). Design, Setting, and Participants: We identified 1170 patients with biopsy-proven GG 5 PCa from 11 centers in the United States and one in Norway treated between 2000 and 2013 (734 with EBRT and 436 with EBRT+BT). Outcome Measurements and Statistical Analysis: Biochemical recurrence-free survival (bRFS), distant metastasis-free survival (DMFS), and prostate cancer-specific survival (PCSS) were compared using Cox proportional hazards models with propensity score adjustment. Results and Limitations: A total of 299 EBRT patients (41%) and 320 EBRT+BT patients (73%) received WPRT. The adjusted 5-yr bRFS rates with WPRT in the EBRT and EBRT+BT groups were 66% and 88%, respectively. Without WPRT, these rates for the EBRT and EBRT+BT groups were 58% and 78%, respectively. The median follow-up was 5.6yr. WPRT was associated with improved bRFS among patients treated with EBRT+BT (hazard ratio [HR] 0.5, 95% confidence interval [CI] 0.2-0.9, p=0.02), but no evidence for improvement was found in those treated with EBRT (HR 0.8, 95% CI 0.6-1.2, p=0.4). WPRT was not significantly associated with improved DMFS or PCSS in the EBRT group (HR 1.1, 95% CI 0.7-1.7, p=0.8 for DMFS and HR 0.7, 95% CI 0.4-1.1, p=0.1 for PCSS), or in the EBRT+BT group (HR 0.6, 95% CI 0.3-1.4, p=0.2 for DMFS and HR 0.5 95% CI 0.2-1.2, p=0.1 for PCSS). Conclusions: WPRT was not associated with improved PCSS or DMFS in patients with GG 5 PCa who received either EBRT or EBRT+BT. However, WPRT was associated with a significant improvement in bRFS among patients receiving EBRT+BT. Strategies to optimize WPRT, potentially with the use of advanced imaging techniques to identify occult nodal disease, are warranted. Patient Summary: When men with a high Gleason grade prostate cancer receive radiation with external radiation and brachytherapy, the addition of radiation to the pelvis results in a longer duration of prostate-specific antigen control. However, we did not find a difference in their survival from prostate cancer or in their survival without metastatic disease. We also did not find a benefit for radiation to the pelvis in men who received radiation without brachytherapy.

Sandrone S, Berthaud JV, Carlson C, Cios J, Dixit N, Farheen A, Kraker J, Owens JWM, **Patino G**, Sarva H, Weber D and Schneider LD (2020). "Strategic considerations for applying the flipped classroom to neurology education." Annals of Neurology 87(1): 4-9.
Full Text
Department of Foundational Medical Studies (OU)

Schafer E, Bazydlo M, Schultz L, Park P, Chang V, **Easton RW**, Schwalb J, **Khalil J**, **Perez-Cruet M**, Abdulhak M, Aleem I and for the MI (2020). "Rates and risk factors associated with 90-day readmission following cervical spine fusion surgery: analysis of the Michigan Spine Surgery Improvement Collaborative (MSSIC) registry." Spine Journal. ePub Ahead of Print.

Request Form

Department of Orthopaedic Surgery

Department of Neurosurgery

Background Context: Hospital readmission rates are an increasingly important focus. Identifying patients at risk for readmission can help decrease those rates and thus decrease the overall cost of care. Purpose: We sought to report the rates and the risk factors associated with 90-day hospital readmission after degenerative cervical spine surgery via either an anterior or posterior approach. Study Design: Retrospective review of prospectively collected database. Patient Sample: Michigan Spine Surgery Improvement Collaborative (MSSIC) registry. Outcome Measures: Hospital readmission at 90 days. Methods: The MSSIC registry prospectively enrolls patients undergoing surgery for degenerative cervical spine disease. The registry was queried over a 4-year period to determine patient characteristics and risk factors associated with unplanned readmission at 90 days following degenerative cervical spine fusion surgery through either an anterior or posterior approach. Univariate and multivariate regression modeling was used to compare patient characteristics and odds of readmission. Results: Of 3,762 patients who underwent an anterior approach, 202 (5.4%) were readmitted within 90 days. Of 693 patients who underwent a posterior approach, 85 (12.3%) were readmitted within 90 days. Risk factors associated with increased likelihood of readmission after the anterior approach were male sex (odds ratio [OR] 1.56, confidence interval [CI] 1.10–2.20), American Society of Anesthesiologists class >2 (OR 1.70, CI 1.26–2.30), and increased length of stay (OR 1.10, CI 1.03–1.19). Factors associated with decreased likelihood of readmission after the anterior approach were being independently ambulatory preoperatively (OR 0.59, CI 0.46–0.76) and holding private insurance (OR 0.67, CI 0.50–0.90). A history of previous spine surgery was associated with increased risk of readmission after the posterior approach (OR 1.76, CI 1.37–2.25). Pain was the most common single reason cited for readmission after either approach (9% anterior, 13% posterior). After an anterior approach, common surgical reasons for readmission include new radicular findings (8%), dysphagia (6%), and surgical site hematoma (5%), whereas common medical reasons include pneumonia (7%), infection outside the surgical site (6%), and an electrolyte issue. After a posterior approach, common surgical reasons for readmission after 90 days include surgical site infection (8%) and new radicular findings (6%), whereas common medical reasons include infection outside the surgical site (9%), urinary tract infection (8%), and an abdominal issue (8%). Conclusions: Analysis of a large multicentered, spine-specific database for elective cervical spine fusion surgery demonstrated an unplanned 90-day readmission rate of 5.4% for the anterior approach and 12.3% for the posterior approach. Factors associated with readmission for the anterior approach include male sex, American Society of Anesthesiologists class >2, increased length of stay, holding private insurance, and being ambulatory preoperatively. A history of previous spine surgery was associated with increased odds of readmission after the posterior approach.

Scherzer ZA, Alvarez C, Renner JB, Murphy LB, Schwartz TA, Jordan JM, Golightly YM and Nelson AE (2020). "Effects of comorbid cardiovascular disease and diabetes mellitus on hand osteoarthritis, pain, and functional state transitions." The Journal of Rheumatology. ePub Ahead of Print.

Request Form

OUWB Medical Student Author

Objective: The purpose of this study is to examine the course of hand osteoarthritis (HOA) and its relationship with cardiovascular disease (CVD) and diabetes (DM). Methods: Data were collected at 3 time points from 845 Johnston County Osteoarthritis Project participants (2/3 women, 1/3 African-Americans, mean age 60 years) with and without HOA, CVD, or DM. A diagnosis of radiographic hand osteoarthritis (rHOA) required a Kellgren-Lawrence severity grade of ≥2 in at least 3 joints in each hand. A four-state progressive model included transitions based on rHOA and pain or function as defined using the AUStralian CANadian Osteoarthritis Hand Index (AUSCAN). Markov multi-state models estimated hazard ratios and 95% confidence intervals (aHR [95%]) for associations between DM or CVD and specific state transitions, adjusting for baseline and time-varying covariates. Results: Participants with DM (vs those without DM) were more

likely to experience worsening pain with rHOA. Individuals who had or developed CVD (vs those who did not) were significantly less likely to experience symptomatic improvement, regardless of rHOA status. Those with DM or CVD (vs those without these comorbidities) were less likely to experience improvement in function, although this was statistically significant only for those with DM and no rHOA. Conclusion: Overall, having or developing DM and/or CVD reduced the likelihood of symptomatic and functional improvement over time, suggesting an impact of comorbid CVD and DM on the clinical and radiographic course of HOA. Additional studies are needed to confirm these findings.

Schmidt BM, **Allison S** and Wrobel JS (2020). "Describing normative foot temperatures in patients with diabetes-related peripheral neuropathy." Journal of Diabetes Science and Technology 14(1): 22-27.
Full Text
OUWB Medical Student Author

Background: Prior research shows increased foot temperatures are predictive of diabetes-related foot complications. Our aim was to describe normative skin foot temperatures for individuals with diabetic peripheral neuropathy to better inform new technologies. We also explored for potential risk factors which correlate with changes in foot temperatures. Methods: We conducted a retrospective chart review of adult patients >18 years of age with diabetes mellitus and clinically diagnosed diabetic peripheral neuropathy with pedal digital thermometry performed between 2009 and 2018. A total of 58 patients met these criteria. Univariate modeling was based on covariates that may affect foot temperature including age, peripheral arterial disease, toe pressure, seasonality of measurement, smoking pack-years, caffeine use, insulin use, and calcium channel blocker use. Results: In patients with diabetic peripheral neuropathy, mean toe temperatures of 27.67 degrees C (6.300 degrees C), forefoot of 28.58 degrees C (5.36 degrees C), midfoot of 29.21 degrees C (3.81 degrees C), and rearfoot of 29.88 degrees C(3.83 degrees C) were demonstrated. A modest negative correlation between seasonality and toe and metatarsal temperatures ($r = -0.38$, $P < .05$; $r = -0.43$ $P < .01$, respectively) was demonstrated. Midfoot temperatures were modestly and positively correlated to the presence of small fiber symptoms ($r = 0.33$, $P = .03$). Positive modest correlation with rearfoot temperatures and amount of pack-year history ($r = 0.30$, $P = .03$) was seen. Conclusion: Normative foot temperatures in neuropathic patients were found to be inversely associated with seasonality at the toe and metatarsal level. Smoking and pack-year history demonstrate modest correlation previously unseen in temperature analyses and warrant further exploration. Normative temperatures in neuropathic patients can better inform new technologies for the prevention of diabetic foot ulcer and Charcot neuroarthropathy.

Sebai M, **Karabon PE**, **Luan T**, Sayee K and **Dekhne N** (2020). "Gender differences and survival outcomes in breast cancer patients: Stage stratified propensity scoring analysis of the National Cancer Database." Annals of Surgical Oncology 27(SUPPL 1): S145-S146.
Request Form
Department of Medical Education
OUWB Medical Student Author
Department of Surgery

Selkie E, Adkins V, Masters E, **Bajpai A** and Shumer D (2020). "Transgender adolescents' uses of social media for social support." Journal of Adolescent Health 66(3): 275-280.
Full Text
OUWB Medical Student Author

Transgender adolescents are at higher risk for negative mental health outcomes, such as depression, anxiety, and suicidality, compared with cisgender adolescents. Social media may be an effective venue for addressing these health disparities because most adolescents have access to online information and socialization. This study used qualitative inquiry to explore transgender adolescents' uses of social media for social support. Transgender adolescents between the ages of 15 and 18 years with a social media profile were recruited from a pediatric gender clinic in the Midwestern U.S. A 30- to 60-minute semistructured interview assessed ways participants used social media to access transgender-related support. Thematic analysis was used to develop categories and code the transcripts. Coding discrepancies were resolved by two researchers following initial coding. Results represent data from 25 interviews comprising 13 transmasculine, 11 transfeminine, and one nonbinary participant(s), with 68% of the sample identifying as white, non-Hispanic.

Categories emerged regarding forms of support participants received from transgender-related online communities including emotional support through peers and role models, appraisal support for validating their experiences, and informational support for navigating health decisions and educating family and friends. Participants also referenced negative experiences, including harassment and exclusionary behavior online. Social media platforms represent hubs of community for transgender adolescents. These communities provide emotional, appraisal, and informational support that transgender youth may not otherwise be able to access. Future research should use the affordances of social media to identify approaches to addressing health disparities and improving the well-being of transgender adolescents.

Seymour ZA, Chan JW, Sneed PK, Kano H, Lehocky CA, Jacobs RC, Ye H, Chytka T, Liscak R, Lee CC, Yang HC, Ding D, Sheehan J, Feliciano CE, Rodriguez-Mercado R, Chiang VL, Hess JA, Sommaruga S, McShane B, Lee J, Vasas LT, Kaufmann AM, **Grills I** and McDermott MW (2020). "Dose response and architecture in volume staged radiosurgery for large arteriovenous malformations: A multi-institutional study." Radiotherapy and Oncology 144: 180-188.
Request Form
Department of Radiation Oncology

Background: Optimal treatment paradigm for large arteriovenous malformations (AVMs) is controversial. Volume-staged stereotactic radiosurgery (VS-SRS) provides an effective option for these high-risk lesions, but optimizing treatment for these recalcitrant and rare lesions has proven difficult. Methods: This is a multi-centered retrospective review of patients treated with a planned prospective volume staging approach to stereotactically treat the entire nidus of an AVM with volume stages separated by intervals of 3–6 months. A total of 9 radiosurgical centers treated 257 patients with VS-SRS between 1991 and 2016. We evaluated near complete response (nCR), obliteration, cure, and overall survival. Results: With a median age of 33 years old at the time of first SRS volume stage, patients received 2–4 total volume stages and a median follow up of 5.7 years after VS-SRS. The median total AVM nidus volume was 23.25 cc (range: 7.7–94.4 cc) with a median margin dose per stage of 17 Gy (range: 12–20 Gy). Total AVM volume, margin dose per stage, compact nidus, lack of prior embolization, and lack of thalamic location involvement were all associated with improved outcomes. Dose >/= 17.5 Gy was strongly associated with improved rates of nCR, obliteration, and cure. With dose >/= 17.5 Gy, 5- and 10-year cure rates were 33.7% and 76.8% in evaluable patients compared to 23.7% and 34.7% of patients with 17 Gy and 6.4% and 20.6% with <17 Gy per volume-stage (p = 0.004). Obliteration rates in diffuse nidus architecture with <17 Gy were particularly poor with none achieving obliteration compared to 32.3% with doses >/= 17 Gy at 5 years (p = 0.007). Comparatively, lesions with a compact nidus architecture exhibited obliteration rates at 5 years were 10.7% vs 9.3% vs 26.6% for dose >17 Gy vs 17 Gy vs >/=17.5 Gy. Conclusion: VS-SRS is an option for upfront treatment of large AVMs. Higher dose was associated with improved rates of nCR, obliteration, and cure suggesting that larger volumetric responses may facilitate salvage therapy and optimize the chance for cure.

Shore ND, Antonarakis ES, Cookson MS, Crawford ED, Morgans AK, Albala DM, **Hafron J**, Harris RG, Saltzstein D, Brown GA, Henderson J, Lowentritt B, Spier JM and Concepcion R (2020). "Optimizing the role of androgen deprivation therapy in advanced prostate cancer: Challenges beyond the guidelines." Prostate 80(6): 527-544.
Full Text
Department of Urology

Background: For specific clinical indications, androgen deprivation therapy (ADT) will induce disease prostate cancer (PC) regression, relieve symptoms and prolong survival; however, ADT has a well-described range of side effects, which may have a detrimental effect on the patient's quality of life, necessitating additional interventions or changes in PC treatment. The risk-benefit analysis for initiating ADT in PC patients throughout the PC disease continuum warrants review. Methods: A 14-member panel comprised of urologic and medical oncologists were chosen for an expert review panel, to provide guidance on a more judicious use of ADT in advanced PC patients. Panel members were chosen based upon their academic and community experience and expertise in the management of PC patients. Four academic members of the panel served as group leaders; the remaining eight panel members were from Large Urology Group Practice Association practices with proven experience in leading their advanced PC clinics. The panel members were assigned to four separate working groups, and were tasked with addressing the role of ADT in specific PC settings. Results: This article describes the practical recommendations of an expert panel for the use of ADT throughout the PC disease continuum, as well as an algorithm summarizing the key recommendations. The

target for this publication is all providers (urologists, medical oncologists, radiation oncologists, or advanced practice providers) who evaluate and manage advanced PC patients, regardless of their practice setting. Conclusion: The panel has provided recommendations for monitoring PC patients while on ADT, recognizing that PC patients will progress despite testosterone suppression and, therefore, early identification of conversion from castrate-sensitive to castration resistance is critical. Also, the requirement to both identify and mitigate side effects of ADT as well as the importance of quality of life maintenance are essential to the optimization of patient care, especially as more combinatorial therapeutic strategies with ADT continue to emerge.

Siljander MP, Whaley JD, Koueiter DM, Alsaleh M and **Karadsheh MS** (2020). "Length of stay, discharge disposition, and 90-day complications and revisions following primary total hip arthroplasty: A comparison of the direct anterior, posterolateral, and direct superior approaches." Journal of Arthroplasty. ePub Ahead of Print.
Request Form
Department of Orthopaedic Surgery

Background: The direct anterior (DA) approach is becoming increasingly popular for primary total hip arthroplasty (THA). The aim of this study is to evaluate early postoperative complication and revision rates based on surgical approach, comparing DA, posterolateral (PL), and direct superior (DS) approaches. Methods: After institutional review board approval, a total joint arthroplasty database from a single institution was used to identify all patients who underwent elective primary THA between July 2013 and November 2017 with a DA, PL, or DS hip approach. Patients were followed for complications out to 90 days postsurgery. Patients were divided into groups based on surgical approach and compared on length of stay, discharge disposition, and 90-day complication and revision rates. Results: There were 5341 THA procedures performed, with 3162 PL, 1846 DA, and 333 DS approaches. Length of stay was shorter for DS (1.7 +/- 0.9 days) and DA (1.8 +/- 0.9 days) than for PL approaches (2.3 +/- 1.4 days, P < .001) The DS approach had the highest rate of home discharges (93.1%), but the highest short-term revision rate (1.5%, P = .011). The DA approach had the lowest intraoperative fracture rate (0.1%, P = .019) but the highest incidence of postoperative fractures (1.3%, P = .021). There were no differences in readmission (P = .056), 90-day events (P = .062), emergency department visits (P = .210), dislocations (P = .090), combined perioperative fractures (P = .289), venous thromboembolic events (P = .059), or acute infection rates (P = .287). Conclusion: In the era of bundled payments, the DA, PL, and DS approaches can all be effectively used.

Šoupal J, Petruželkov L, **Grunberger G**, Haskova A, Flekač M, Matoulek M, Mikeš O, Pelcl T, Škrha J, Jr., Horov E, Škrha J, Parkin CG, Svačina S and Přazńy M (2020). "Glycemic outcomes in adults with T1D are impacted more by continuous glucose monitoring than by insulin delivery method: 3 years of follow-up from the comisair study." Diabetes Care 43(1): 37-43.
Full Text
Department of Internal Medicine

Objective: This study assessed the clinical impact of four treatment strategies in adults with type 1 diabetes (T1D): real-Time continuous glucose monitoring (rtCGM) with multiple daily insulin injections (rtCGM1MDI), rtCGM with continuous subcutaneous insulin infusion (rtCGM1CSII), self-monitoring of blood glucose with MDI (SMBG1MDI), and SMBG with CSII (SMBG1CSII). Research, Design, and Methods: This 3-year, nonrandomized, prospective, real-world, clinical trial followed 94 participants with T1D (rtCGM1MDI, n522; rtCGM1CSII, n526; SMBG1MDI, n521; SMBG1CSII, n525). The main end points were changes in A1C, time in range (70- 180 mg/dL [3.9-10 mmol/L]), time below range (<70 mg/dL [<3.9 mmol/L]), glycemic variability, and incidence of hypoglycemia. RESULTS At 3 years, the rtCGM groups (rtCGM1MDIand rtCGM1CSII) had significantly lower A1C (7.0% [53 mmol/mol], P 5 0.0002, and 6.9% [52 mmol/mol], P < 0.0001, respectively), compared with the SMBG1CSII and SMBG1MDI groups (7.7% [61 mmol/mol], P 5 0.3574, and 8.0% [64 mmol/mol], P 5 1.000, respectively), with no significant difference between the rtCGM groups. Significant improvements in percentage of time in rangewereobserved in thertCGMsubgroups (rtCGM1MDI, 48.7-69.0%, P < 0.0001; and rtCGM1CSII, 50.9-72.3%, P < 0.0001) and in the SMBG1CSII group (50.6-57.8%, P 5 0.0114). Significant reductions in time below range were found only in the rtCGM subgroups (rtCGM1MDI, 9.4-5.5%, P50.0387; and rtCGM1CSII, 9.0-5.3%, P 5 0.0235). Seven severe hypoglycemia episodes occurred: SMBG groups, n 5 5; sensor-Augmented insulin regimen groups, n 5 2. Conclusions: rtCGM was superior to SMBG in reducing A1C, hypoglycemia, and other end points in individuals with T1Dregardless of their insulin

delivery method.rtCGM1MDIcan be considered an equivalent but lower-cost alternative to sensor-Augmented insulin pump therapy and superior to treatment with SMBG1MDI or SMBG1CSII therapy.

Starke RM, McCarthy DJ, Chen CJ, Kano H, McShane B, Lee J, Mathieu D, Vasas LT, Kaufmann AM, Wang WG, **Grills IS**, Patibandla MR, Cifarelli CP, Paisan G, Vargo JA, Chytka T, Janouskova L, Feliciano CE, Rodriguez-Mercado R, Tonetti DA, Lunsford LD and Sheehan JP (2020). "Evaluation of stereotactic radiosurgery for cerebral dural arteriovenous fistulas in a multicenter international consortium." Journal of Neurosurgery 132(1): 114-121.
Request Form
Department of Radiation Oncology

Objective: In this multicenter study, the authors reviewed the results obtained in patients who underwent Gamma Knife radiosurgery (GKRS) for dural arteriovenous fistulas (dAVFs) and determined predictors of outcome. Methods: Data from a cohort of 114 patients who underwent GKRS for cerebral dAVFs were compiled from the International Gamma Knife Research Foundation. Favorable outcome was defined as dAVF obliteration and no posttreatment hemorrhage or permanent symptomatic radiation-induced complications. Patient and dAVF characteristics were assessed to determine predictors of outcome in a multivariate logistic regression analysis; dAVF-free obliteration was calculated in a competing-risk survival analysis; and Youden indices were used to determine optimal radiosurgical dose. Results: A mean margin dose of 21.8 Gy was delivered. The mean follow-up duration was 4 years (range 0.5-18 years). The overall obliteration rate was 68.4%. The postradiosurgery actuarial rates of obliteration at 3, 5, 7, and 10 years were 41.3%, 61.1%, 70.1%, and 82.0%, respectively. Post-GRKS hemorrhage occurred in 4 patients (annual risk of 0.9%). Radiation-induced imaging changes occurred in 10.4% of patients; 5.2% were symptomatic, and 3.5% had permanent deficits. Favorable outcome was achieved in 63.2% of patients. Patients with middle fossa and tentorial dAVFs (OR 2.4, $p = 0.048$) and those receiving a margin dose greater than 23 Gy (OR 2.6, $p = 0.030$) were less likely to achieve a favorable outcome. Commonly used grading scales (e.g., Borden and Cognard) were not predictive of outcome. Female sex (OR 1.7, $p = 0.03$), absent venous ectasia (OR 3.4, $p < 0.001$), and cavernous carotid location (OR 2.1, $p = 0.019$) were predictors of GKRS-induced dAVF obliteration. Conclusions: GKRS for cerebral dAVFs achieved obliteration and avoided permanent complications in the majority of patients. Those with cavernous carotid location and no venous ectasia were more likely to have fistula obliteration following radiosurgery. Commonly used grading scales were not reliable predictors of outcome following radiosurgery.

Swanberg SM, Thielen J and **Bulgarelli N** (2020). "Faculty knowledge and attitudes regarding predatory open access journals: a needs assessment study." Journal of the Medical Library Association 108(2): 208-218.
Full Text
Department of Foundational Medical Studies (OU)
Medical Library

Objective: The purpose of predatory open access (OA) journals is primarily to make a profit rather than to disseminate quality, peer-reviewed research. Publishing in these journals could negatively impact faculty reputation, promotion, and tenure, yet many still choose to do so. Therefore, the authors investigated faculty knowledge and attitudes regarding predatory OA journals. Methods: A twenty-item questionnaire containing both quantitative and qualitative items was developed and piloted. All university and medical school faculty were invited to participate. The survey included knowledge questions that assessed respondents' ability to identify predatory OA journals and attitudinal questions about such journals. Chi-square tests were used to detect differences between university and medical faculty. Results: A total of 183 faculty completed the survey: 63% were university and 37% were medical faculty. Nearly one-quarter (23%) had not previously heard of the term "predatory OA journal." Most (87%) reported feeling very confident or confident in their ability to assess journal quality, but only 60% correctly identified a journal as predatory, when given a journal in their field to assess. Chi-square tests revealed that university faculty were more likely to correctly identify a predatory OA journal ($p=0.0006$) and have higher self-reported confidence in assessing journal quality, compared with medical faculty ($p=0.0391$). Conclusions: Survey results show that faculty recognize predatory OA journals as a problem. These attitudes plus the knowledge gaps identified in this study will be used to develop targeted educational interventions for faculty in all disciplines at our university.

Taye A, Inabnet WB, 3rd, Pan S, Carty SE, Cotton T, **Czako P**, Doherty G, Gauger P, Hanks J, McAneny D, Milas M,

Perrier N, Rosen J, Schneider DF, Sharma J, Siperstein A and Sosa JA (2020). "Post-thyroidectomy emergency room visits and readmissions: Assessment from the Collaborative Endocrine Surgery Quality Improvement Program (CESQIP)." American Journal of Surgery. ePub Ahead of Print.
Full Text
Department of Surgery

Background: This study analyzed independent factors associated with post-thyroidectomy Emergency Room (ER) visits and Hospital Readmissions (HR). Methods: This is a retrospective review from the CESQIP registry of 8381 thyroidectomy patients by 173 surgeons at 46 institutions. A total of 7142 ER visits and 7265 HR were analyzed. Multivariable logistic regression analysis was performed to determine the risk factors for an ER visit or HR. Results: Within 30-days of surgery, rates of all ER visits were 3.4% (n = 250) and all HR were 2.3% (n = 170). Hypocalcemia was the reason for 21.9% of ER encounters and 36.4% of HR. BMI >40 kg/m(2) was a risk factor for both ER visit (OR1.86) and HR (OR1.94). Surgical duration >3 h (OR2.63), and transection of recurrent laryngeal nerve (OR4.58) were risk factors for HR. Conclusions: Strategies to decrease hypocalcemia and improve perioperative care of patients with BMI >40 kg/m(2) may improve post-thyroidectomy outcome.

Tennyson L, Turner K, Vollstedt A and **Peters K** (2020). "Cyclosporine for the treatment of Hunner's lesion interstitial cystitis." Neurourology and Urodynamics 39: S141-S142.
Request Form
Department of Urology

Todd B, **Nierenberg L** and Price J (2020). "Mondor's Disease: A rare cause of chest pain in the emergency department." Cureus 12(2): e6917.
Full Text
Department of Emergency Medicine
OUWB Medical Student Author

Thrombophlebitis of a subcutaneous vein, known as Mondor's disease, is a rare cause of chest pain and can mimic several more life-threatening diseases. Mondor's disease can be caused by trauma, or hypercoagulable states; however, in many cases the etiology is unknown. Mondor's disease is usually self-limited and can be managed conservatively. In this case report, we highlight a 52-year-old male patient who presented to our emergency department with chest pain caused by Mondor's disease mimicking a pulmonary embolism. Although a rare and benign diagnosis, Mondor's disease should be part of the differential diagnosis of chest pain and can be made on the basis of a thorough history and physical examination alone. Recognition of Mondor's disease could reduce costs and risks of further testing for patients presenting with chest pain.

van Rosendael AR, Bax AM, Smit JM, van den Hoogen IJ, Ma X, Al'Aref S, Achenbach S, Al-Mallah MH, Andreini D, Berman DS, Budoff MJ, Cademartiri F, Callister TQ, Chang HJ, **Chinnaiyan K**, Chow BJW, Cury RC, DeLago A, Feuchtner G, Hadamitzky M, Hausleiter J, Kaufmann PA, Kim YJ, Leipsic JA, Maffei E, Marques H, de Araujo Goncalves P, Pontone G, **Raff GL**, Rubinshtein R, Villines TC, Gransar H, Lu Y, Pena JM, Lin FY, Shaw LJ, Min JK and Bax JJ (2020). "Clinical risk factors and atherosclerotic plaque extent to define risk for major events in patients without obstructive coronary artery disease: The long-term coronary computed tomography angiography CONFIRM registry." European Heart Journal Cardiovascular Imaging. ePub Ahead of Print.
Full Text
Department of Internal Medicine

Aims: In patients without obstructive coronary artery disease (CAD), we examined the prognostic value of risk factors and atherosclerotic extent. Methods and Results: Patients from the long-term CONFIRM registry without prior CAD and without obstructive (>/=50%) stenosis were included. Within the groups of normal coronary computed tomography angiography (CCTA) (N = 1849) and non-obstructive CAD (N = 1698), the prognostic value of traditional clinical risk factors and atherosclerotic extent (segment involvement score, SIS) was assessed with Cox models. Major adverse cardiac events (MACE) were defined as all-cause mortality, non-fatal myocardial infarction, or late revascularization. In total, 3547 patients were included (age 57.9 +/- 12.1 years, 57.8% male), experiencing 460 MACE during 5.4 years of follow-up. Age, body mass index, hypertension, and diabetes were the clinical variables associated with increased MACE risk, but the

magnitude of risk was higher for CCTA defined atherosclerotic extent; adjusted hazard ratio (HR) for SIS >5 was 3.4 (95% confidence interval [CI] 2.3-4.9) while HR for diabetes and hypertension were 1.7 (95% CI 1.3-2.2) and 1.4 (95% CI 1.1-1.7), respectively. Exclusion of revascularization as endpoint did not modify the results. In normal CCTA, presence of >/=1 traditional risk factors did not worsen prognosis (log-rank P = 0.248), while it did in non-obstructive CAD (log-rank P = 0.025). Adjusted for SIS, hypertension and diabetes predicted MACE risk in non-obstructive CAD, while diabetes did not increase risk in absence of CAD (P-interaction = 0.004). Conclusion: Among patients without obstructive CAD, the extent of CAD provides more prognostic information for MACE than traditional cardiovascular risk factors. An interaction was observed between risk factors and CAD burden, suggesting synergistic effects of both.

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. ePub Ahead of Print.
Request Form
Department of Internal Medicine

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 mm3, (2) percent atheroma volume (PAV) in % [which equaled: PV/vessel volume * 100%], and (3) normalized total atheroma volume (TAVnorm) in mm3 [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 then PV and TAVnorm and may be the preferred method to report coronary atherosclerotic burden.

Van Rosendael AR, Narula J, Lin FY, Van Den Hoogen IJ, Gianni U, Al Hussein Alawamlh O, Dunham PC, Penã JM, Lee SE, Andreini D, Cademartiri F, **Chinnaiyan K**, Chow BJW, Conte E, Cury RC, Feuchtner G, Hadamitzky M, Kim YJ, Leipsic J, Maffei E, Marques H, De Araújo Gonçalves P, Plank F, Pontone G, **Raff GL**, Villines TC, Weirich HG, Al'Aref SJ, Baskaran L, Cho I, Danad I, Han D, Heo R, Lee JH, Rivzi A, Stuijfzand WJ, Gransar H, Lu Y, Sung JM, Park HB, Samady H, Stone PH, Virmani R, Budoff MJ, Berman DS, Chang HJ, Bax JJ, Min JK and Shaw LJ (2020). "Association of high-density calcified 1K plaque with risk of acute coronary syndrome." JAMA Cardiology 5(3): 282-290.
Full Text
Department of Internal Medicine

Importance: Plaque morphologic measures on coronary computed tomography angiography (CCTA) have been associated with future acute coronary syndrome (ACS). However, the evolution of calcified coronary plaques by noninvasive imaging is not known. Objective: To ascertain whether the increasing density in calcified coronary plaque is associated with risk for ACS. Design, Setting, and Participants: This multicenter case-control cohort study included individuals enrolled in ICONIC (Incident Coronary Syndromes Identified by Computed Tomography), a nested case-control study of patients drawn from the CONFIRM (Coronary CT

Angiography Evaluation for Clinical Outcomes: An International Multicenter) registry, which included 13 study sites in 8 countries. Patients who experienced core laboratory-verified ACS after baseline CCTA (n = 189) and control individuals who did not experience ACS after baseline CCTA (n = 189) were included. Patients and controls were matched 1:1 by propensity scores for age; male sex; presence of hypertension, hyperlipidemia, and diabetes; family history of premature coronary artery disease (CAD); current smoking status; and CAD severity. Data were analyzed from November 2018 to March 2019. Exposures: Whole-heart atherosclerotic plaque volume was quantitated from all coronary vessels and their branches. For patients who underwent invasive angiography at the time of ACS, culprit lesions were coregistered to baseline CCTA lesions by a blinded independent reader. Low-density plaque was defined as having less than 130 Hounsfield units (HU); calcified plaque, as having more than 350 HU and subcategorized on a voxel-level basis into 3 strata: 351 to 700 HU, 701 to 1000 HU, and more than 1000 HU (termed 1K plaque). Main Outcomes and Measures: Association between calcium density and future ACS risk. Results: A total of 189 patients and 189 matched controls (mean [SD] age of 59.9 [9.8] years; 247 [65.3%] were male) were included in the analysis and were monitored during a mean (SD) follow-up period of 3.9 (2.5) years. The overall mean (SD) calcified plaque volume (>350 HU) was similar between patients and controls (76.4 [101.6] mm3 vs 99.0 [156.1] mm3; P =.32), but patients who experienced ACS exhibited less 1K plaque (>1000 HU) compared with controls (3.9 [8.3] mm3 vs 9.4 [23.2] mm3; P =.02). Individuals within the highest quartile of 1K plaque exhibited less low-density plaque, as a percentage of total plaque, when compared with patients within the lower 3 quartiles (12.6% [10.4%] vs 24.9% [20.6%]; P <.001). For 93 culprit precursor lesions detected by CCTA, the volume of 1K plaque was lower compared with the maximally stenotic lesion in controls (2.6 [7.2] mm3 vs 7.6 [20.3] mm3; P =.01). The per-patient and per-lesion results were similar between the 2 groups when restricted to myocardial infarction cases. Conclusions and Relevance: Results of this study suggest that, on a per-patient and per-lesion basis, 1K plaque was associated with a lower risk for future ACS and that measurement of 1K plaque may improve risk stratification beyond plaque burden.

Vishweswaraiah S, **Singh RB**, Talbot C, Aydas B, Southekal S, Mishra NK, Friedman P, **Yilmaz A**, Guda C and **Radhakrishna U** (2020). "Artificial intelligence and epigenomic analysis of cell-free fetal DNA for Congenital Heart Defect (CHD) detection." American Journal of Obstetrics and Gynecology 222(1): S392-S393.
Full Text
Department of Obstetrics & Gynecology

Vollstedt A, Luke N, Wonjo K, Kelly C, Smith D, Baunoch D, Opel M, **Korman H**, Keating P, **Burks F**, **Jafri M**, Cline K, LaBelkoff L, Milbank A, Sherman N, Haverkorn R, Yore L, Shore N and **Sirls L** (2020). "Agreement of traditional urinary culture and multiplex PCR: Results from a prospective study." Neurourology and Urodynamics 39: S71-S72.
Request Form
Department of Urology

Vollstedt A, Luke N, Wonjo K, Kelly C, Smith D, Baunoch D, Opel M, **Korman H**, Keating P, **Burks F**, **Jafri M**, Cline K, LaBelkoff L, Milbank A, Sherman N, Haverkorn R, Yore L, Shore N and **Sirls L** (2020). "Urinary tract infection presentation of elderly patients and the decision to empirically treat." Neurourology and Urodynamics 39: S253-S254.
Request Form
Department of Urology

Vu CC, **Jawad MS** and **Krauss DJ** (2020). "The cost-effectiveness and value proposition of brachytherapy." Seminars in Radiation Oncology 30(1): 87-93.
Full Text
Department of Radiation Oncology

Brachytherapy is an effective treatment modality for a wide range of malignancies. However, brachytherapy utilization for both prostate and gynecologic malignancies has significantly declined over the last 20 years in favor of external beam radiation techniques. The cause of this decline is multifactorial, with logistical challenges, lower reimbursement, and inadequate training contributing to the preference of many radiation oncologists to more frequently recommend external beam radiation therapy. While the authors recognize the application of brachytherapy to a wider range of disease presentations among which include breast, skin, head and neck, and connective tissue cancers, in this review, we will review the analyses supporting

brachytherapy as a cost-effective component of the management in patients with prostate, cervix, and endometrial cancer.

Wang C, Kraus CN, **Patel KG**, Ganesan AK and Grando SA (2020). "Real-world experience of dupilumab treatment for atopic dermatitis in adults: A retrospective analysis of patients' records." International Journal of Dermatology 59(2): 253-256.
Full Text
OUWB Medical Student Author

Background: Clinical trial data for dupilumab, a monoclonal antibody against the interleukin-4 receptor (IL-4Rα), have shown that it is safe and effective for the treatment of moderate to severe atopic dermatitis in patients whose disease is resistant to other therapies. However, little real-world experience with dupilumab use has been reported thus far. The aim of this retrospective study was to assess overall outcomes in adult patients with atopic dermatitis (AD) treated with dupilumab. Methods: A retrospective review of electronic medical records was conducted for patients treated with dupilumab in the Department of Dermatology at the University of California, Irvine. Results: We analyzed the medical records of 77 AD patients who received dupilumab according to standard dosing and had at least one documented follow-up visit. In 66 patients (86%), dupilumab improved clinical disease severity, with 23 patients (30%) experiencing complete clearance on dupilumab. Dupilumab was generally well-tolerated and caused no serious adverse events. The most common side effects included dry eyes, conjunctivitis, and keratitis. The most common reason for discontinuation of treatment was lack of substantial clinical improvement or progression of disease severity, followed by ophthalmologic side effects. Conclusions: Overall, dupilumab was well-tolerated and resulted in clinical improvement in our patient population. These results provide additional important information on the safety and utility of dupilumab treatment for moderate to severe atopic dermatitis in the real-world clinical setting.

Wasserman JA, Redinger M and Gibb T (2020). "Responding to unprofessional behavior by trainees - A "just culture" framework." New England Journal of Medicine 382(8): 773-777.
Request Form
Department of Foundational Medical Studies (OU)

The article discusses the complexity of medical professionalism. It mentions that professionalism has been formally considered a medical education competency by the Accreditation Council for Graduate Medical Education and the American Board of Medical Specialties. It also talks about faculty report discomfort with identifying and responding to unprofessional behavior.

Wilson TG, Hanna A, **Recknagel J**, Pruetz BL, Baschnagel AM and **Wilson GD** (2020). "Prognostic significance of MTOR expression in HPV positive and negative head and neck cancers treated by chemoradiation." Head and Neck 42(2): 153-162.
Full Text
Department of Radiation Oncology
OUWB Medical Student Author

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

Wu JY, Deebajah M, Lai ZS, **Micale M** and Yu LM (2020). "Utilization of deep neural network in recognition of BCR/ABL gene rearrangements in fluorescence in situ hybridization images." Laboratory Investigation 100(SUPPL 1):

1493-1494.
Request Form
Department of Pathology

Yamamoto MH, Maehara A, Stone GW, Kini AS, Brilakis ES, Rizik DG, Shunk K, Powers ER, Tobis JM, Maini BS, **Dixon SR**, **Goldstein JA**, Petersen JL, Genereux P, Shah PR, Crowley A, Nicholls SJ, Mintz GS, Muller JE and Weisz G (2020). "2-Year outcomes after stenting of lipid-rich and nonrich coronary plaques." Journal of the American College of Cardiology 75(12): 1371-1382.
Request Form
Department of Internal Medicine

Background: Autopsy studies suggest that implanting stents in lipid-rich plaque (LRP) may be associated with adverse outcomes. Objectives: The purpose of this study was to evaluate the association between LRP detected by near-infrared spectroscopy (NIRS) and clinical outcomes in patients with coronary artery disease treated with contemporary drug-eluting stents. Methods: In this prospective, multicenter registry, NIRS was performed in patients undergoing coronary angiography and possible percutaneous coronary intervention (PCI). Lipid core burden index (LCBI) was calculated as the fraction of pixels with the probability of LRP >0.6 within a region of interest. MaxLCBI(4mm) was defined as the maximum LCBI within any 4-mm-tong segment. Major adverse cardiac events (MACE) included cardiac death, myocardial infarction, definite or probable stent thrombosis, or unplanned revascularization or rehospitalization for progressive angina or unstable angina. Events were subcategorized as culprit (treated) lesion-related, nonculprit (untreated) lesion-related, or indeterminate. Results: Among 1,999 patients who were enrolled in the COLOR (Chemometric Observations of Lipid Core Plaques of Interest in Native Coronary Arteries Registry), PCI was performed in 1,621 patients and MACE occurred in 18.0% of patients, of which 8.3% were culprit lesion-related, 10.7% were nonculprit lesion-related, and 31% were indeterminate during 2-year follow-up. Complications from NIRS imaging occurred in 9 patients (0.45%), which resulted in 1 peri-procedural myocardial infarction and 1 emergent coronary bypass. Pre-PCI NIRS imaging was obtained in 1,189 patients, and the 2-year rate of culprit lesion-related MACE was not significantly associated with maxLCBI(4mm) (hazard ratio of maxLCBI(4mm) per 100: 1.06; 95% confidence interval: 0.96 to 1.17; p = 0.28) after adjusting clinical and procedural factors. Conclusions: Following PCI with contemporary drug-eluting stents, stent implantation in NIRS-defined LRPs was not associated with increased periprocedural or late adverse outcomes compared with those without significant lipid.

Youn A (2020). "Commentary on: Predicting public interest in nonsurgical cosmetic procedures using Google Trends." Aesthetic Surgery Journal. ePub Ahead of Print.
Request Form
Department of Surgery

Yuhan BT, **Trang A**, Hutz MJ and Leonetti JP (2020). "Primary paraganglioma of the facial canal: An evidence-based approach." Otolaryngology-Head and Neck Surgery. ePub Ahead of Print.
Full Text
OUWB Medical Student Author

Objectives: To perform an evidence-based review evaluating presenting symptoms, imaging, and management for primary paragangliomas of the facial canal (PPFCs). Data Sources: PubMed/MEDLINE, Embase, Cochrane Library, and Web of Science. Review Methods: Studies were assessed for quality of evidence and bias with the Cochrane bias tool, GRADE, and MINORS criteria. Demographic data, imaging modalities, management strategies, and status at last follow-up were obtained. Results: Sixteen studies met inclusion criteria. In total, 21 patients with PPFCs were identified, 19 of which were histologically confirmed. Most common presenting symptoms included unilateral facial nerve dysfunction (n = 14, 73.7%) and pulsatile tinnitus (n = 8, 42.1%). Mean time from reported onset of facial dysfunction was 17.8 months. Computed tomography findings included an expanded descending facial nerve canal (n = 13, 76.5%). All cases with magnetic resonance imaging reported enhancement with contrast. Of the 18 patients who had surgery, 16 (88.9%) underwent full tumor resection while 1 (5.6%) had partial tumor debulking with adjuvant radiotherapy. Overall improvement in facial weakness was documented in 5 of 9 patients (55.6%) with initial facial nerve dysfunction and >6-month follow-up. No evidence of tumor recurrence was reported.

Conclusions: PPFCs are extraordinarily rare vascular neoplasms of the temporal bone. Early imaging with both computed tomography and magnetic resonance imaging is essential for narrowing the differential diagnosis, assessing the extent of tumor invasion, and accurate surgical planning. Surgical tumor resection with subsequent facial nerve reconstruction is recommended for patients with facial nerve dysfunction, while tumor biopsy or debulking may be indicated when normal facial movement in present.

Zakaria HM, Lipphardt M, Bazydlo M, Xiao SJ, Schultz L, Chedid M, Abdulhak M, Schwalb JM, Nerenz D, **Easton R**, Chang V and Investigators M (2020). "The preoperative risks and two-year sequelae of postoperative urinary retention: Analysis of the Michigan Spine Surgery Improvement Collaborative (MSSIC)." World Neurosurgery 133: E619-E626.

Full Text

Department of Orthopaedic Surgery

Objective: Although postoperative urinary retention (POUR) is common after spine surgery, the association of this adverse event with other morbidities and patient-reported outcomes is not fully understood. We sought to examine the sequelae of POUR after lumbar spine surgery. Methods: The Michigan Spine Surgery Improvement Collaborative (MSSIC) is a large prospective multicenter registry. MSSIC was queried with multivariate analysis for factors that are associated with POUR, the association of POUR with 90-day adverse events, and the effect of POUR on 2-year patient-reported outcomes and satisfaction. Results: Multivariate analysis identified hardware revision (odds ratio [OR], 0.61), 1 operative level (OR, 0.74), and ambulation on postoperative day zero (OR, 0.65) to be protective for POUR. Factors associated with POUR included age (OR, 1.19), male gender (OR, 1.58), body mass index <25 (OR, 1.22), diabetes (OR, 1.28), coronary artery disease (OR, 1.20), fusion surgery (OR, 1.27), and longer surgery (OR, 1.11). Patients who had POUR were more likely to be readmitted, develop a urinary tract infection, and develop an infection ($P < 0.001$). POUR was associated with decreased likelihood of achieving Oswestry Disability Index minimal clinically important difference at 90 days ($P < 0.001$), but not at 1 year after surgery. POUR was associated with dissatisfaction with surgery at 90 days ($P< 0.001$), 1 year ($P = 0.004$), and 2 years after surgery ($P = 0.011$). Conclusions: POUR is common after lumbar spine surgery, and the demographic, diagnostic, and surgical factors that are associated with POUR are identified. POUR is associated with several adverse events, and patients who have POUR were less likely to be satisfied with surgery up to 2 years after surgery.

Zwaans BMM, Wegner KA, Bartolone SN, Vezina CM, **Chancellor MB** and **Lamb LE** (2020). "Radiation cystitis modeling: A comparative study of bladder fibrosis radio-sensitivity in C57BL/6, C3H, and BALB/c mice." Physiological Reports 8(4): e14377.

Full Text

Department of Urology

A subset of patients receiving radiation therapy for pelvic cancer develop radiation cystitis, a complication characterized by mucosal cell death, inflammation, hematuria, and bladder fibrosis. Radiation cystitis can reduce bladder capacity, cause incontinence, and impair voiding function so severely that patients require surgical intervention. Factors influencing onset and severity of radiation cystitis are not fully known. We tested the hypothesis that genetic background is a contributing factor. We irradiated bladders of female C57BL/6, C3H, and BALB/c mice and evaluated urinary voiding function, bladder shape, histology, collagen composition, and distribution of collagen-producing cells. We found that the genetic background profoundly affects the severity of radiation-induced bladder fibrosis and urinary voiding dysfunction. C57BL/6 mice are most susceptible and C3H mice are most resistant. Irradiated C57BL/6 mouse bladders are misshapen and express more abundant collagen I and III proteins than irradiated C3H and BALB/c bladders. We localized Col1a1 and Col3a1 mRNAs to FSP1-negative stromal cells in the bladder lamina propria and detrusor. The number of collagen I and collagen III-producing cells can predict the average voided volume of a mouse. Collectively, we show that genetic factors confer sensitivity to radiation cystitis, establish C57BL/6 mice as a sensitive preclinical model, and identify a potential role for FSP1-negative stromal cells in radiation-induced bladder fibrosis.