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Full Text
Department of Ophthalmology
OUWB Medical Student Author

Background and Objective: A retrospective clinical study was performed to assess whether photographically screened and remotely read images for retinopathy of prematurity (ROP) allowed for timely and accurate diagnosis of treatment-warranted ROP compared to bedside examination. Patients and Methods: The study included 130 eyes of 65 premature neonates in born at William Beaumont Hospital, Royal Oak NICU. Bedside examined (2006 to 2010) and telemedicine screened (2010 to 2014) neonates were compared to identify whether there is a statistical difference in postmenstrual age (PMA) at the time of treatment. Results: One hundred thirty eyes of 65 infants met the inclusion and exclusion criteria. Thirty-five infants who needed laser treatment were screened bedside with an average PMA at treatment of 36.5 weeks. Thirty infants who needed treatment were photographically screened, with an average PMA at treatment of 36.4 weeks. Neither group had statistically different PMAs (P = .58). Conclusion: This study confirms that telemedicine also allows for appropriately timed treatment for early ROP.


Full Text
Department of Diagnostic Radiology and Molecular Imaging

While it is well accepted that CT is not an optimal imaging study to evaluate the breasts, findings on chest CT may be the first indication of an occult malignancy. The nonspecific appearance of breast findings and the lack of consensus guidelines for managing incidental breast findings may dissuade radiologists from thoroughly evaluating the breasts on CT. We review commonly encountered breast findings on CT and present an algorithm for managing incidentally detected breast findings.
Hepatitis A is a common viral infection with a benign course but in rare cases can progress to acute liver failure. It usually presents with abdominal pain, nausea, vomiting, diarrhea, jaundice, anorexia, or asymptomatically, but it can also present atypically with relapsing hepatitis and prolonged cholestasis. In addition, extrahepatic manifestations have been reported, including urticarial and maculopapular rash, acute kidney injury, autoimmune hemolytic anemia, aplastic anemia, acute pancreatitis, mononeuritis, reactive arthritis, glomerulonephritis, cryoglobulinemia, Guillain–Barre syndrome, and pleural or pericardial effusion. A rare manifestation of hepatitis A is acute myocarditis. We report a case of a young woman who presented with “flu-like symptoms” and was found to have severe elevation of liver enzymes due to acute hepatitis A infection. On her 3rd day of admission, the patient developed chest pain and nonspecific electrocardiographic changes. Her troponins rose to 16.4 ng/mL, and a transthoracic echocardiogram revealed global hypokinesis and a depressed ejection fraction at 30%. A CT angiography showed no evidence of significant coronary artery disease. The patient was managed supportively, and symptoms and laboratory findings slowly improved over the next 7 days. Her chest pain resolved and a follow-up echocardiogram showed improved ejection fraction to 45%.

Thermal ring injuries are rarely reported in the literature. For this reason, treatment is varied without a standard approach. We describe a case of a thermal wedding ring injury sustained during a welding accident. It is critical to understand the 3 zones of burn injuries when managing these infrequent cases. Furthermore, the dynamic progression that ensues a thermal burn will directly affect outcome. A case is presented along with a graduated approach to the management of such injuries.

Early career otolaryngologists (≤10 years) offered fewer prescriptions compared to those who had greater experience (31.1 vs 39.3, P = .02). Moreover, 73.6% of fellowship-trained otolaryngologists offered >10 prescriptions versus 82.7% of nonfellowship-trained otolaryngologists (P = .02). Practitioners in the South on average prescribed the greatest amount of opioids (P < .05). Conclusion: A majority of sinus surgeons prescribe ≥25 opioid prescriptions annually, with otolaryngologists who write a greater amount of prescriptions writing lengthier courses. As the mean opioid prescription length is 5.4 days, recent legislation limiting opioid prescriptions to 5 days may only have a modest impact for preventing the diversion of perioperative opioid prescriptions. These data suggest further standardized guidelines may be beneficial in elucidating the appropriate indications for the prescription of opioids among sinus surgeons.

**Background:** The objective of this work was to evaluate factors associated with antibiotic and oral corticosteroid (OCS) prescription among otolaryngologists regularly performing sinus surgery. Methods: Fellowship-trained rhinologists, including fellowship directors, were identified via the American Rhinologic Society (ARS) website. Non–fellowship-trained otolaryngologists performing ≥25 balloons (frontal/maxillary) or ≥25 functional endoscopic sinus surgeries (FESSs) (frontal/maxillary/ethmoids) were also included in “balloon surgeons” and “sinus surgeon” cohorts, respectively. Prescribing data for Medicare Part D beneficiaries was obtained for 2015. Results: Otolaryngologists included in this analysis wrote a median of 54 scripts for antibiotics, with a 15.1% antibiotic prescription rate. The overall script length per antibiotic was 11.1 days. Of fellowship-trained rhinologists, 90.2% wrote fewer than 100 scripts, compared to 25.6% and 32.5% of sinus surgeons and balloon surgeons, respectively. Fellowship-trained rhinologists wrote lengthier antibiotic scripts (14.1 vs 10.3 days, p < 0.05). Clinicians who have been in practice longer prescribed antibiotics significantly more frequently. Fellowship-trained rhinologists had a greater OCS rate (8.9%) than balloon and sinus surgeons (7.1%), also writing lengthier courses (15.0 vs 8.1 days). Early-career otolaryngologists wrote lengthier steroid prescriptions than those with 11 to 20 years and >20 years in practice. Conclusion: Antibiotic and OCS utilization varies by type of training, as non–fellowship-trained sinus surgeons and balloon surgeons tend to utilize antibiotics more aggressively, and fellowship-trained rhinologists utilize OCS more frequently. Otolaryngologists with more years in practice are more likely to incorporate antibiotics in the management of sinus disorders, although these conclusions must be considered in the context of this resource’s limitations. Further clarification of guidelines may be helpful for minimizing divergent practices and maintaining a consensus.


**Background:** This analysis explores the increasing heterogeneity of trends in allergy management under the premise that the practice of allergy has undergone significant changes in national economics, healthcare delivery, and treatment options from 2007 to 2016. Methods: Centers for Medicare and Medicaid Services (CMS) data were obtained for: (1) temporal trends in allergy immunotherapy injection (Current Procedural Terminology [CPT] codes 95115, 95117) and testing (CPT 95004, 95024) from 2007 to 2016; (2) geographic trends; and (3) practitioners administering immunotherapy. Although there are no sublingual immunotherapy (SLIT) CPT codes, billing for unlisted allergy/immunologic services (CPT 95199) were obtained. Results: Since 2007, there were 99.5 million allergy tests and 33.5 million immunotherapy injections billed to Medicare beneficiaries. Increases in testing have outpaced rising immunotherapy administration (49.7% vs 19.6% increase). Significant regional variation in testing rates was noted, with the greatest ratio of testing to immunotherapy in the South (0.35) and smallest ratio in the Northeast (0.18). The maximum unlisted allergy services billed was 594 (of which includes SLIT), compared to annual subcutaneous immunotherapy (SCIT) totals in the millions. The majority of immunotherapy in 2016 was administered by allergists/immunologists (51.6%) followed by otolaryngologists (31.2%), trends that have remained consistent since 2012. Conclusion: Physicians have been more aggressive in the workup of allergy-mediated disorders in recent years. Although differences in allergen load exist, there is tremendous geographic variation in the ratio of testing to immunotherapy. While the role otolaryngologists play in immunotherapy remains stable, allergists manage the majority of patients, reinforcing the importance of interdisciplinary cooperation and outreach. SLIT does not appear to play a significant role in this population.


**Background:** This analysis explores the increasing heterogeneity of trends in allergy management under the premise that the practice of allergy has undergone significant changes in national economics, healthcare delivery, and treatment options from 2007 to 2016. Methods: Centers for Medicare and Medicaid Services (CMS) data were obtained for: (1) temporal trends in allergy immunotherapy injection (Current Procedural Terminology [CPT] codes 95115, 95117) and testing (CPT 95004, 95024) from 2007 to 2016; (2) geographic trends; and (3) practitioners administering immunotherapy. Although there are no sublingual immunotherapy (SLIT) CPT codes, billing for unlisted allergy/immunologic services (CPT 95199) were obtained. Results: Since 2007, there were 99.5 million allergy tests and 33.5 million immunotherapy injections billed to Medicare beneficiaries. Increases in testing have outpaced rising immunotherapy administration (49.7% vs 19.6% increase). Significant regional variation in testing rates was noted, with the greatest ratio of testing to immunotherapy in the South (0.35) and smallest ratio in the Northeast (0.18). The maximum unlisted allergy services billed was 594 (of which includes SLIT), compared to annual subcutaneous immunotherapy (SCIT) totals in the millions. The majority of immunotherapy in 2016 was administered by allergists/immunologists (51.6%) followed by otolaryngologists (31.2%), trends that have remained consistent since 2012. Conclusion: Physicians have been more aggressive in the workup of allergy-mediated disorders in recent years. Although differences in allergen load exist, there is tremendous geographic variation in the ratio of testing to immunotherapy. While the role otolaryngologists play in immunotherapy remains stable, allergists manage the majority of patients, reinforcing the importance of interdisciplinary cooperation and outreach. SLIT does not appear to play a significant role in this population.


**Full Text**
Cancer is a major public health problem, and cancer patients and survivors face many physical and emotional challenges after the initial diagnosis, through treatment, and in the post-treatment period. Different integrative medicine (IM) modalities can be used to mitigate some of the physical issues that originate from the cancer itself or the treatment and to promote well-being and emotional health. Here, we discuss how an IM Department can function in a hospital system, particularly with regard to oncology patients, the modalities appropriate for oncology patients, how these modalities can benefit this patient population, and the role of IM in cancer survivorship. A dedicated IM Department that works with oncologists provides support and care for the whole person. These different modalities work together to reduce pain, anxiety, and chemotherapy-induced nausea and peripheral neuropathy, while promoting immune function and improving sleep, range of motion, and an overall sense of well-being. However, each modality has different contraindications for the oncology patient, and proper training is required for safe and effective care. We illustrate how IM can be a valuable component of the care of the oncology patient.


Full Text

Department of Emergency Medicine

Introduction: Establishing peripheral intravenous (IV) access is a vital step in providing emergency care. Ten to 30% of Emergency Department (ED) patients have difficult vascular access (DVA). Even after cannulation, early failure of US-guided IV catheters is a common complication. The primary goal of this study was to compare survival of a standard long IV catheter to a longer extended dwell catheter. Methods: This study was a prospective, randomized comparative evaluation of catheter longevity. Two catheters were used in the comparison: [1] a standard long IV catheter, the 4.78 cm 20 gauge Becton Dickinson (BD); and [2] a 6 cm 3 French (19.5 gauge) Access Scientific POWERWAND™ extended dwell catheter (EDC). Adult DVA patients in the ED with vein depths of 1.20 cm–1.60 cm and expected hospital admissions of at least 24 h were recruited. Results: 120 patients were enrolled. Ultimately, 70 patients were included in the survival analysis, with 33 patients in the EDC group and 37 patients in the standard long IV group. EDC catheters had lower rates of failure (p = 0.0016). Time to median catheter survival was 4.04 days for EDC catheters versus 1.25 days for the standard long IV catheter. Multivariate survival analysis also showed a significant survival benefit for the EDC catheter (p = 0.0360). Conclusion: A longer extended dwell catheter represents a viable and favorable alternative to the standard longer IVs used for US-guided cannulation of veins >1.20 cm in depth. These catheters have significantly improved survival rates with similar insertion success characteristics.


Full Text

Department of Surgery


Full Text

Department of Internal Medicine

Essentials: Warfarin typically requires International Normalized Ratio (INR) testing at least every 4 weeks. We implemented extended INR testing for stable warfarin patients in six anticoagulation clinics. Use of extended INR testing increased from 41.8% to 69.3% over the 3 year study. Use of extended INR testing appeared safe and effective. Summary: Background A previous single-center randomized trial suggested that patients with stable International Normalized Ratio (INR) values could safely receive INR testing as infrequently as every 12 weeks. Objective To test the success of implementation of an extended INR testing interval for stable warfarin patients in a practice-based, multicenter collaborative of anticoagulation clinics. Methods: At six
anticoagulation clinics, patients were identified as being eligible for extended INR testing on the basis of prior INR value stability and minimal warfarin dose changes between 2014 and 2016. We assessed the frequency with which anticoagulation clinic providers recommended an extended INR testing interval (> 5 weeks) to eligible patients. We also explored safety outcomes for eligible patients, including next INR values, bleeding events, and emergency department visits. Results: At least one eligible period for extended INR testing was identified in 890 of 3362 (26.5%) warfarin-treated patients. Overall, the use of extended INR testing in eligible patients increased from 41.8% in the first quarter of 2014 to 69.3% in the fourth quarter of 2016. The number of subsequent out-of-range next INR values were similar between eligible patients who did and did not have an extended INR testing interval (27.3% versus 28.4%, respectively). The numbers of major bleeding events were not different between the two groups, but rates of clinically relevant non-major bleeding (0.02 per 100 patient-years versus 0.09 per 100 patient-years) and emergency department visits (0.07 per 100 patient-years versus 0.19 per 100 patient-years) were lower for eligible patients with extended INR testing intervals than for those with non-extended INR testing intervals. Conclusions: Extended INR testing for stable warfarin patients can be successfully and safely implemented in diverse, practice-based anticoagulation clinic settings.


Full Text

Department of Urology

Infection with Zika virus (ZIKV) can be asymptomatic in adults, however, infection during pregnancy can lead to miscarriage and severe neurological birth defects. The goal of this protocol is to quickly detect ZIKV in both human and mosquito samples. The current gold standard for ZIKV detection is quantitative reverse transcription PCR (qRT-PCR); reverse transcription loop-mediated isothermal amplification (RT-LAMP) may allow for a more efficient and low-cost testing without the need for expensive equipment. In this study, RT-LAMP is used for ZIKV detection in various biological samples within 30 min, without first isolating the RNA from the sample. This technique is demonstrated using ZIKV infected patient urine and serum, and infected mosquito samples. 18S ribosomal ribonucleic acid and actin are used as controls in human and mosquito samples, respectively.


Full Text

Department of Emergency Medicine

Atrial fibrillation and flutter (AF) is a common condition among emergency department (ED) patients in the United States. Traditionally, ED care for primary complaints related to AF focus on rate control, and patients are often admitted to an inpatient setting for further care. Inpatient care may include further telemetry monitoring and diagnostic testing, rhythm control, a search for identification of AF etiology, and stroke prophylaxis. However, many patients are eligible for safe and effective outpatient management pathways. They are widely used in Canada and other countries but less widely adopted in the United States. In this project, we convened an expert panel to create a practical framework for the process of creating, implementing, and maintaining an outpatient AF pathway for emergency physicians to assess and treat AF patients, safely reduce hospitalization rates, ensure appropriate stroke prophylaxis, and effectively transition patients to longitudinal outpatient treatment settings from the ED and/or observation unit. To support local pathway creation, the panel also reached agreement on a protocol development plan, a sample pathway, consensus recommendations for pathway components, sample pathway metrics, and a structured literature review framework using a modified Delphi technique by a technical expert panel of emergency medicine, cardiology, and other stakeholder groups.

Full Text
Department of Surgery
Background: Negative pressure wound therapy (NPWT) has been described for closure of complex neonatal abdominal wounds, but advanced techniques for stoma or fistula control, skin protection, and the use of high pressure therapy not as well established. Cases: We identified neonatal patients at our institution who received NPWT for a complex abdominal wound, defined as a wound associated with a stoma or fistula with partial or complete dehiscence of the abdominal fascia or skin. We then reviewed techniques for decreasing wound contamination and protecting the newborn's skin. One patient had an especially complex wound; she was born at ∼23 weeks' gestational age (birth weight 580 g). She developed necrotizing enterocolitis and strictures, requiring multiple surgeries to relieve obstruction, ultimately resulting in an end ileostomy with mucous fistula. She suffered from wound dehiscence and retraction of her surgically created stoma, resulting in a complex abdominal wound with significant damage to the surrounding skin. We used advanced NPWT techniques to heal her wound, including topical skin protectants, placement of an adhesive dressing over the skin prior to placement of negative pressure dressing, placement of a negative pressure sponge directly on the wound bed and stoma, diversion of enteric contents away from the wound using a Malecot catheter, and an increase in the negative pressure applied. Conclusion: Complex neonatal abdominal wounds can be treated effectively using NPWT. The techniques we describe divert enteric contents away from the wound bed while maintaining negative pressure and protecting the surrounding skin. In addition, we used negative pressure up to ∼125 mm Hg and found it was well tolerated by our patients.


Full Text
Department of Pediatrics
Aim: To identify neonates at risk of haemolytic hyperbilirubinaemia through near-concurrent measurements of total serum/plasma bilirubin (TB) or transcutaneous bilirubin (TcB) and end-tidal breath carbon monoxide (CO), corrected for ambient CO (ETCOc), an index of bilirubin production and haemolysis. Methods: Paired TB/TcB (mg/dL) and ETCOc (ppm) measurements were obtained in newborns (n = 283) at 20 to <60 hours of age in five nurseries. TB/TcB values were assigned TB/TcB percentile risk values using the Bhutani hour-specific nomogram. In infants having two serial TB/TcB measurements (n = 76), TB rate of rise (ROR, mg/dL/h) was calculated. Results: For the entire cohort (n = 283), 67.1% and 32.9% had TB/TcB <75th and ≥75th percentile, respectively. TB/TcB (5.79 ± 1.84 vs 9.14 ± 2.25 mg/dL) and ETCOc (1.61 ± 0.45 vs 2.02 ± 1.35 ppm, p = 0.0002) were different between the groups. About 36.6% of infants with TB/TcB ≥75th percentile had ETCOc ≥ 2.0 ppm. In the subcohort of infants with serial TB/TcB measurements (n = 76), 44.7% and 55.3% had TB/TcB <75th and ≥75th percentile, respectively. TB/TcB (5.28 ± 1.97 vs 9.53 ± 2.78 mg/dL), ETCOc (1.72 ± 0.48 vs 2.38 ± 1.89 ppm, p = 0.05) and TB ROR (0.011 ± 0.440 vs 0.172 ± 0.471 mg/dL/h) were different between the groups. Conclusion: The combined use of TB/TcB percentile risk assessments and ETCOc measurements can identify infants with haemolytic hyperbilirubinaemia. The addition of TB ROR can identify those infants with elimination disorders.


Full Text
Department of Internal Medicine
OUWB Medical Student Author
Purpose: Few data on the effect of exercise interventions in black women at risk for cardiovascular disease are available. Methods: Women ≥18 yr of age without known cardiovascular disease with ≥1 coronary risk factor were enrolled in a community-based exercise program ≥3 d·wk−1 for ≥30 min per session for 6 months. Exercise training intensity ~50% to 80% of functional capacity, using heart rate (HR) and/or rating of perceived exertion (RPE) as the primary intensity modulators. Preconditioning versus postconditioning quality of life assessments (depression and level of daytime sleepiness), dietary fat intake, Duke Activity Status Index score, changes in cardiovascular efficiency (systolic/diastolic blood pressure (SBP/DBP), HR, RPE during a standardized submaximal workload), and anthropometric measures, including body weight, body mass index, and waist circumference, were evaluated. Results: Of 556 volunteers, 143 were excluded, leaving
413 women (222 white, 191 black; mean ± SD age, 61 ± 9 yr) who met compliance criteria. Both groups demonstrated significant (<italic>P</italic> < 0.05) postconditioning decreases in body mass index, waist circumference, resting SBP/DBP, and total and LDL cholesterol, and reductions in HR, SBP/DBP, and RPE at a fixed submaximal workload, and in fat screen, depression, and sleep scores. Duke Activity Status Index scores increased significantly (<italic>P</italic> < 0.0001) for both groups, signifying increases in self-reported functional capacity. Although 87 women (21%) experienced a musculoskeletal injury/discomfort during the program, there were no exercise-related cardiovascular events. Conclusions: A progressive moderate-to-vigorous exercise intervention without preliminary exercise testing elicited comparable improvements in coronary risk factors, anthropometric and quality of life measures, and cardiovascular efficiency in “at-risk” black and white women. These adaptations were achieved at exercise levels below those recommended in contemporary physical activity guidelines.


Full Text
Department of Internal Medicine
Department of Pathology

Aim: To systematically review liver disease associated with hemophagocytic lymphohistiocytosis (HLH), propose reasonable contraindications for liver transplantation for liver failure in HLH, and report an illustrative case. Methods: Systematic review according to PRISMA guidelines of hepatic manifestations of HLH using computerized literature search via PubMed of articles published since 1980 with keywords ("hemophagocytic lymphohistiocytosis" or "HLH") AND ("liver" or "hepatic"). Two authors independently performed literature search and incorporated articles into this review by consensus. Illustrative case report presented based on review of medical chart, and expert re-review of endoscopic photographs, radiologic images, and pathologic slides. Results: A 47-year-old Caucasian male, was hospitalized with high-grade pyrexia, rash, total bilirubin = 45 g/dL, moderately elevated hepatic transaminases, ferritin of 3300 ng/dL, leukopenia, and profound neutropenia (absolute neutrophil count < 100 cells/mm³). Viral serologies for hepatitis A, B, and C were negative. Abdominal computed tomography scan and magnetic resonance imaging revealed no hepatic or biliary abnormalities. Pathologic analysis of liver biopsy revealed relatively well-preserved hepatic parenchyma without lymphocytic infiltrates or macrophage invasion, except for sparse, focal hepatocyte necrosis. Bone marrow biopsy and aspirate revealed foamy macrophages engulfing mature and precursor erythrocytes, consistent with HLH. Interleukin-2 receptor (CD25) was highly elevated, confirming diagnosis of HLH according to Histiocytic Society criteria. Patient initially improved after high-dose prednisone therapy. Patient was judged not to be a liver transplant candidate despite model for end stage liver disease (MELD) score = 33 because liver failure was secondary to severe systemic disease from HLH, including septic shock, focal centrilobular hepatocyte necrosis from hypotension, bone marrow failure, and explosive immune activation from HLH. The patient eventually succumbed to overwhelming sepsis, progressive liver failure, and disseminated intravascular coagulopathy. Systematic review reveals liver injury is very common in HLH, and liver failure can sometimes occur. Data on liver transplantation for patients with HLH are very limited, and so far the results have shown a generally much worse prognosis than for other liver transplant indications. Liver transplantation should not be guided solely by MELD score, but should include liver biopsy results and determination whether liver failure is from intrinsic liver injury vs multisystem (extrahepatic) organ failure from HLH. Conclusion: This case report illustrates that liver transplantation may not be warranted when liver failure associated with HLH is primarily from multisystem failure from HLH. Liver biopsy may be very helpful in determining the severity and pathophysiology of the liver disease.


Full Text
Department of Orthopedic Surgery

Recently, indications for reverse total shoulder arthroplasty have expanded to include glenohumeral arthritis, rotator cuff arthropathy, irreparable rotator cuff tears, complex proximal humerus fractures, sequelae of trauma, and failed shoulder prostheses. Dislocation is a common complication, with rates ranging from 1.5% to 31%. The literature pertaining to management of instability in reverse total shoulder arthroplasty is scanty. Assessment of the patient and biomechanical and surgical factors is critical in determining the best course of treatment. Future studies involving patient selection, prosthetic design, surgical technique, and biomechanics may help reduce the rate of instability.


Full Text
Department of Radiation Oncology

Chang AM, Hollander JE, Su E, Weiss RE, Yagapen AN, Malveau SE, Adler DH, Bastani A, Baugh CW, Caterino JM,
Almost 20% of patients with syncope will experience another event. It is unknown whether recurrent syncope is a marker for a higher or lower risk etiology of syncope. The goal of this study is to determine whether older adults with recurrent syncope have a higher likelihood of 30-day serious clinical events than patients experiencing their first episode. Methods This study is a pre-specified secondary analysis of a multicenter prospective, observational study conducted at 11 emergency departments in the US. Adults 60 years or older who presented with syncope or near syncope were enrolled. The primary outcome was occurrence of 30-day serious outcome. The secondary outcome was 30-day serious cardiac arrhythmia. In multivariate analysis, we assessed whether prior syncope was an independent predictor of 30-day serious events. Results The study cohort included 3580 patients: 1281 (35.8%) had prior syncope and 2299 (64.2%) were presenting with first episode of syncope. 498 (13.9%) patients had 1 prior episode while 771 (21.5%) had >1 prior episode. Those with recurrent syncope were more likely to have congestive heart failure, coronary artery disease, previous diagnosis of arrhythmia, and an abnormal ECG. Overall, 657 (18.4%) of the cohort had a serious outcome by 30 days after index ED visit. In multivariate analysis, we found no significant difference in risk of events (adjusted odds ratio 1.09; 95% confidence interval 0.90–1.31; p = 0.387). Conclusion In older adults with syncope, a prior history of syncope within the year does not increase the risk for serious 30-day events.


This article describes a case of endometrial stromal sarcoma arising in a background of endometriosis presenting several years after total abdominal hysterectomy. Discussion of endometrial stromal sarcoma ensues as well as review of pertinent imaging findings.
observational cohort study included 135 clinical sites in the United States and Canada. A total of 5761 participants with coronary heart disease who did not qualify for primary prevention implantable cardioverter defibrillator therapy based on left ventricular ejection fraction (LVEF) of more than 35% or New York Heart Association (NYHA) heart failure class (LVEF >30%, NYHA I). EXPOSURES Clinical risk factors measured at baseline including age, LVEF, and NYHA heart failure class. Main Outcomes and Measures: Primary outcome of SAD, which is a composite of SAD and resuscitated ventricular fibrillation arrest. RESULTS The mean (SD) age of the cohort was 64 (11) years. During a median of 3.9 years, the cumulative incidence of SAD and non-SAD was 2.1% and 7.7%, respectively. Sudden and/or arrhythmic death was the most common mode of cardiovascular death accounting for 114 of 202 cardiac deaths (56%), although noncardiac death was the primary mode of death in this population. The 4-year cumulative incidence of SAD was lowest in those with an LVEF of more than 60% (1.0%) and highest among those with LVEF of 30% to 40% (4.9%) and class III/IV heart failure (5.1%); however, the cumulative incidence of non-SAD was similarly elevated in these latter high-risk subgroups. Patients with a moderately reduced LVEF (40%-49%) were more likely to die of SAD, whereas those with class II heart failure and advancing age were more likely to die of non-SAD. The proportion of deaths due to SAD varied widely, from 14% (18 of 131 deaths) in patients with NYHA II to 49% (37 of 76 deaths) in those younger than 60 years. Conclusions and Relevance: In a contemporary population of patients with coronary heart disease without severe systolic dysfunction, SAD accounts for a significant proportion of overall mortality. Moderately reduced LVEF, age, and NYHA class distinguished SAD and non-SAD, whereas other markers were equally associated with both modes of death. Absolute and proportional risk of SAD varied significantly across clinical subgroups, and both will need to be maximized in future risk stratification efforts.


Department of Family Medicine and Community Health

In an interesting investigation by Khoury-Hanold et al. (1), genital infection of mice with herpes simplex virus 1 (HSV1) were reported to cause multiple pelvic organ involvement and obstruction. A small subset of mice succumbed after the first week of HSV1 infection. The authors inferred that the mice died due to toxic megacolon. In a severe form of mechanical and/or functional obstruction involving gross dilation of the colon and profound toxemia, the presentation is called "toxic megacolon." The representative observations by Khoury-Hanold likely do not resemble toxic megacolon. The colon was only slightly dilated and benign appearing. Importantly, HSV1 infection affected the postjunctional mechanisms of smooth muscle relaxation like the sildenafil-response proteins, which may have been responsible for defective nitrergic neurotransmission and the delayed transit. Orally administered polyethylene glycol reversed the gastrointestinal "obstruction," suggesting a mild functional type of slowed luminal transit, resembling constipation, rather than toxic megacolon, which cannot be reversed by an osmotic laxative without perforating the gut. The authors suggest that the mice did not develop HSV1 encephalitis, the commonly known cause of mortality. The premature death of some of the mice could be related to the bladder outlet obstruction, whose backflow effects may alter renal function, electrolyte abnormalities and death. Muscle strip recordings of mechanical relaxation after electrical field stimulation of gastrointestinal, urinary bladder or cavernosal tissues shall help obtain objective quantitative evidence of whether HSV infection indeed cause pelvic multi-organ dysfunction and impairment of autonomic neurotransmission and postjunctional electromechanical relaxation mechanisms of these organs.


Department of Radiation Oncology

Background and Purpose: The aim of this international, multicenter, retrospective matched cohort study is to directly compare the outcomes after stereotactic radiosurgery (SRS) for brain arteriovenous malformations (AVM) in pediatric versus adult patients. Methods: We performed a retrospective review of patients with
AVM who underwent SRS at 8 institutions participating in the International Gamma Knife Research Foundation from 1987 to 2014. Patients were categorized into pediatric (<18 years of age) and adult (≥18 years of age) cohorts and matched in a 1:1 ratio using propensity scores. Favorable outcome was defined as AVM obliteration, no post-SRS hemorrhage, and no permanently symptomatic radiation-induced changes. Results: From a total of 2191 patients who were eligible for inclusion in the overall study cohort, 315 were selected for each of the matched cohorts. There were no significant differences between matched pediatric versus adult cohorts with respect to the rates of favorable outcome (59% versus 58%; \(P=0.936\)), AVM obliteration (62% versus 63%; \(P=0.934\)), post-SRS hemorrhage (9% versus 7%; \(P=0.298\)), radiological radiation-induced changes (26% versus 26%; \(P=0.837\)), symptomatic radiation-induced changes (2% versus 3%; \(P=0.589\)), or permanent radiation-induced changes (2% versus 3%; \(P=0.589\)). The all-cause mortality rate was significantly lower in the matched pediatric cohort (3% versus 10%; \(P=0.003\)). Conclusions: The outcomes after SRS for comparable AVMs in pediatric versus adult patients were not found to be appreciably different. SRS remains a reasonable treatment option for appropriately selected pediatric patients with AVM, who harbor a high cumulative lifetime hemorrhage risk. Age seems to be a poor predictor of AVM outcomes after SRS.


NeoCRT concurrently with IMRT or 3DCRT. PR was recorded as none, partial, or complete. Common terminology for adverse events version 4 was used to grade toxicities. Toxicity rates were compared using Chi-square analysis. Multivariable models were fit adjusting for age, gender, pre-tx CT to identify independent predictors of PR and toxicity. RESULTS: A total of 128 patients were analyzed: 60.1% male and 39.8% female, median age 57.7 years (range, 31-85 years). Clinical characteristics were similar across RT groups. The outcome of partial and complete PR was similar for IMRT and 3DCRT (48.1%, 23.1% vs. 31.7%, 23.3%), respectively. After adjusting for gender, age, and pre-RT chemotherapy type, IMRT and pretreatment PET and/or MRI imaging was significantly associated with increased odds for complete and partial response (OR =2.95, 95% CI: 1.21-7.25, P=0.018; OR =14.70, 95% CI: 3.69-58.78, P<0.0001). Additionally, IMRT was associated with reduced rates of dehydration, dermatitis, rectal pain, rectal bleeding, and diverting ostomy (P<0.05). Overall rates of grade 2 and higher toxicities were significantly reduced in IMRT vs. 3DCRT after adjusting for confounders (OR =0.27, 95% CI: 0.08-0.87). Conclusions: NeoCRT IMRT with pretreatment PET and/or MRI for LARC leads to reduced acute toxicities and improved PR compared to 3DCRT. Given the challenges associated with prospective validation of these data, IMRT with pretreatment PET and/or MRI should be considered standard treatment for LARC.


Department of Surgery


OUWB Medical Student Author

Department of Radiation Oncology


Department of Surgery

Background: This study was designed to determine the effect of statins on colorectal postoperative complications related to sepsis. Previous studies have reported conflicting results. Methods: This is a retrospective propensity score analysis of postoperative outcomes from a large regional database of patients who underwent elective colorectal resection from June 2012–July 2015. Results: 7285 patients met inclusion criteria: 34.5% received statins. Propensity score matching revealed that patients taking statins had reduced risk of sepsis (3.75% vs 5.32%, p = .03). Subgroup analysis revealed that this difference was driven by patients undergoing rectal resections. Among the rectal resection group, anastomotic leaks were more common in the non-statins group (4.1% vs. 1.3%, p = .01). There was no significant difference between those taking statins and those not on statin medications with respect to composite SSI or 30-day mortality. Conclusions: Statin medications are associated with decreased risk of sepsis after colorectal surgery and anastomotic leaks after rectal resection. Future studies should focus on medication type, dosage, and duration to confirm these results and identify patient populations that would benefit most from statin therapy.


Department of Internal Medicine

Purpose of Review: The “Extreme Exercise Hypothesis” is characterized by a U-shaped or reverse J-shaped, dose-response curve between physical activity volumes and cardiovascular health outcomes. In this review, we summarize recent findings that may support or refute the “Extreme Exercise Hypothesis.” Furthermore, we discuss potential cardiovascular health implications of the cardiac anatomical, structural, contractility, and
biomarker abnormalities that have been reported in some veteran endurance athletes. Recent Findings:
Emerging evidence from epidemiological studies and observations in cohorts of endurance athletes suggest that potentially adverse cardiovascular manifestations may occur following high-volume and/or high-intensity long-term exercise training, which may attenuate the health benefits of a physically active lifestyle. Accelerated coronary artery calcification, exercise-induced cardiac biomarker release, myocardial fibrosis, atrial fibrillation, and even higher risk of sudden cardiac death have been reported in athletes. There is primarily circumstantial evidence that supports the "Extreme Exercise Hypothesis." Subclinical and atherosclerotic coronary artery disease (CAD) as well as structural cardiovascular abnormalities and arrhythmias are present in some of the most active veteran endurance athletes and need appropriate clinical follow-up to reduce the risk for adverse cardiovascular outcomes. Future studies are warranted to establish the long-term cardiovascular health effects of these findings in veteran endurance athletes.


ultrasound guided renal mass biopsy. Median age in this group was 69.5 years, median body mass index was 29.5 kg/m² and 61.4% of the patients (43) were male. A total of 103 patients underwent hospital based, ultrasound guided biopsy. Median age in this group was 68.0 years, median body mass index was 29.3 kg/m² and 53.4% of the patients (55) were male. Finally, 52 patients underwent hospital based, computerized tomography guided biopsy. Median age in this group was 69 years, median body mass index was 30.1 kg/m² and 51.9% of the patients (27) were male. Median tumor size was 2.7 cm in patients undergoing office based, ultrasound guided renal mass biopsy, 2.2 cm in those undergoing hospital based, ultrasound guided biopsy and 2.1 cm in those undergoing hospital based, computerized tomography guided biopsy (p = 0.001). Renal cell carcinoma was found in 43 of 70 (61.4%), 74 of 103 (71.8%) and 33 of 52 (63.5%) respective biopsies. Respective diagnostic rates were 81.4% (57 of 70 cases), 88.3% (91 of 103) and 86.5% (45 of 52, p = 0.434). Concordance with surgical pathology was 97.7% (42 of 43 cases), 100% (35 of 35) and 100% (15 of 15), respectively. Complication rates were 4.3% (3 of 70 patients), 13.6% (14 of 103) and 13.5% (7 of 52), respectively (p = 0.096). Cost analysis revealed that when available, office based, ultrasound guided renal mass biopsy provides the health care system a total savings of approximately $46,011 yearly.

Conclusions: Office based, ultrasound guided renal mass biopsy for small renal masses is a safe and efficacious option for select patients, and potentially offers greater convenience and availability as well as decreased health care costs.


Department of Internal Medicine

Klebsiella oxytoca hemorrhagic colitis is a rare form of antibiotic associated hemorrhagic colitis that is Clostridium difficile negative. Klebsiella oxytoca colitis has been shown to be triggered by penicillin administration, yet other antibiotics have been implicated as well. It can mimic the appearance of ischemic colitis on endoscopy; however it will generally be found in young, otherwise healthy patients without risk factors. We present a case of a 33-year-old Caucasian female who presented to the emergency room with profuse, bloody diarrhea for 5 days, after a one-week course of ampicillin. Colonoscopy was notable for ulcerated mucosa with erythema and easy friability and the biopsy was suggestive of ischemic colitis. Stool culture was positive for many Klebsiella oxytoca. The patient was discharged home with resolution of symptoms after three days in the hospital. She was instructed to avoid penicillin antibiotics and minimize nonsteroidal anti-inflammatory drug use.


Department of Neurology


Department of Internal Medicine


Department of Internal Medicine
Outcomes in acute myeloid leukemia (AML) have been correlated with predictive and prognostic factors including age, performance status, comorbidities, cytogenetics, and molecular mutations. Retrospective review of 137 adult AML patients identified 3+7 (3 days of anthracycline and 7 days of cytarabine) induction and absence of monosomal karyotype to positively predict complete remission whereas positive predictors of overall survival were younger age and the absence of monosomal karyotype. Background: Acute myeloid leukemia (AML) is a heterogeneous malignancy with diverse genetic abnormalities, clinical presentations, and outcomes. Known predictive and prognostic factors in AML include age, performance status, comorbidities, cytogenetics, and molecular mutations. Identifying prognostic and predictive factors can inform the choice of induction therapy and outcomes prediction. Patients and Methods: A retrospective review was performed of 137 adult AML patients from 2010 to 2015. Predictors of complete remission (CR) and overall survival (OS) were determined for patients treated with 3+7 (3 days of anthracycline and 7 days of cytarabine) or hypomethylating agent. Variables associated with CR or OS were assessed using univariate Cox regression and a multivariate Cox model. Results: The average age was 65 years and 91 patients (66%), sample size is 137 patients had primary AML. Patients in the 3+7 induction group were younger, had a higher bone


Department of Urology
Written by OUWB Medical Student Author

Background: Persistent genital arousal disorder (PGAD) is a rare life-altering condition characterized by unwanted, uncomfortable genital sensations or spontaneous orgasms without physical or emotional stimulation. Its etiology remains unclear, and a variety of treatments have been attempted with incomplete resolution. We propose that chronic pudendal neuromodulation (CPN) may be a useful treatment for PGAD symptoms. Methods: A retrospective chart review was performed for women older than 18 years with a diagnosis of PGAD that had staged neuromodulation with placement of a tined lead at the pudendal nerve. Demographic, operative, and postoperative data were collected. A survey was then sent to these women to assess additional demographic data, preoperative and postoperative symptoms, and patient satisfaction. Descriptive statistics were performed. Results: Six women underwent CPN for PGAD. Mean age was 52 (SD, 9) years. Five (83%) of 6 were still implanted at time of survey, at a mean of 38 months after implantation; 1 device was removed for nonuse. Four of 6 completed surveys and were still using their device. Three of 4 had met their treatment goals and were satisfied with CPN; 3 of 4 felt CPN was the most useful treatment modality they had used overall. Chronic pudendal neuromodulation also improved chronic pelvic pain (4/4), bowel function (3/4), and bladder function (3/4). Conclusions: Chronic pudendal neuromodulation can be an effective treatment for decreasing frequency of PGAD symptoms and providing symptom relief.

Department of Internal Medicine

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Department of Internal Medicine

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marrow blast percentage, and more de novo AML compared with those in the hypomethylating agent group (P < .001, P < .001, P = .005, respectively). Univariate logistic regression for CR showed a significant association between age (P < .001), choice of induction (P < .001), and monosomy (P = .015), although only induction with 3+7 (P < .001) and absence of monosomy (P = .042) remained significant in multivariate analysis. Univariate Cox regression indicated that age (P = .003), AML status (de novo or secondary; P = .0277), choice of induction (P = .030), and monosomy (P = .010) had a significant association with OS. Only younger age (P = .018) and absence of monosomy (P = .022) were predictive of OS in multivariate Cox analysis. Conclusion: Positive predictors of CR in adult AML include absence of monosomy and induction treatment with 3+7; whereas positive predictors of OS are younger age and absence of monosomy.

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**Department of Internal Medicine**

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**Department of Obstetrics and Gynecology**

Huntington’s disease (HD) is a devastating, progressive neurodegenerative disease with a distinct phenotype characterized by chorea and dystonia, incoordination, cognitive decline and behavioral difficulties. The precise mechanisms of HD progression are poorly understood; however, it is known that there is an expansion of the trinucleotide cytosine-adenine-guanine (CAG) repeat in the Huntingtin gene. Herein DI/LC-MS/MS was used to accurately identify and quantify 185 metabolites in post mortem frontal lobe and striatum from HD patients and healthy control cases. The findings link changes in energy metabolism and phospholipid metabolism to HD pathology and also demonstrate significant reductions in neurotransmitters. Further investigation into the oxidation of fatty acids and phospholipid metabolism in pre-clinical models of HD are clearly warranted for the identification of potential therapies. Additionally, panels of 5 metabolite biomarkers were identified in both the frontal lobe (AUC = 0.962 (95% CI: 0.85–1.00) and striatum (AUC = 0.988 (95% CI: 0.899–1.00). This could have clinical utility in more accessible biomatrices such as blood serum for the early detection of those entering the prodromal phase of the disease, when treatment is believed to be most effective. Further evaluation of these biomarker panels in human cohorts is justified to determine their clinical efficacy.

[Full Text](#)  
**Department of Obstetrics and Gynecology**  
**Department of Internal Medicine**

Parkinson’s disease is the second most common neurodegenerative disease. In the vast majority of cases the origin is not genetic and the cause is not well understood, although progressive accumulation of alpha-synuclein aggregates appears central to the pathogenesis. Currently, treatments that slow disease progression are lacking, and there are no robust biomarkers that can facilitate the development of such treatments or act as aids in early diagnosis. Therefore, we have defined metabolomic changes in the brain and serum in an animal model of prodromal Parkinson’s disease. We biochemically profiled the brain tissue and serum in a mouse model with progressive synucleinopathy propagation in the brain triggered by unilateral injection of preformed alpha-synuclein fibrils in the olfactory bulb. In total, we accurately identified
and quantified 71 metabolites in the brain and 182 in serum using NMR and targeted mass spectrometry, respectively. Using multivariate analysis, we accurately identified which metabolites explain the most variation between cases and controls. Using pathway enrichment analysis, we highlight significantly perturbed biochemical pathways in the brain and correlate these with the progression of the disease. Furthermore, we identified the top six discriminatory metabolites and were able to develop a model capable of identifying animals with the pathology from healthy controls with high accuracy (AUC (95% CI) = 0.861 (0.755-0.968)). Our study highlights the utility of metabolomics in identifying elements of Parkinson’s disease pathogenesis and for the development of early diagnostic biomarkers of the disease.


OUWB Medical Student Author


Department of Pathology


Department of Internal Medicine

Background: Millions of Americans are currently living with diabetes and approximately 1.5 million cases are being diagnosed each year. Diabetes is now the seventh leading cause of death in the United States. In addition, the economic burden of the disease has resulted in billions of dollars in health care costs. In spite of these investments, the United States lags behind other developed countries on diabetes life expectancy and disease-related deaths. The purpose of this study is to assess the impact of a pharmacist-managed diabetes clinic (PMDC) model on diabetes core measures. Our hypothesis is that a PMDC would have a significant positive impact on the diabetes measures and will result in higher-quality care at a lower price.

Methods: This study is a randomized, open-label, controlled, parallel-group trial which will be conducted in the outpatient clinic at Beaumont Hospital, Royal Oak, Michigan. Patients will be randomly assigned to one of two groups: standard of care (SOC) or standard of care plus PMDC (SOC + PMDC). Included in the study will be patients older than 18 years of age with a diagnosis of type 2 diabetes mellitus and a hemoglobin A1c ≥ 9%, who are established with a primary care resident and who have not been seen in the PMDC within the last 3 months. The primary outcome is the change in hemoglobin A1c, measured at 6 and 12 months. Secondary outcomes include the impact on all diabetes core measures, patient quality of life, harms, and cost impact related to the intervention. Discussion: If the results of this trial are consistent with the previous retrospective analysis that a pharmacy clinic has a significant impact in controlling hemoglobin A1c levels as well as other diabetes core measures to improve clinical outcomes, it will constitute a scaffold for a future multicenter, randomized controlled trial. In addition, these results may influence future diabetes guidelines, leading to the inclusion of a PMDC as the standard of care. The impact of these results on the economic burden, life expectancy, and diabetes-related deaths are needed and have yet to be studied.


Department of Surgery

Background: The standard treatment of primary palmar hyperhidrosis had been thoracoscopic R2 sympathectomy, yet this sympathectomy level has been associated with serious unwanted side effects. Therefore, some recent experiences have recommended R2-sparing R3 or R4 thoracoscopic sympathectomy with less side effects, particularly compensatory hyperhidrosis (CH). The aim of this study is to compare the
Department of Emergency Medicine

Department of Anesthesiology

Full Text


Department of Urology

Introduction: Over the last 100 years, the terminology and diagnosis criteria for interstitial cystitis have evolved. Many therapeutic options have changed, but others have endured. This article will review the idea of separating ‘classic’ Hunner lesion interstitial cystitis (HL IC) from non-Hunner lesion interstitial cystitis and bladder pain syndrome (N-HL IC/BPS) and their respective treatment algorithms. Methods/Results: A literature search was performed to identify articles and research on HL IC and N-HL IC/BPS including definitions, etiological theories, and treatments. This article is an overview of the existing literature. We also offer insight into how HL IC and N-HL IC/BPS are approached at our tertiary referral center. Additionally, American Urological Association guidelines have been integrated and newer treatment modalities and research will be introduced at the conclusion. Conclusion: The AUA guidelines have mapped out a stepwise fashion to treat IC/BPS; at our institution we separate patients with HL IC from those with N-HL IC/BPS prior to them entering a treatment pathway. We identify the rarer patient with HL as having classic ‘IC’; this cystoscopic finding is critical in guiding treatment. We believe HL IC is a distinct disease from N-HL IC/BPS and therapy should focus on the bladder. The vast majority of patients with N-HL IC/BPS need management of their pelvic floor muscles as the primary therapy, complemented by bladder-directed therapies as needed as well as a multidisciplinary team to manage a variety of other regional/systemic symptoms. Ongoing research into IC/BPS will help us better understand the pathophysiology and phenotypes of this complex disease while exciting and novel research studies are developing promising treatments.


Department of Anesthesiology

Department of Emergency Medicine

Objectives: Syncope and near-syncope are common in patients with dementia and a leading cause of emergency department (ED) evaluation and subsequent hospitalization. The objective of this study was to describe the clinical trajectory and short-term outcomes of patients who presented to the ED with syncope or near-syncope and were assessed by their ED provider to have dementia. Methods: This multisite prospective cohort study included patients 60 years of age or older who presented to the ED with syncope or near-syncope between 2013 and 2016. We analyzed a subcohort of 279 patients who were identified by the treating ED provider to have baseline dementia. We collected comprehensive patient-level, utilization, and outcomes data through interviews, provider surveys, and chart abstraction. Outcome measures included...
serious conditions related to syncope and death. Results: Overall, 221 patients (79%) were hospitalized with a median length of stay of 2.1 days. A total of 46 patients (16%) were diagnosed with a serious condition in the ED. Of the 179 hospitalized patients who did not have a serious condition identified in the ED, 14 (7.8%) were subsequently diagnosed with a serious condition during the hospitalization, and an additional 12 patients (6.7%) were diagnosed postdischarge within 30 days of the index ED visit. There were seven deaths (2.5%) overall, none of which were cardiac-related. No patients who were discharged from the ED died or had a serious condition in the subsequent 30 days. Conclusions: Patients with perceived dementia who presented to the ED with syncope or near-syncope were frequently hospitalized. The diagnosis of a serious condition was uncommon if not identified during the initial ED assessment. Given the known iatrogenic risks of hospitalization for patients with dementia, future investigation of the impact of goals of care discussions on reducing potentially preventable, futile, or unwanted hospitalizations while improving goal-concordant care is warranted.


**Importance** The appropriate duration of antibiotics for staphylococcal bacteremia is unknown. **Objective:** To test whether an algorithm that defines treatment duration for staphylococcal bacteremia vs standard of care provides noninferior efficacy without increasing severe adverse events. **Design, Setting, and Participants:** A randomized trial involving adults with staphylococcal bacteremia was conducted at 16 academic medical centers in the United States (n = 15) and Spain (n = 1) from April 2011 to March 2017. Patients were followed up for 42 days beyond end of therapy for those with *Staphylococcus aureus* and 28 days for those with coagulase-negative staphylococcal bacteremia. Eligible patients were 18 years or older and had 1 or more blood cultures positive for *S aureus* or coagulase-negative staphylococci. Patients were excluded if they had known or suspected complicated infection at the time of randomization. **Interventions:** Patients were randomized to algorithm-based therapy (n = 255) or usual practice (n = 254). Diagnostic evaluation, antibiotic selection, and duration of therapy were predefined for the algorithm group, whereas clinicians caring for patients in the usual practice group had unrestricted choice of antibiotics, duration, and other aspects of clinical care. **Main Outcomes and Measures:** Coprimary outcomes were (1) clinical success, as determined by a blinded adjudication committee and tested for noninferiority within a 15% margin; and (2) serious adverse event rates in the intention-to-treat population, tested for superiority. The prespecified secondary outcome measure, tested for superiority, was antibiotic days among per-protocol patients with simple or uncomplicated bacteremia. **Results:** Among the 509 patients randomized (mean age, 56.6 [SD, 16.8] years; 226 [44.4%] women), 480 (94.3%) completed the trial. Clinical success was documented in 209 of 255 patients assigned to algorithm-based therapy and 207 of 254 randomized to usual practice (82.0% vs 81.5%; difference, 0.5% [1-sided 97.5% CI, −6.2% to ∞]). Serious adverse events were reported in 32.5% of algorithm-based therapy patients and 28.3% of usual practice patients (difference, 4.2% [95% CI, −3.8% to 12.2%]). Among per-protocol patients with simple or uncomplicated bacteremia, mean duration of therapy was 4.4 days for algorithm-based therapy vs 6.2 days for usual practice (difference, −1.8 days [95% CI, −3.1 to −0.6]). **Conclusions and Relevance:** Among patients with staphylococcal bacteremia, the use of an algorithm to guide testing and treatment compared with usual care resulted in a noninferior rate of clinical success. Rates of serious adverse events were not significantly different, but interpretation is limited by wide confidence intervals. Further research is needed to assess the utility of the algorithm.

Full Text

Department of Obstetrics and Gynecology

Germline BRCA1 or BRCA2 mutations (mtBRCA1 and mtBRCA2) increase risk for high-grade serous ovarian cancer (HGSOC), the most commonly diagnosed epithelial ovarian cancer histotype. Other identified risk factors for this cancer, which originates primarily in the distal fallopian tube epithelium (FTE), implicate ovulation, during which the FTE cells become transiently exposed to follicular fluid (FF). To test whether mtBRCA1 or mtBRCA2 nonmalignant FTE cells respond differently to periovulatory FF exposure than control patient FTE cells, gene expression profiles from primary FTE cultures derived from BRCA1 or BRCA2 mutation carriers or control patients were compared at baseline, 24 hours after FF exposure, and 24 hours after FF replacement with culture medium. Hierarchical clustering revealed both FF exposure and BRCA mutation status affect gene expression, with BRCA1 mutation having the greatest impact. Gene set enrichment analysis revealed increased NFκB and EGFR signaling at baseline in mtBRCA1 samples, with increased interferon target gene expression, including members of the ISGylation pathway, observed after recovery from FF exposure. Gene set enrichment analysis did not identify altered pathway signaling in mtBRCA2 samples. An inverse relationship between EGFR signaling and ISGylation with BRCA1 protein levels was verified in an immortalized FTE cell line, OE-E6/E7, stably transfected with BRCA1 cDNA. Suppression of ISG15 and ISGylated protein levels by increased BRCA1 expression was found to be mediated by decreased NFκB signaling. These studies indicate that increased NFκB signaling associated with decreased BRCA1 expression results in increased ISG15 and protein ISGylation following FF exposure, which may be involved in predisposition to HGSOC.


Full Text

OUWB Medical Student Author

Department of Emergency Medicine

Background: Prolonged emergency department (ED) length of stay (LOS) is associated with poorer clinical outcomes and patient experience. At our community hospital, trauma patients were experiencing extended ED LOS incommensurate with their clinical status. Our objective was to determine if operational modifications to patient flow would reduce the LOS for trauma patients. Method: We conducted a retrospective chart review of admitted trauma patients from January 1, 2015 to June 30, 2016 to study two interventions. First, a communication intervention [INT1], which required the ED provider to directly notify the trauma service, was studied. Second, a bed intervention [INT2], which reserved two temporary beds for trauma patients, was added. The primary outcome was the average ED LOS change across three time periods: (1) Baseline data [BASE] collected from January 1, 2015 to June 30, 2015, (2) INT1 data collected from July 1, 2015 to October 18, 2015, and (3) INT2 data collected from October 19, 2015 to June 30, 2016. Data was analyzed using descriptive statistics, two-sample t-tests, and multivariate linear regression. Results: A total of 777 trauma patients were reviewed, with 151, 150 and 476 reviewed during BASE, INT1, and INT2 time periods, respectively. BASE LOS for trauma patients was 389 min. After INT1, LOS decreased by 74.35 min (±31.92; p < 0.0001). After INT2 was also implemented, LOS decreased by 164.56 min (±22.97; p < 0.0001) from BASE LOS. Conclusion: Direct communication with the trauma service by the ED provider and reservation of two temporary beds significantly decreased the LOS for trauma patients.


Full Text

Department of Internal Medicine

The purpose of this study was to examine the subject and combined associations of cardiorespiratory fitness (fitness) and body mass index (BMI) with the risk of sudden cardiac death (SCD) in middle-aged men. This prospective study was based on a population sample of 2,357 men aged 42 to 60 years, who were followed up in the Kuopio Ischemic Heart Disease cohort study. Fitness was directly measured by peak oxygen uptake
(VO2peak) during progressive exercise testing to volitional fatigue. Participants were divided into 4 groups (fit-normal weight, unfit-normal weight, fit-overweight/obese, and unfit-overweight/obese) based on the median values of fitness and BMI. A total of 253 (10.7 %) SCDs occurred during an average follow-up of 22 years. After adjusting for potential confounders, the hazard ratio (HR) and 95% confidence interval (CI) for SCD was 1.80 (95% CI 1.21 to 2.68) for BMI \geq 30.0 kg/m(2) versus normal weight cohort, that is, BMI corresponding to 18.5 to 24.9 kg/m(2). However, these associations were no longer statistically significant after adjusting for VO2peak (1.49, 95% CI 0.98 to 2.24). Compared with the lower levels of fitness, upper levels of fitness had a 39% lower risk of SCD (HR 0.61, 95% CI 0.40 to 0.92) after adjusting for potential confounders, including BMI. In the combined associations of fitness and BMI with the risk of SCD, unfit-overweight/obese men had 1.80 times (95% CI 1.06 to 3.06) increased risk of SCD, but fit-overweight/obese men were not at increased risk of SCD (HR 1.22, 95% CI 0.66 to 2.25) as compared with their fit-normal weight counterparts. In conclusion, both overweight/obesity and fitness were independently associated with the risk of SCD; however, fitness appears to attenuate the risk of SCD in overweight/obese men, suggesting that improving fitness may reduce the risk of SCD in this population.


**Department of Internal Medicine**

**Objective**: To the association between metabolically healthy overweight/obesity and the risk of sudden cardiac death in middle-aged men. Participants and Methods: This prospective study was based on a population sample of 2185 men aged 42 to 60 years from the Kuopio Ischaemic Heart Disease Risk Factor Study. Participants were divided into 4 groups on the basis of body mass index and metabolic health status. Metabolically healthy overweight/obesity was defined as body mass index 25 kg/m(2) or greater without metabolic abnormalities, and metabolically unhealthy normal weight was defined as body mass index less than 25 kg/m(2) with 1 or more metabolic abnormalities. Results: During a median follow-up of 26 years (interquartile range, 18.7-28.1 years), 240 sudden cardiac deaths (11%) occurred. Compared with metabolically healthy normal weight men, metabolically unhealthy overweight/obese men had a higher risk of sudden cardiac death (hazard ratio, 1.99; 95% CI, 1.03-3.85) after adjusting for potential confounders. However, metabolically healthy overweight/obese men were not at increased risk of sudden cardiac death (hazard ratio, 0.95; 95% CI, 0.40-2.24) as compared with their metabolically healthy normal weight counterparts after adjusting for age, smoking, low-density lipoprotein cholesterol level, high-sensitivity C-reactive protein level, insulin level, history of myocardial infarction, and directly measured peak oxygen uptake. Conclusion: Our findings indicate that metabolically healthy normal weight men and metabolically healthy overweight/obese men were at comparable risk of sudden cardiac death over a 26-year follow-up period, suggesting that a baseline body mass index of 25 kg/m(2) or greater per se does not adversely affect the risk of sudden cardiac death.


**OUWB Medical Student Author**

**Purpose**: Timing of bone grafting for maxillary alveolar clefts is not standardized. Secondary bone grafting is often performed; however, consensus does not exist regarding use of chronologic versus dental age to guide treatment. Several authors suggest an early chronologic age is associated with greater success. Available literature was systematically reviewed for evidence for optimal timing for grafting maxillary alveolar clefts. Methods: PubMed, MEDLINE, and Cochrane Central Registrar of Controlled Trials databases were queried for manuscripts pertaining to maxillary alveolar cleft bone grafting. Inclusion criteria included manuscripts with level of evidence 4 or greater. Studies not using bone graft, lacking postoperative follow up, and clinical reports were excluded. Seventeen articles met criteria. Results: Nine manuscripts recommended grafting based on dental age prior to eruption of the permanent canines, while 8 recommended grafting between ages 7 to 12. The most commonly reported complication was wound dehiscence, followed by graft-site infection. Ten studies used perioperative treatment protocols, 8 of which included preoperative and/or postoperative orthodontia for maxillary expansion. Correlation between chronologic age and success was
not significant, but trended towards greater success with increasing age. Conclusion: Success of secondary grafting is high, but significant variability exists in the timing of grafting. Evidence is lacking to support specific chronologic age; rather, perioperative protocols, systematic surgical technique, and a multidisciplinary discussion are likely more substantial in achieving success, and may be confounders in studies where an early age at grafting appears associated with success. The timing of bone grafting for maxillary alveolar clefts would benefit from a prospective randomized study.


Department of Obstetrics and Gynecology
Department of Radiation Oncology
Department of Pediatrics

Purpose: Immune checkpoint inhibitors designed to revert tumor-induced immunosuppression have emerged as potent anticancer therapies. Tryptophan metabolism represents an immune checkpoint, and targeting this pathway's rate-limiting enzyme IDO1 is actively being investigated clinically. Here, we studied the intermediary metabolism of tryptophan metabolism in glioblastoma and evaluated the activity of the IDO1 inhibitor GDC-0919, both alone and in combination with radiation (RT). Experimental Design: LC/GC-MS and expression profiling was performed for metabolomic and genomic analyses of patient-derived glioma. Immunocompetent mice were injected orthotopically with genetically engineered murine glioma cells and treated with GDC-0919 alone or combined with RT. Flow cytometry was performed on isolated tumors to determine immune consequences of individual treatments. Results: Integrated cross-platform analyses coupling global metabolomic and gene expression profiling identified aberrant tryptophan metabolism as a metabolic node specific to the mesenchymal and classical subtypes of glioblastoma. GDC-0919 demonstrated potent inhibition of this node and effectively crossed the blood-brain barrier. Although GDC-0919 as a single agent did not demonstrate antitumor activity, it had a strong potential for enhancing RT response in glioblastoma, which was further augmented with a hypofractionated regimen. RT response in glioblastoma involves immune stimulation, reflected by increases in activated and cytotoxic T cells, which was balanced by immune checkpoint reactivation, reflected by an increase in IDO1 expression and regulatory T cells (Treg). GDC-0919 mitigated RT-induced Tregs and enhanced T-cell activation. Conclusions: Tryptophan metabolism represents a metabolic node in glioblastoma, and combining RT with IDO1 inhibition enhances therapeutic response by mitigating RT-induced immunosuppression.


Department of Internal Medicine

Purpose: To describe and quantify SD-OCTA metrics among subjects with varying severities of diabetic retinopathy (DR) and determine correlation with disease severity. Methods: Retrospective, observational, multicenter, Institutional Review Board-approved study of patients with and without DR at 3 tertiary-care centers using ZEISS AngioPlex™ SD-OCTA (Cirrus, Carl Zeiss Meditec, Dublin, CA). A total of 110 subjects and 201 eyes were included (38 normal, 61 mild non-proliferative DR (NPDR), 27 moderate NPDR, 24 severe NPDR, and 51 proliferative DR (PDR) eyes). A semi-automated segmentation algorithm was used to assess retinal microvasculature in superficial (SRL), deep (DRL), and full-thickness (RET) retinal layers with 3x3-mm scans centered on the fovea. Quantified capillary metrics included vessel skeletal density (VSD), flow impairment region (FIR), and flux. Associations between SD-OCTA metrics and DR status were analyzed with
generalized estimating equations accounting for correlations between two eyes from one subject. Results: When comparing normal to mild NPDR eyes, mean VSD was decreased in SRL (0.153±0.007 vs 0.147±0.010) and DRL (0.151±0.008 vs 0.143±0.013) (p<0.05 for both). Mean FIR were greater in RET (1.27±0.35 mm² vs 1.60±0.61 mm²), SRL (1.57±0.37 mm² vs 1.92±0.58 mm²), and DRL (2.03±0.48 mm² vs 2.56±0.88 mm²) (p<0.05 for all). Mean FIR in all 3 layers were significantly greater for progressively worse DR stages (p<0.05 for all). No differences in flux were observed in normal versus mild NPDR eyes. Significant interactions between age and mild NPDR were seen in FIR of SRL and DRL (p<0.05 for both). Significant trends were also noted in other OCTA morphology parameters.

Conclusions: There are significant differences in capillary density (SRL and DRL) and morphology among normal eyes compared to mild NPDR eyes. Progressively greater changes in density and morphology are seen with worsening DR status. The OCTA-based metrics may objectively assess DR severity.


Department of Diagnostic Radiology and Molecular Imaging
Department of Orthopedic Surgery


Department of Orthopedic Surgery

Polyethylene wear is a known complication in total joint arthroplasty, however, in vivo wear rates in reverse total shoulder arthroplasty (RTSA) remain largely unknown. This study aimed to quantify volumetric and surface deviation changes in retrieved RTSA humeral liners using a novel micro-computed tomography (μCT)-based technique. After IRB-approval, 32 humeral liners (single manufacturer and model) with term-of-service greater than 90 days were analyzed. Clinical demographics and surgical data were collected via chart review. Unworn liners were used as geometric controls. Retrieved and unworn liners underwent μCT scanning. Retrieved liner volumes were isolated, co-registered to controls of matching geometry, and surface deviations of the articulation surface and rim were computed. Differences in total volume loss (TVL), volumetric wear rate (VWR), and surface deviation were reported. Semi-quantitative grading evaluated rim damage presence and severity. Mean term-of-service for all liners was 2.07 ± 1.33 years (range: 0.30–4.73). Mean TVL and VWR were 181.3 ± 208.2 mm³ and 114.5 ± 160.3 mm³/year, respectively. Mean articulation and rim surface deviations were 0.084 ± 0.065 and 0.177 ± 0.159 mm, respectively. Articulation surface deviation was positively correlated to term-of-service. Rim damage was present on 63% of liners and correlated significantly to rim surface deviation. This study reports in vivo wear rates of retrieved RTSA implants. Our results demonstrate volumetric and articulation surface wear in select RTSA liners that is correlated to term-of-service. Calculation of in vivo wear rates can help bridge the gap between clinical outcomes and experimental models such as wear simulations and computational models.


Department of Radiation Oncology

Purpose: Data errors caught late in treatment planning require time to correct, resulting in delays up to 1 week. In this work, we identify causes of data errors in treatment planning and develop a software tool that detects them early in the planning workflow. Methods: Two categories of errors were studied: data transfer errors and TPS errors. Using root cause analysis, the causes of these errors were determined. This information was incorporated into a software tool which uses ODBC-SQL service to access TPS’s Postgres and Mosaiq MSSQL databases for our clinic. The tool then uses a read-only FTP service to scan the TPS unix file system for errors. Detected errors are reviewed by a physicist. Once confirmed, clinicians are notified to correct the error and educated to prevent errors in the future. Time-cost analysis was performed to estimate
the time savings of implementing this software clinically. Results: The main errors identified were incorrect patient entry, missing image slice, and incorrect DICOM tag for data transfer errors and incorrect CT-density table application, incorrect image as reference CT, and secondary image imported to incorrect patient for TPS errors. The software has been running automatically since 2015. In 2016, 84 errors were detected with the most frequent errors being incorrect patient entry (35), incorrect CT-density table (17), and missing image slice (16). After clinical interventions to our planning workflow, the number of errors in 2017 decreased to 44. Time savings in 2016 with the software is estimated to be 795 h. This is attributed to catching errors early and eliminating the need to replan cases. Conclusions: New QA software detects errors during planning, improving the accuracy and efficiency of the planning process. This important QA tool focused our efforts on the data communication processes in our planning workflow that need the most improvement.


Department of Internal Medicine

Background: Diagnosis of coronary artery disease and management strategies have relied solely on the presence of diameter stenosis ≥50%. We assessed whether direct quantification of plaque burden (PB) and plaque characteristics assessed by coronary computed tomography angiography could provide additional value in terms of predicting rapid plaque progression. Methods and Results: From a 13-center, 7-country prospective observational registry, 1345 patients (60.4±9.4 years old; 57.1% male) who underwent repeated coronary computed tomography angiography >2 years apart were enrolled. For conventional angiographic analysis, the presence of stenosis ≥50%, number of vessel involved, segment involvement score, and the presence of high-risk plaque feature were determined. For quantitative analyses, PB and annual change in PB (ΔPB/y) in the entire coronary tree were assessed. Clinical outcomes (cardiac death, nonfatal myocardial infarction, and coronary revascularization) were recorded. Rapid progressors, defined as a patient with an annual change in PB ≥0.33%/y (0.33%/y), were older, more frequently male, and had more clinical risk factors than nonrapid progressors (all P<0.05). After risk adjustment, addition of baseline PB improved prediction of rapid progression to each angiographic assessment of coronary artery disease, and the presence of high-risk plaque further improved the predictive performance (all P<0.001). For prediction of adverse outcomes, adding both baseline PB and ΔPB/y showed best predictive performance (C statistics, 0.763; P<0.001). Conclusions: Direct quantification of atherosclerotic PB in addition to conventional angiographic assessment of coronary artery disease might be beneficial for improving risk stratification of coronary artery disease.


OUWB Medical Student Author

Proteins and microRNAs (miRNAs) within the axon locally regulate axonal development. However, protein profiles of distal axons of cortical neurons have not been fully investigated. In particular, networks of genes encoding axonal proteins and their related miRNAs in sub compartments of neurons such as axons remain unknown. Using embryonic cortical neurons cultured in a microfluidic device and proteomic approaches, we found that distal axons contain 883 proteins. Bioinformatics analysis revealed that 94 out of these 883 proteins are related to regulating axonal growth. Of the 94 genes encoding these proteins, there were 56 candidate genes that can be putatively targeted by axon-enriched 62 miRNAs with 8mer sites that exactly match these target genes. Among them, we validated 11 proteins and 11 miRNAs, by means of western blot and RT-PCR, respectively. Treatment of distal axons with chondroitin sulfate proteoglycans (CSPGs) that inhibit axonal growth elevated miR-133b, -203a, -29a, and -92a, which were associated with reduced protein level of AKT, MTOR, PI3K, DPYSL2, MAP1B, and PPP2CA. In contrast, reduction of miR-128, -15b, -195, -26b, -34b, -376b, and -381 by CSPGs was accompanied by increased EZR, KIF5A, DCX, GSX3B, and ROCK2 proteins. In silico pathway analysis revealed an interconnected network of these miRNAs and protein coding genes.
that is highly related to regulating axonal growth. Our data provide new insights into networks of miRNAs and their related proteins in distal axons in mediating axonal growth.


Full Text

Department of Pathology

Background: Intrahepatic cholestasis of pregnancy is an incompletely understood disease that poses significant fetal risks, including stillbirth. Treatment of intrahepatic cholestasis of pregnancy is aimed at relieving maternal symptoms and improving fetal outcomes. Case: A 21-year-old gravida woman, 3 para 0111, presented at 27 2/7 weeks of gestation with severe intrahepatic cholestasis of pregnancy. Her clinical course was refractory to first-line therapy with ursodiol, and she was started on rifampin with rapid improvement of symptoms and transaminitis. Despite maternal improvement, she was delivered at 31 weeks of gestation for persistent nonreassuring fetal status. Conclusion: Rifampin may be an effective adjunctive therapy for intrahepatic cholestasis of pregnancy refractory to ursodiol alone. Additional research is needed to assess short-term and long-term maternal and newborn outcomes, because fetal deterioration still occurred in spite of maternal improvement.


Full Text

Department of Radiation Oncology

Purpose: Four-dimensional (4D) adaptive radiation therapy (ART) treatment planning is an alternative to the conventional margin-based treatment planning approach. In 4D ART, interfraction patient geometric variations, gathered from computed tomography (CT) or cone beam CT (CBCT) images acquired during the patient treatment course, are directly incorporated into the adaptive plan optimization using a probabilistic treatment planning method. The goal of the present planning study was to evaluate the dosimetric differences between 4D ART and conventional margin-based adaptive planning strategies for head and neck cancers. In addition, we examined whether the dose differences achieved with 4D ART would translate into clinically relevant toxicity reductions using the existing normal tissue complication probability (NTCP) models. Methods and Materials: For 18 head and neck cancer patients, the treatment plans were retrospectively generated for 4 different treatment strategies, including a solely image guided radiation therapy (IGRT) strategy (IGRT-only), 2 conventional adaptive treatment planning strategies using 3- and 0-mm planning target volume (PTV) margins, and the 4D ART strategy. In the IGRT-only strategy, a conventional 3-mm PTV margin treatment plan was applied for the entire treatment course. In the 2 conventional adaptive strategies, 2 new treatment plans were generated during the treatment course using diagnostic planning CT scans acquired after the 10th and 22nd fractions. The 4D ART followed the same adaptive schedule, except that the 4D adaptive plan was generated using 5 CBCT images acquired during the 5 most recent treatment fractions. For each strategy, the actual delivered dose for the entire treatment course was constructed by calculating the daily doses on 35 CBCT scans, deforming back to the pretreatment planning CT scan, and accumulating over all 35 fractions. The target coverage was evaluated using the percentage of target volume receiving >= 100% of the prescription dose (V-100%) and the minimum dose to 99% of the target volume (D-99). It was considered adequate if the V-100% was >= 95% and the dose deficit in D-99 was <= 2 Gy (with respect to the prescription dose). For each strategy, the dose received by the organs at risk (OARs) was also evaluated, and the corresponding NTCP values were subsequently calculated using 3 NTCP models. Results: Adequate target coverage was achieved for the primary clinical target volume (CTV1) and elective nodal CTV (CTV2) with a 3-mm PTV margin, regardless of adaptation. The 3-mm ART plan reduced the OAR mean dose by 1 to 2 Gy compared with the IGRT-only plan. The 0-mm ART plan further reduced the OAR dose by another 2 to 3 Gy at the expense of target coverage: 3 and 1 patient had V-100% <95%, and 6 and 5 patients had a >2 Gy dose deficit in D(99) for the CTV1 and CTV2, respectively. Use of 4D ART improved target coverage and attained OAR sparing similar to that with 0-mm ART. The number of patients with V 100% <95% and >2 Gy D-99 deficit decreased to 0 and 0 for CTV1 and 0 and 2 for CTV2, respectively. The NTCP calculations suggested that 4D ART could benefit a substantial
portion of patients compared with IGRT-only because 17 and 12 patients had >= 5% and >= 10% NTCP reductions for parotid toxicity and 18 and 3 patients had >= 5% and >= 10% NTCP reductions for swallowing toxicity, respectively. Conclusions: Compared with margin-based adaptive planning strategies, 4D ART provides a better balance between target coverage and OAR sparing. NTCP estimation predicted for theoretical clinical benefits that warrant further clinical validation.


Full Text

Department of Surgery

Background: Medial plantar artery perforator (MPAP) flap was proposed as proper option for finger pulp reconstruction. To provide the previously unavailable vessel information required for this small flap design, this study aimed to gather all necessary anatomy of MPA, MPAP, and their territories of blood supply to apply in clinical MPAP flap reconstruction minimizing perforator injury. Methods: Dissection of 30 Thai cadaveric feet for visualizing superficial branch of MPA and its perforators (MPAP) using acrylic dye cannulation were performed. Diameter, length, number of branches, course, distributing areas of these vessels, and also their areas of blood supply were recorded in relation to specified landmarks, eg. C-MTH line; medial calcaneal tuberosity to plantar side of the first metatarsal head and S point; emerging point of superficial branch of MPA from deep fasciae into subcutaneous layer. Results: Average diameter of MPA at its origin and total length are 1.63 ± 0.3 and 52.8 ± 16.1 mm, respectively. It provides 1–3 perforators, with an average size and length of 0.36 ± 0.11 and 23.2 ± 5.47 mm, respectively. Its distribution is mostly in the posteromedial quadrant within 50 and 30 mm from the midpoint of C-MTH line and the S point, respectively. The estimated perforator flap area is 2.5 cm × 1.5 cm and 4.5 cm × 2.5 cm for single and double perforators, respectively. Conclusions: MPAP flap was proved as another ideal option for finger pulp reconstruction. Its limitation is small size of perforators but this can be overcome by using MPA for microsurgical anastomosis instead.


Full Text

OUWB Medical Student Author

Department of Orthopedic Surgery

Background: The underlying cause of glenohumeral arthritis is poorly understood. Glenohumeral arthrosis patterns have been classified and described, and differential contact stresses within the joint have been implicated as a cause of joint degeneration, but the intrinsic cause of degeneration patterns in the glenohumeral joint (GHJ) remains largely unknown. Purpose/Hypothesis: The purpose of this study was to assess morphological and mechanical differences in articular cartilage (AC) and subchondral bone (SCB) of the glenoid and humeral head in matched cadaveric specimens. We hypothesized that there would be significant zone-dependent differences between the intrinsic characteristics (AC thickness, SCB thickness, compressive forces) of the glenoid and humeral head in matched cadaveric specimens. We hypothesized that there would be significant zone-dependent differences between the intrinsic characteristics (AC thickness, SCB thickness, compressive forces) of the glenoid and humeral head. Study Design: Descriptive laboratory study. Methods: Ten human cadaveric GHJs (mean age, 60.2 years) were dissected to expose articular surfaces to facilitate biomechanical testing. A 2-mm and 6-mm osteochondral plug was harvested at 5 zones (central, anterior, posterior, inferior, superior) on the glenoid and humeral head (N = 200 plugs). Each 2-mm core was histologically sectioned and stained with hematoxylin and eosin. AC thickness measurements were taken using light microscopy. The 6-mm plugs were imaged using micro-computed tomography to measure SCB thickness. After imaging, AC specimens were removed from the SCB and tested in confined compression. The compressive aggregate modulus (HA0), compressive stiffening coefficient (β), and compressive modulus at 16% strain (HA0.16) and at 50% strain (HA0.50) were calculated. Results: The overall AC thickness was significantly greater on the glenoid. The glenoid also had significantly thicker AC at the inferior, posterior, and superior zones as well as significantly higher SCB thickness overall and significantly greater SCB thickness at the anterior and central zones. The glenoid had significantly greater overall HA0.50 and HA0.50
values at the superior zone and had a significantly greater overall compressive stiffening coefficient ($\beta$).
Conclusion: The glenoid had thicker AC, thicker SCB, and greater compressive stiffness at high strain. Clinical Relevance: These intrinsic differences may help better elucidate the cause of differential degeneration patterns between the glenoid and humeral head.


Full Text

Department of Internal Medicine

Background: Obesity can develop during any life stage. Understanding the contexts within which obesity develops can inform our understanding of the disease and help tailor interventions specific to life stages.
Objective: Using life-course theory as a guiding framework, this study aimed to explain the development of obesity in bariatric surgery patients by creating personalized weight trajectories. Design: Qualitative methods using semistructured interviews were used to uncover participants' experiences with and explanations for the development of obesity. A grounded theory approach using the constant comparative method was used to analyze transcripts for categories and themes. Participants/Setting: Thirty pre-bariatric surgery patients (24 women, 6 men) were recruited from a bariatric surgery center; 25 participants were available for follow-up. Participants were interviewed before surgery and at 6 and 12 months postsurgery. Results: Four weight history groups were created based on patterns of weight changes from adolescence through adulthood: Always Heavy, Late Peak, Steady Progression, and Weight Cycling. Participants' explanations for weight changes centered around themes of transitions and life-course events or stressors. Differences in the weight history groups could be explained by the timing of transitions, life events, and responses to stress. Conclusions: The development of obesity does not follow the same pattern for all individuals. Weight gain patterns can be explained by the timing of life-course events, stressors, and the type and effects of environmental transitions. Weight management counseling should include strategies tailored to an individual's current life-stage and circumstance, but also acknowledge previous responses to transitions and stressors.


Full Text

OUWB Medical Student Author

Myxomas are the most common benign cardiac neoplasms in adults. The vast majority of cardiac myxomas arise from the left atrium near the fossa ovalis of the intra-atrial septum. There have been reports of myxomas arising from the ventricles accounting for about 5% of cases. In our literature review, we have found 55 reported cases of myxomas originating from the mitral valve reported in the adult population dating back to 1871. The majority of these cases presented with embolic complications or syncope. We present an incidental mitral valve myxoma which we excised in efforts to prevent debilitating complications.


Full Text

Department of Radiation Oncology

Objective: Meningiomas are the most common benign extramedullary lesions of the foramen magnum;
However, their optimal management remains undefined. Given their location, foramen magnum meningiomas (FMMs) can cause significant morbidity, and complete microsurgical removal can be challenging. Anterior and anterolateral FMMs carry greater risks with surgery, but they comprise the majority of these lesions. As an alternative to resection, stereotactic radiosurgery (SRS) has been used to treat FMMs in small case series. To more clearly define the outcomes of SRS and to delineate a rational management paradigm for these lesions, the authors analyzed the safety and efficacy of SRS for FMM in an international multicenter trial. Methods: Seven medical centers participating in the International Gamma Knife Research Foundation (IGKRF) provided data for this retrospective cohort study. Patients who were treated with Gamma Knife radiosurgery and whose clinical and radiological follow-up was longer than 6 months were eligible for study inclusion. Data from pre- and post-SRS radiological and clinical evaluations were analyzed. Stereotactic radiosurgery treatment variables were recorded. Results: Fifty-seven patients (39 females and 18 males, with a median age of 64 years) met the study inclusion criteria. Thirty-two percent had undergone prior microsurgical resection. Patients most frequently presented with cranial neuropathy (39%), headache (35%), numbness (32%), and ataxia (30%). Median pre-SRS tumor volume was 2.9 cm³. Median SRS margin dose was 12.5 Gy (range 10–16 Gy). At the last follow-up after SRS, 49% of tumors were stable, 44% had regressed, and 7% had progressed. Progression-free survival rates at 5 and 10 years were each 92%. A greater margin dose was associated with a significantly increased likelihood of tumor regression, with 53% of tumors treated with &gt; 12 Gy regressing. Fifty-two percent of symptomatic patients noted some clinical improvement. Adverse radiation effects were limited to hearing loss and numbness in 1 patient (2%). Conclusions: Stereotactic radiosurgery for FMM frequently results in tumor control or tumor regression, as well as symptom improvement. Margin doses &gt; 12 Gy were associated with increased rates of tumor regression. Stereotactic radiosurgery was generally safe and well tolerated. Given its risk-benefit profile, SRS may be particularly useful in the management of small- to moderate-volume anterior and anterolateral FMMs.


Department of Internal Medicine
Traumatic vessel perforation is a potential complication of chronic total occlusion (CTO) percutaneous coronary artery intervention (PCI). A rare consequence of this complication is a coronary-cameral fistula. The management of this condition is not well elucidated. Herein, we present such a case of symptomatic left anterior descending to the right ventricle (LAD-RV) fistula which was treated with coil embolization.


Department of Diagnostic Radiology and Molecular Imaging
Renal angiomyolipoma (AML) is the most commonly encountered mesenchymal tumor of the kidney which can present spontaneously or in association with tuberous sclerosis complex. Rarely, renal AMLs may demonstrate aggressive features such as renal vein invasion. This common entity and its uncommon complications are diagnosed based on physical examination and computed tomography results. Here we report imaging findings of a renal AML with renal vein and inferior vena cava invasion resulting in pulmonary tumor embolus and pulmonary infarction.


OUWB Medical Student Author
Department of Ophthalmology


Background: Pelvic fracture urethral injuries (PFUI) occur in up to 10% of pelvic fractures. It remains controversial whether initial primary urethral realignment (PR) after PFUI decreases the incidence of urethral obstruction and the need for subsequent urethral procedures. We present methodology for a prospective cohort study analyzing the outcomes of PR versus suprapubic cystostomy tube (SPT) after PFUI. Methods: A prospective cohort trial was designed to compare outcomes between PR (group 1) and SPT placement (group 2). Centers are assigned to a group upon entry into the study. All patients will undergo retrograde attempted catheter placement; if this fails a cystoscopy exam is done to confirm a complete urethral disruption and attempt at gentle retrograde catheter placement. If catheter placement fails, group 1 will undergo urethral realignment and group 2 will undergo SPT. The primary outcome measure will be the rate of urethral obstruction preventing atraumatic passage of a flexible cystoscope. Secondary outcome measures include: subsequent urethral interventions, post-injury complications, urethroplasty complexity, erectile dysfunction (ED) and urinary incontinence rates. Results: Prior studies demonstrate PR is associated with a 15% to 50% reduction in urethral obstruction. Ninety-six men (48 per treatment group) are required to detect a 15% treatment effect (80% power, 0.05 significance level, 20% loss to follow up/death rate). Busy trauma centers treat complete PFUI approximately 1–6 times per year, thus our goal is to recruit 25 trauma centers and enroll patients for 3 years with a goal of 100 or more total patients with complete urethral obstruction.
disruption. Conclusions: The proposed prospective multi-institutional cohort study should determine the utility of acute urethral realignment after PFUI.


Department of Ophthalmology


Objective: To evaluate the frequency, age at phototherapy (PT) initiation, and duration of PT use in infants 23(0/7) to 34(6/7) weeks of gestation in two neonatal intensive care units (NICUs) over 4 time periods. Study Design: We reviewed the charts of all infants born at 23(0/7)-34(6/7) weeks of gestational age (GA) and admitted to the NICUs of two hospitals between January 2009 and September 2015. We calculated the proportion of infants who received PT and the total duration of PT exposure. Results: Overall 2023 (81.8%) received PT, and PT use was inversely related to GA and birthweight. More infants received PT when GA was added as a criterion for initiating PT. The median duration (interquartile range (IQR)) of PT for all infants was 50 (27-85) h and in the lowest GA group was 74 (42-111) h. Conclusions: Recent US consensus guidelines appear to have led to an increased use of PT in our NICUs and studies from Norway indicate that we use PT considerably more frequently and for longer durations than do our Norwegian colleagues.


Department of Orthopedic Surgery

Mechanical characterization of the intervertebral disc involves labor-intensive and destructive experimental methodology. Contrast-enhanced micro-computed tomography is a nondestructive imaging modality for high-resolution visualization and glycosaminoglycan quantification of cartilaginous tissues. The purpose of this study was to determine whether anionic and cationic contrast-enhanced micro-computed tomography of the intervertebral disc can be used to indirectly assess disc mechanical properties in an ex vivo model of disc degeneration. L3/L4 motion segments were dissected from female Lewis rats. To deplete glycosaminoglycan, samples were treated with 0 U/ml (Control) or 5 U/ml papain. Contrast-enhanced micro-computed tomography was performed following incubation in 40% Hexabrix (anionic) or 30 mg I/ml CA4+ (cationic) for 24 h (n = 10/contrast agent/digestion group). Motion segments underwent cyclic mechanical testing to determine compressive and tensile modulus, stiffness, and hysteresis. Glycosaminoglycan content was determined using the dimethylmethylene blue assay. Correlations between glycosaminoglycan content, contrast-enhanced micro-computed tomography attenuation, and mechanical properties were assessed via the Pearson correlation. The predictive accuracy of attenuation on compressive properties was assessed via repeated random sub-sampling cross validation. Papain digestion produced significant decreases in glycosaminoglycan content and corresponding differences in attenuation and mechanical properties. Attenuation correlated significantly to glycosaminoglycan content and corresponding differences in attenuation and mechanical properties. Predictive linear regression models demonstrated a predictive accuracy of attenuation on compressive modulus and stiffness of 79.8–86.0%. Contrast-enhanced micro-computed tomography was highly predictive of compressive mechanical properties in an ex vivo simulation of disc degeneration and may represent an effective modality for indirectly assessing disc compressive properties.


Request Form

Department of Pediatrics

Objective: To describe the accuracy of the Bayley Scales of Infant Development-Second Edition (BSID-II) Mental Development Index (MDI) at 2 years of age for prediction of cognitive function at school age of children born extremely preterm. Design: Study participants were enrolled in the Extremely Low Gestational Age Newborn Study between 2002 and 2004. Two-thirds of surviving children (n = 795) were assessed at 2 years with the BSID-II and at 10 years with an intelligence quotient (IQ) test. We computed test characteristics for a low MDI (<70), including predictive value positive. Results: Almost two-thirds of children with a low MDI had a normal IQ (≥70) at 10 years. Concordance between MDI and IQ was highest among children with major motor and/or sensory impairment, and when MDI was adjusted for gestational age. Conclusion: Most children born extremely preterm with low BSID-II MDI at 2 years have normal intelligence at school age.


Full Text

Department of Internal Medicine

Background: In May 2017, the Alliance for Academic Internal Medicine (AAIM) published guidelines intending to standardize and improve internal medicine residency program director (PD) letters of recommendation (LORs) for fellowship applicants. Objectives: This study aimed to examine fellowship PDs impressions of the new guidelines, letter writers’ adherence to the guidelines, and the impact of LORs that conformed to guidelines compared to non-standardized letters. Methods: The authors anonymously surveyed fellowship PDs from January to March 2018 to gather input about LORs submitted to their programs during the 2017 fellowship application cycle. Results: A total of 78% of survey respondents were satisfied with letters that followed the AAIM guidelines, whereas 48% of respondents were satisfied with letters that did not. Fellowship PDs felt that letters that followed the AAIM guidelines were more helpful than letters that did not, especially for differentiating between applicants from the same institution and for understanding residents’ performance across the six core competency domains. Fellowship PDs provided several suggestions for residency PDs to make the LORs even more helpful. Conclusion: Fellowship PD respondents indicated that LORs that followed the new AAIM guidelines were more helpful than letters that did not.


Full Text

Department of Pathology

Department of Obstetrics and Gynecology

OUWB Medical Student Author

Objective: To determine independent perinatal associations of anxiety and depression in women who were and were not treated with psychotropic drugs in comparison to unaffected pregnancies. Study Design: From 2013 to 2014, 978 (6.3%) cases of anxiety/depression, of which 35% used psychotropic drugs, were compared with 14,514 (93.7%) unaffected pregnancies using logistic regression. Results: Subjects were more likely to be Non-Hispanic Whites, use tobacco and illegal substances, be unmarried, use public insurance, and have medical complications of pregnancy. For independent maternal outcomes, untreated
anxiety/depression was associated with labor induction (adjusted odds ratio [aOR] = 2.02), cesarean deliveries (aOR = 1.69), longer length of stay (aOR = 1.96), readmission (aOR = 2.40), fever (aOR = 2.03), magnesium exposure (aOR = 1.82), and postpartum hemorrhage (aOR = 2.57), whereas treated cases were associated with increased blood transfusion (aOR = 4.81), severe perineal lacerations (aOR = 2.93), and postpartum hemorrhage (aOR = 3.85), but decreased risk of cesarean deliveries (aOR = 0.59). Independent neonatal outcomes included small for gestational age (aOR = 3.04), meconium-stained fluid (aOR = 1.85; 2.61), respiratory failure (aOR = 5.84), neonatal adaptation syndrome (aOR = 11; 10.2), and neonatal seizures (aOR = 12.3) in treated cases, whereas untreated cases were associated with hypoxia (aOR = 2.83), low Apgar score (aOR = 3.82), and encephalopathy (aOR = 18.3). Exposure to multiple psychotropic medications independently increased the risk of neonatal adaptation syndrome, neonatal length of stay, and hypoglycemia. Conclusion: Untreated cases were associated with increased maternal adverse outcomes, whereas treated cases were associated with more adverse neonatal outcomes when compared with unaffected pregnancies.


Full Text
Department of Obstetrics and Gynecology
Department of Internal Medicine


Full Text
Department of Internal Medicine

Background: The Impella percutaneous ventricular assist device (PVAD) rapidly deploys mechanical circulatory support (MCS) in patients with acute myocardial infarction complicated by cardiogenic shock (AMICS). We present findings from a quality improvement (IQ) registry for US patients with AMICS who received Impella devices. Methods and Results: From January 2009 to December 2016, 46,949 patients from 1010 US hospitals were entered into the IQ registry; of these, 15,259 had AMICS. Limited de-identified patient information, product performance, and survival to explantation were recorded. Of those with AMICS, 51% survived to explantation of PVAD. There was a significant difference between survival at explantation with quintile volume at hospitals (range: 0–100%; 30% survival rate in lowest quintile vs. 76% in top quintile; P < .0001). Use of the Impella device as first-line treatment pre-PCI was associated with a 59% survival rate, compared with 52% when used as a salvage strategy (P < .001). The survival rate among those who received hemodynamic monitoring with pulmonary artery catheters was 63% as compared with 49% in those who did not (P < .0001). Overall institutional Impella volume was related to survival (56% survival at sites with >7/year vs. 51% at sites with ≤1; P < .001). Conclusions: In this early clinical experience with Impella support for AMICS, wide variation in outcomes existed across centers. Survival was higher when Impella was used as first support strategy, when invasive hemodynamic monitoring was used, and at centers with higher Impella implantation volume.


Full Text
Department of Physical Medicine & Rehabilitation

Children with cleft palate frequently show speech and language disorders. In the related scientific literature, several reports have described the use of different strategies for treating speech disorders in children with cleft palate. However, only a few studies have addressed the use of these strategies within a meaningful linguistic context. Deliberate practice is a procedure or strategy, which proposes that the key for achieving high levels of expert performance is dedicating long time for practice. Deliberate practice has been studied mainly in the areas of sports and intellectual games. The purpose of this article is to study whether the use of a strategy originally designed for achieving expert performance in sports and intellectual games, can be
useful for the speech intervention of children with cleft palate. For this project, 32 children with cleft palate were studied. The children were randomly assigned to 2 independent groups. Both groups received speech therapy based on the principles of the Whole Language Model. In addition, deliberate practice was used in the children included in the active group. After a speech intervention, although both groups of children demonstrated significant improvement in articulation placement, the active group demonstrated a significantly higher improvement as compared with the control group. In conclusion, these preliminary results seem to suggest that the use of deliberate practice can be effective for enhancing articulation in children with cleft palate.


**Request Form**

**Department of Emergency Medicine**

Objective: Ultrasound (US)-guided peripheral IVs have a high failure rate. We explore the relationship between the quantity of catheter residing within the vein and the functionality of the catheter over time.

Methods: This was a prospective, observational single-site study. Adult ED patients with US-guided IVs had the catheter visualised under ultrasound post-placement. IV placement time and catheter length residing in the vein was obtained. Exclusions included catheter not visualised, patient discharged from ED unless IV failed, 24 hour hospitalisation unless IV failed or patient self-removed IV. Inpatient follow-up occurred within 24, 48 and 72 hours from the IV placement time. Catheter functionality was noted. If the catheter failed, the time and reason for failure was documented. Results: 113 patients were enrolled; 27 were excluded. Of the 86 study subjects, 29 (33.7%) patients' IVs failed and 57 (66.3%) remained functional. Median time to IV failure was 15.6 hours. 100% of IVs failed when 30% of the catheter was in the vein; 32.4% of IVs failed when 30%–64% of the catheter was in the vein; no IVs failed when ≥65% of the catheter was in the vein (p<0.0002). The HR was 0.71 (95% CI 0.60 to 0.83), and for every 5% increase of catheter in vein, the hazard of the IV failing decreases by 29% (0.0001). Conclusion: The quantity of catheter residing in the vein is a key predictor of long-term functionality of US-guided IVs and is strongly associated with the hazard of failure within 72 hours. Catheter failure is high when 30% of the catheter resided in the vein. Optimum catheter survival occurs when ≥65% of the catheter is placed in the vein.


**Full Text**

**Department of Obstetrics and Gynecology**

Objective: To evaluate trends in surgical approach for hysterectomy following the introduction and implementation of a comprehensive robotic surgery program. Methods: A retrospective review of all hysterectomies done at two institutions, a community hospital and a suburban, tertiary-care teaching hospital, in the same health system over a five-year period, January 2010 through December 2014. A robotic surgery training program was implemented during the first year of the study and trends in route of hysterectomy were evaluated in the subsequent years. Results: A total of 5175 patients undergoing hysterectomy, for both benign and malignant indications, were included in the study. There was a significant decrease in the percent of cases performed through an abdominal approach at both the community and teaching hospitals (19.3% decline at each institution). There was an inversely related significant increase in the percent of robotic procedures at both the community and teaching hospitals (44.5% and 17%, respectively). A decrease in number of cases performed vaginally over this period was only noted in the community hospital site (25.2% decrease), and there was a slightly higher rate of vaginal hysterectomies at the teaching hospital over this study period (21.9% in 2010, 24.1% in 2014). Conclusion: The decrease in number of abdominal and laparoscopic hysterectomies and increase in number of robotic hysterectomies that was seen are consistent with national trends. The initiation of a robotic training program did not prevent the proliferation of use of the robot but did aim to ensure proficiency on the robot prior to gaining privileges for patient use. This type of comprehensive training and monitoring program could be applied to future technologic advances to ensure a standard level of surgical proficiency. Trends in route of hysterectomy are clearly multifactorial and involve patient, provider, and location-specific factors that are likely to continue to change.

Department of Ophthalmology

Purpose: We report a case series of advanced ischemic vitreoretinopathies in premature infants that were more consistent with familial exudative vitreoretinopathy (FEVR) than with retinopathy of prematurity (ROP).

Methods: The charts of three consecutive patients who met ROP screening criteria and were diagnosed with FEVR-like, non-ROP aggressive posterior neonatal vitreoretinopathy were retrospectively reviewed.

Results: Table 1 shows clinical characteristics of each case. Severe, rapidly progressive retinal vascular abnormalities were noted in all cases (Figure 1). Average time to intervention (laser or surgery) was 39 weeks gestational age (range 35-46), and prompt treatment resulted in anatomic stabilization or improvement in the retinal detachment and maintenance of at least light perception vision in all cases. Conclusions: This series supports the existence of a clinical entity more consistent with a FEVR-like ischemic vitreoretinopathy than ROP in premature infants and suggests that early diagnosis and intervention may mitigate the typical aggressive course and poor prognosis of this condition.


OUWB Medical Student Author

Histone chaperones, chromatin remodelers, and histone modifying complexes play a critical role in alleviating the nucleosomal barrier for DNA-dependent processes. Here, we have examined the role of two highly conserved yeast (Saccharomyces cerevisiae) histone chaperones, facilitates chromatin transcription (FACT) and Spt6, in regulating transcription. We show that the H3 tail contributes to the recruitment of FACT to coding sequences in a manner dependent on acetylation. We found that deleting a H3 histone acetyltransferase Gcn5 or mutating lysines on the H3 tail impairs FACT recruitment at ADH1 and ARG1 genes. However, deleting the H4 tail or mutating the H4 lysines failed to dampen FACT occupancy in coding regions. Additionally, we show that FACT depletion reduces RNA polymerase II (Pol II) occupancy genome-wide. Spt6 depletion leads to a reduction in Pol II occupancy toward the 3′-end, in a manner dependent on the gene length. Severe transcription and histone-eviction defects were also observed in a strain that was impaired for Spt6 recruitment (spt6Δ202) and depleted of FACT. Importantly, the severity of the defect strongly correlated with wild-type Pol II occupancies at these genes, indicating critical roles for Spt6 and Spt16 in promoting high-level transcription. Collectively, our results show that both FACT and Spt6 are important for transcription globally and may participate during different stages of transcription.


Request Form

Department of Radiation Oncology

Objective: Due to the complexity of Spetzler-Martin (SM) Grade IV–V arteriovenous malformations (AVMs), the management of these lesions remains controversial. The aims of this multicenter, retrospective cohort study were to evaluate the outcomes after single-session stereotactic radiosurgery (SRS) for SM Grade IV–V AVMs and determine predictive factors.

Methods: The authors retrospectively pooled data from 233 patients (mean age 33 years) with SM Grade IV (94.4%) or V AVMs (5.6%) treated with single-session SRS at 8 participating centers in the International Gamma Knife Research Foundation. Pre-SRS embolization was performed in 71 AVMs (30.5%). The mean nidus volume, SRS margin dose, and follow-up duration were 9.7 cm3, 17.3 Gy, and 84.5 months, respectively. Statistical analyses were performed to identify factors associated with post-SRS outcomes. Results: At a mean follow-up interval of 84.5 months, favorable outcome was defined as AVM obliteration, no post-SRS hemorrhage, and no permanently symptomatic radiation-
induced changes (RIC) and was achieved in 26.2% of patients. The actuarial obliteration rates at 3, 7, 10, and 12 years were 15%, 34%, 37%, and 42%, respectively. The annual post-SRS hemorrhage rate was 3.0%. Symptomatic and permanent RIC occurred in 10.7% and 4% of the patients, respectively. Only larger AVM diameter (p = 0.04) was found to be an independent predictor of unfavorable outcome in the multivariate logistic regression analysis. The rate of favorable outcome was significantly lower for unruptured SM Grade IV–V AVMs compared with ruptured ones (p = 0.042). Prior embolization was a negative independent predictor of AVM obliteration (p = 0.024) and radiologically evident RIC (p = 0.05) in the respective multivariate analyses. Conclusions: In this multi-institutional study, single-session SRS had limited efficacy in the management of SM Grade IV–V AVMs. Favorable outcome was only achieved in a minority of unruptured SM Grade IV–V AVMs, which supports less frequent utilization of SRS for the management of these lesions. A volume-staged SRS approach for large AVMs represents an alternative approach for high-grade AVMs, but it requires further investigation.


Full Text
Department of Ophthalmology


Request Form
OUWB Medical Student Author

Objective: Gamma Knife radiosurgery (GKRS) is frequently used to treat residual or recurrent nonfunctioning pituitary macroadenomas. There is no consensus as to whether GKRS should be used early after surgery or if radiosurgery should be withheld until there is evidence of imaging-defined progression of tumor. Given the high incidence of adenoma progression after subtotal resection over time, the present study intended to evaluate the effect of timing of radiosurgery on outcome. Methods: This is a multicenter retrospective review of patients with nonfunctioning pituitary macroadenomas who underwent transsphenoidal surgery followed by GKRS from 1987 to 2015 at 9 institutions affiliated with the International Gamma Knife Research Foundation. Patients were matched by adenoma and radiosurgical parameters and stratified based on the interval between last resection and radiosurgery. Operative results, imaging data, and clinical outcomes were compared across groups following early (= 6 months after resection) or late (> 6 months after resection) radiosurgery. Results: After matching, 222 patients met the authors' study criteria (from an initial collection of 496 patients) and were grouped based on early (n = 111) or late (n = 111) GKRS following transsphenoidal surgery. There was a greater risk of tumor progression after GKRS (p = 0.013) and residual tumor (p = 0.038) in the late radiosurgical group over a median imaging follow-up period of 68.5 months. No significant difference in the occurrence of post-GKRS endocrinopathy was observed (p = 0.68). Thirty percent of patients without endocrinopathy in the early cohort developed new endocrinopathies during the follow-up period versus 27% in the late cohort (p = 0.84). Fourteen percent of the patients in the early group and 25% of the patients in the late group experienced the resolution of endocrine dysfunction after original presentation (p = 0.32). Conclusions: In this study, early GKRS was associated with a lower risk of radiological progression of subtotally resected nonfunctioning pituitary macroadenomas compared with expectant management followed by late radiosurgery. Delaying radiosurgery may increase patient risk for long-term adenoma progression. The timing of radiosurgery does not appear to significantly affect the rate of delayed endocrinopathy.


Full Text

Department of Neurosurgery

Purpose: Surgical excision of keloids can result in an insidious cycle of tissue injury and repeat keloid formation unless combined with adjuvant therapy to halt this cycle. We present our results of postoperative radiation therapy for keloids with various dose regimens. Methods and Materials: A retrospective review of 124 patients with 250 keloid lesions treated with postoperative radiation therapy was analyzed. In this institutional review board-approved study, 125 keloids were treated to 20 Gy in 5 fractions and 125 keloids were treated to 12 to 16 Gy in 3 to 4 fractions. Local failure was defined as redevelopment of any clinically apparent keloid at the treated site. The median age was 34 years (14-84 years). Keloids were located on the ear (34%), neck/shoulder (19%), abdomen (13%), chest (10%), face (9%), breast (7%), extremities (4%), and back (3%). Median keloid size was 4 cm (0.5-20 cm). Results: At a median follow-up of 40 months, the recurrence rate for all lesions was 5.6%. Lesions treated to 20 Gy had a recurrence rate of 1.6% compared with 9.6% with <20 Gy and an odds ratio of 0.16 (P = .02). Upon univariate and multivariate analysis there were no differences in recurrence rate with respect to location, race, gender, age, previously treated lesions, and presence of multiple keloids. The lone predictor for improved control rate was the dose of 20 Gy in 5 fractions compared with less than that. Control rate for lesions treated to a biologically equivalent dose2 of 35 to 36 Gy2, 48 to 52.5 Gy2, and 60 to 72 Gy2 were 10% (P = .007), 8.9% (P = .16), and 1.6% (P = .02), respectively. Conclusions: Surgical excision followed by immediate adjuvant radiation therapy for keloids provides excellent local control and cosmesis. Treatment with a biologically equivalent dose2 > 60 (20 Gy in 5 fractions) yielded superior local control over lower dose regimens.

and in mechanisms used. Consumption of green tea has been shown to distribute these compounds and/or their metabolites throughout the body, which allows for not only the possibility of treatment of infections but also the prevention of infections.


Department of Orthopedic Surgery

Background: Bone graft substitutes have been developed to circumvent donor site morbidity associated with iliac crest bone graft, but sparse literature compares the efficacy of various substitutes. Two commonly used bone graft substitutes used in lumbar fusion are β-tricalcium phosphate (BTP) and demineralized bone matrix (DBM). Methods: A retrospective review of patients who underwent instrumented posterolateral lumbar fusion was conducted by a single surgeon from January 2013 to December 2016. Patients were divided into two groups based on whether DBM or BTP as graft in conjunction with local autograft. Clinical outcomes scores were collected at a minimum of 1-year follow-up. Postoperative CT scans were evaluated to assess fusion. Results: Forty-one patients (DBM, 21 and BTP, 20) were reviewed. No significant differences were found in terms of age, sex, body mass index, smoking, diabetes, steroids, osteoporosis, American Society of Anesthesiologists classification, number of levels fused, estimated blood loss, length of stay, or surgical time between the DBM and BTP groups. A trend was found toward lower revision surgery (zero versus 15%), improved visual analog scale scores (postoperative change of 1.81 versus 3.25; P = 0.09), and higher rates of fusion (90% versus 70%; P = 0.09) in the DBM group compared with the BTP group. Conclusions: No significant difference was found in clinical outcomes at 1 year, with a trend toward a higher fusion rate and lower revision surgery with DBM.


Department of Foundational Medical Studies

There are few graduate programs available for pursuing a doctorate in anatomy where students gain specific training in gross anatomy dissection and the responsibilities of a medical educator. In light of this fact, the University of Kentucky created a Graduate Certificate in Anatomical Sciences Instruction in 2006. This 12-credit hour curriculum includes detailed training in gross anatomy and/or neuroscience courses, practicum experiences, a seminar class in pedagogical literature, and a course in educational strategies for the anatomical sciences. The award of certificate completion affirms that the candidate has demonstrated faculty-supervised proficiency in anatomy dissection, instruction in anatomy topics, and teaching strategies for anatomy. Seventeen graduate students have earned the certificate since its inception; nine students accepted teaching positions in anatomy following their graduate training and currently nine certificate graduates have assistant (six) or associate (three) professor positions in academia. In 2016, an anonymous survey including Likert-style and open-ended questions was emailed to all certificate graduates. Graduates favorably responded (each question averaged 4.4 or greater out of 5) that the certificate increased their awareness of teaching-faculty responsibilities, adequately prepared them for teaching-related duties, and positively contributed toward their first employment. Graduates indicated that the lecturing and dissection experience, awareness of faculty responsibilities, and job preparation (e.g., teaching philosophy development) were the most helpful aspects of the certificate. These results indicate that the Graduate Certificate in Anatomical Sciences Instruction is viewed by its graduates and their employers as a valuable teaching credential that can be attained alongside a basic science degree. Anat Sci Educ 11: 516–524. © 2018 American Association of Anatomists.


Department of Radiation Oncology
Objectives: Although treatment of superior sulcus tumors with induction chemoradiotherapy (CRT) followed by surgery employed in the Intergroup INT-0160 trial is widely adopted as a standard of care, there may be significant associated morbidity and mortality. We describe our experience using standard and alternative induction regimens to assess survival rates and treatment toxicity in these patients. Materials and Methods: Electronic medical records of all patients who underwent multimodality treatment including resection of lung cancer invading the superior pulmonary sulcus between 1994 and 2016 were retrospectively reviewed. Multivariable Cox Proportional Hazards model was constructed. Results: Of 102 consecutive patients, 53 (52%) underwent induction CRT, 34 (33%) underwent induction chemotherapy only (Ch) followed by adjuvant radiotherapy, and 15 (15%) underwent no induction therapy followed by adjuvant therapy. There were 2 postoperative deaths (1.9%). To date, 42 patients are alive with a median follow-up 72.5 months. Overall 5-year survival rate was 45.4%. Survival was significantly influenced by age, FEV1, positive resection margins, surgical complications, but not the induction regimen. CRT resulted in higher complete pathological response rate than Ch: 38% vs. 3% (p < 0.001). CRT was associated with higher post-operative re-intubation rate: 13% vs. 0% (p = 0.03). Conclusions: Our single-institutional experience indicated that while induction CRT produced greater complete pathological response than Ch, it also increased the risk of post-operative complications. With careful patient selection, induction Ch followed by adjuvant radiotherapy may provide comparable survival outcomes to induction CRT. Since induction Ch is associated with lower risk of complications, it may be a particularly desirable choice for patients with impaired performance status.


Full Text
Department of Ophthalmology

Purpose: Vitrectomy can be performed either with non-contact wide-angle viewing systems or wide-angle contact lenses. It is unknown whether there are differences in surgical outcomes based on choice of viewing system. The purpose of this study is to assess whether there are differences in anatomic vitrectomy outcomes of primary non-complex retinal detachment (RD) repair, based on viewing system used. Methods: This is a multicenter, interventional, retrospective, comparative study. Eyes that underwent non-complex primary RD repair by either pars plana vitrectomy (PPV) alone or in combination with scleral buckle (SB/PPV) were identified. Eyes that underwent repair by primary SB, pneumatic retinopexy, or retinopexy alone were excluded from the analysis. The viewing system used at the time of RD repair was identified. The primary outcome of our study was single surgery anatomic success (SSAS), which was defined as no re-operations for RD during the post-operative 90-day window. Significance was determined using Pearson’s X² test. Results: A total of 1811 eyes were included in our analysis. Of those, 1529 (84.4%) had RD repaired using non-contact viewing systems, while 282 (15.6%) were repaired using a contact lens system. SSAS for non-contact viewing systems was 86.5% and 86.9% for contact lenses, which was not statistically different (p=0.87). A total of 1073 eyes had PPV alone for RD repair, of which 916 (85.4%) were performed using non-contact viewing systems. Of those eyes repaired by PPV alone, non-contact systems had an 84.3% SSAS compared to 84.1% for contact lenses. This difference was not significant (p=0.94). Similarly, a total of 738 eyes were repaired using a combined SB/PPV approach, 613 (83.1%) of which were repaired using non-contact viewing systems. Of those eyes repaired by a combined SB/PPV approach there was no statistically significant difference between the two viewing systems, with an 89.9% SSAS for non-contact systems vs. 90.4% for contact lenses (p=0.86). Conclusions: There was no significant difference in SSAS for primary RD repair when comparing non-contact viewing systems to contact lens systems.


Full Text
Department of Internal Medicine


Department of Radiation Oncology

Purpose: Gleason score (GS) 10 disease is the most aggressive form of clinically localized prostate adenocarcinoma (PCa). The long-term clinical outcomes and overall prognosis of patients presenting with GS 10 PCa are largely unknown because of its rarity. Methods and Materials: The study included 112 patients with biopsy-determined GS 10 PCa who received treatment with radical prostatectomy (RP, n = 26), external beam radiation therapy (EBRT, n = 48), or EBRT with a brachytherapy boost (EBRT-BT, n = 38) between 2000 and 2013. Propensity scores were included as covariates for comparative analysis. Overall survival, prostate cancer-specific survival, and distant metastasis-free survival (DMFS) were estimated by the Kaplan-Meier method with inverse probability of treatment weighting to control for confounding. Results: The median follow-up period was 4.9 years overall (3.9 years for RP, 4.8 years for EBRT, and 5.7 years for EBRT-BT). Significantly more EBRT patients than EBRT-BT patients received upfront androgen deprivation therapy (98% vs 79%, P < .01 by χ2 test), though the durations were similar (median, 24 months vs 22.5 months). Of the RP patients, 34% received postoperative EBRT, and 35% received neoadjuvant systemic therapy. The propensity score-adjusted 5-year overall survival rate was 80% for the RP group, 73% for the EBRT group, and 83% for the EBRT-BT group. The corresponding adjusted 5-year prostate cancer-specific survival rates were 87%, 75%, and 94%, respectively. The EBRT-BT group trended toward superior DMFS when compared with the RP group (hazard ratio, 0.3; 95% confidence interval 0.1-1.06; P = .06) and had superior DMFS when compared with the EBRT group (hazard ratio, 0.4; 95% confidence interval 0.1-0.99; P = .048). Conclusions: To our knowledge, this is the largest series ever reported on the clinical outcomes of patients with biopsy-determined GS 10 PCa. These data provide useful prognostic benchmark information for physicians and patients. Aggressive therapy with curative intent is warranted, as >50% of patients remain free of systemic disease 5 years after treatment.

Sangal RB (2018). "Baseline sleep efficiency and arousal index do not predict who will benefit from sedatives in improving positive airway pressure adherence in sleep apnea to 90%.” Clinical EEG and Neuroscience 49(4): 285-289. 

Department of Family Medicine and Community Health

Positive airway pressure (PAP) is the preferred treatment for obstructive sleep apnea (OSA), but adherence is low. Educational or ongoing supportive intervention improves the number of PAP adherent patients from the 50% to the 70% range. A common side effect of PAP is increased awakenings. This prospective trial examined baseline polysomnographically derived sleep efficiency and arousal index in PAP adherent and nonadherent patients, and in patients needing sedating medicines to attain PAP adherence versus those who did not need such medicines. Patients with OSA were titrated on PAP during a polysomnography or treated with autotitrating PAP, followed by educational and supportive interventions. Patients with PAP related awakenings (patients describing waking up and taking PAP off in the middle of the night) or difficulty tolerating PAP were additionally treated with medicines that suppress arousals/awakenings (trazodone, mirtazapine, doxepin). A total of 120 of 151 (79%) new patients were 70% PAP adherent over a continuous 30-day period, typically within the first 90 days of starting PAP, without sedating medicines. Nineteen of the remaining patients were treated with medicines that suppress arousals and awakenings, and 16 became adherent, resulting in 136 (90%) of 151 new patients achieving adherence. There were no differences in baseline sleep efficiency or arousal index, between adherent and nonadherent patients, as well as between patients who needed sedating medicines for PAP adherence and those who did not. Adding medicines that suppress arousals and awakenings for patients having trouble tolerating PAP, increases the number of patients who are PAP adherent. The need for such medicines seems to be related to the PAP side effect of increased awakenings rather than baseline impaired sleep.


Department of Orthopedic Surgery
Introduction: A paucity of information exists on the range of femoral version, its effect on hip stability, clinical examination, and presentation in patients with symptomatic acetabular dysplasia. The purpose of this study was to describe the range of version in symptomatic acetabular dysplasia, the association between femoral version and proximal femoral morphology and degree of dysplasia, and the effect of version on clinically measured hip range of motion and on preoperatively measured hip outcome scores. Methods: We reviewed 314 patients prospectively enrolled in a longitudinal clinical study on periacetabular osteotomy between January 2014 and August 2015 and measured femoral version, morphologic characteristics of the upper femur and acetabulum, and preoperative clinical outcome scores. Results: The average femoral version was 19.7° ± 11.2° (range, -20° to 50°). Femoral version correlated strongly with clinically measured hip range of motion but did not correlate linearly with either radiographic severity of acetabular dysplasia or preoperative symptomaticity. Discussion: Despite concerns that transverse plane femoral anatomy influences the stability of the hip joint after skeletal maturity, we did not find a statistical association between femoral version and severity of dysplasia or presenting symptomaticity. This finding suggests that femoral version is not a major influence on the clinical presentation of acetabular dysplasia. Level Of Evidence: Level IIIb.


Full Text
Department of Internal Medicine

Introduction: Tissue plasminogen activator (tPA) is commonly used in ischemic cerebral vascular accidents (CVAs). tPA is generally well tolerated; however, orolinguinal angioedema is a well-documented adverse effect. Angioedema is generally mild, transient, and unilateral but can manifest as severe, life-threatening upper airway obstruction requiring intubation. Reported incidence for all severities ranges from one to five percent, whereas reported incidence of severe cases ranges from 0.18 to 1 percent of patients receiving tPA for ischemic CVA. Angiotensin-converting enzyme (ACE) inhibitors and middle cerebral artery distribution have been associated with a higher risk of developing angioedema. The aim of this study is to evaluate the incidence of severe tPA-induced angioedema and its effects on length of stay (LOS) and death. Methods: A retrospective chart review of patients receiving tPA for ischemic CVA from January 2014 through December 2016 was conducted at a large tertiary center with Comprehensive Stroke Center designation. Subjects were eighteen or older. Baseline demographics and clinical data were collected. Results: 147 patients were included with four developing severe angioedema due to tPA resulting in an incidence of 2.72%. All four were female. The median LOS was thirty days for patients with angioedema and twelve days for those without. The survival probability was higher in the angioedema group and mean time to death was twenty-two days in the angioedema group and twenty-one days in the nonangioedema group. Twenty-five patients died, one from the angioedema group. ACE inhibitor use was found to have an OR of 7.72. Conclusion: This study found a higher incidence of severe angioedema than that reported. Development of severe angioedema increased length of stay but was not shown to worsen outcomes in regards to death. Consistent with previous studies, ACE inhibitor use was associated with a higher risk of developing angioedema.


Full Text
OUWB Medical Student Author
Department of Surgery

Objective: In spite of the recognized benefits of ultrasound, many physicians have little experience with using ultrasound to perform procedures. Many medical schools and residency programs lack a formal ultrasound training curriculum. We describe an affordable ultrasound training curriculum and versatile, inexpensive practice model. Design: Participants underwent a didactic session to teach the theory required to perform ultrasound-guided procedures. Motor skills were taught using a practice model incorporating analogs of common anatomic and pathologic structures into an opacified gelatin substrate. Setting: The Marcia and Eugene Applebaum Simulation Learning Institute, Beaumont Hospital, Royal Oak, MI; a private nonprofit tertiary care hospital associated with the OUWB School of Medicine, Rochester, MI. Participants: The model
was tested in a cohort of 50 medical students and general surgery residents. Results: The gelatin model can be constructed for $1.03 per learner. The solid, cystic, and vascular structural analogs were readily identifiable on ultrasound and easily differentiated based on their echotextures. Eighty-four percent of participants successfully aspirated the cystic structure, 88% successfully biopsied a portion of the solid structure, and 76% successfully cannulated the tubular structure. Overall, 82% of participants achieved a passing score for the exercise based on a validated Objective Structured Assessment of Technical Skill instrument. There were no significant differences between the medical students and residents. Conclusion: This model can be used to teach basic ultrasound skills such as aspiration, biopsy, and vessel cannulation, providing a foundation for the use of ultrasound in a broad range of clinical procedures, as well as providing practice opportunities for medical students and residents to gain increased ultrasound competency and confidence.


Department of Orthopedic Surgery


Full Text

Department of Orthopedic Surgery


Full Text

OUWB Medical Student Author

Department of Orthopedic Surgery

Periprosthetic joint infection is a major complication after both anatomical and reverse total shoulder arthroplasty. Factors such as diabetes mellitus and high body mass index play a role in increasing the risk of infection after shoulder arthroplasty. Infection after shoulder surgery is caused by a variety of organisms, most of which, such as Staphylococcus aureus and Propionibacterium acnes, are normal skin flora. Treatment options include single-stage revision, 2-stage revision, component retention with irrigation and
debridement, and treatment with antibiotics alone. The efficacy of these treatment modalities is discussed. With the increasing prevalence of shoulder arthroplasty, preventive measures such as antibiotic prophylaxis and adequate surgical skin preparation are of the utmost importance.


Full Text

Department of Radiation Oncology

Purpose: A treatment planning/delivery QA tool using linac log files (LF) and Monte Carlo (MC) dose calculation is investigated as a standalone alternative to phantom-based patient-specific QA (ArcCHECK AC). Methods: Delivering a variety of fields onto MapCHECK2 and ArcCHECK, diode sensitivity dependence on dose rate (in-field) and energy (primarily out-of-field) was quantified. AC and LF QAs were analyzed with respect to delivery complexity by delivering 12 × 12 cm static fields/arcs comprised of varying numbers of abutting sub-fields onto ArcCHECK. About 11 clinical dual-arc VMAT patients planned using Pinnacle’s convolution–superposition (CS) were delivered on ArcCHECK and log file dose (LF-CS and LF-MC) calculated. To minimize calculation time, reduced LF-CS sampling (1/2/3/4° control point spacing) was investigated. Planned (“Plan”) and LF-reconstructed CS and MC doses were compared with each other and AC measurement via statistical [mean ± StdDev(σ)] and gamma analyses to isolate dosimetric uncertainties and quantify the relative accuracies of AC QA and MC-based LF QA. Results: Calculation and ArcCHECK measurement differed by up to 1.5% in-field due to variation in dose rate and up to 5% out-of-field. For the experimental segment-varying plans, despite CS calculation deviating by as much as 13% from measurement, Plan-MC and LF-MC doses generally matched AC measurement within 3%. Utilizing 1° control point spacing, 2%/2 mm LF-CS vs AC pass rates (97%) were slightly lower than Plan-CS vs AC pass rates (97.5%). Utilizing all log file samples, 2%/2 mm LF-MC vs AC pass rates (97.3%) were higher than Plan-MC vs AC (96.5%). Phantom-dependent, calculation algorithm-dependent (MC vs CS), and delivery error-dependent dose uncertainties were 0.8 ± 1.2%, 0.2 ± 1.1%, and 0.1 ± 0.9% respectively. Conclusion: Reconstructing every log file sample with no increase in computational cost, MC-based LF QA is faster and more accurate than CS-based LF QA. Offering similar dosimetric accuracy compared to AC measurement, MC-based log files can be used for treatment planning QA.


Full Text

Department of Ophthalmology

Importance: Neovascular age-related macular degeneration (nvAMD) is a leading cause of vision loss. The optimal screening protocol to detect choroidal neovascularization (CNV) in fellow eyes of patients undergoing treatment for unilateral CNV has not been determined. Objective: To compare the visual outcomes of eyes with established, active nvAMD in index eyes with outcomes of fellow eyes that subsequently developed CNV during the management protocol. Design, Setting, and Participants: In this retrospective single-center case series conducted at a private vitreoretinal practice, data were collected for all patients treated for bilateral nvAMD between October 1, 2015, and October 1, 2016, for whom we could determine the date of index eye and fellow eye conversion to nvAMD (n = 1600). Per institutional protocol, patients were screened for new CNV in the fellow eye at every office visit. Patients were excluded if they had a condition that could result in marked asymmetric vision loss. Exposures: Development of nvAMD. Main Outcomes and Measures: Visual acuity (VA) at the time of diagnosis of nvAMD and at equivalent time points following conversion to nvAMD for both index eyes and fellow eyes. Results: A total of 264 patients met the inclusion criteria; 197 (74.6%) were women and 253 (95.8%) were white, and the mean (SD) age was 79.1 (8.2) years at time of index eye conversion to nvAMD and 80.6 (8.2) years at time of fellow eye conversion to nvAMD. Fellow eyes presented with better VA (mean VA, 20/50 [0.40 logMAR]) compared with index eyes (mean VA, 20/90 [0.67 logMAR]) at the time of conversion (difference, 14 letters [0.27 logMAR]; 95%CI, 10-17 [0.20-0.34]; P < .001). Index eyes did not achieve the same level of VA as fellow eyes after an equivalent
postconversion follow-up of approximately 20 months (mean VA: Index eye; 20/70 [0.56 logMAR]; fellow eye, 20/50 [0.40 logMAR]; difference, 8 letters [0.15 logMAR]; 95%CI, 4-11 [0.08-0.22]; P < .001). No difference was detected between the mean number of anti-vascular endothelial growth factor injections received by fellow eyes and index eyes (9.7 vs 10.0 injections, respectively). Conclusions and Relevance: This retrospective study suggests that fellow eyes of previously treated patients with nvAMD may achieve better VA than their index eye counterparts after an equivalent amount of follow-up. This may be because the CNV was detected and treated earlier and at a better level of VA, although it is unknown whether the frequent office visits, VA measurements, or optical coherence tomography testing was responsible for the detection at a better level of VA.


Full Text
Department of Foundational Medical Studies

The article offers information on musculoskeletal rehabilitation and the impact that the words used by therapists can play in the clinical outcome. Topics discussed include the importance of effective communication by therapists in rehabilitation; the role of psychological factors as predictors of pain and disability levels; and the influence of language on pain perception of individuals.


Full Text
Department of Pathology

Cutaneous lymphoproliferative disorders remain a challenging aspect of dermatopathology, in part due to the rarity of the entities and extreme variability in clinical outcomes. Although many of the entities remain unchanged, the approach to some of them has changed in the new 2016 classification scheme of the World Health Organization. Chief among these are Epstein-Barr virus–associated lymphoproliferative disorders such as Epstein-Barr virus–associated mucocutaneous ulcer and hydrosche vciniforme-like lymphoproliferative disorder, primary cutaneous CD8+ aggressive epidermotropic cytotoxic T-cell lymphoma, primary cutaneous acral CD8+ T-cell lymphoma, primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder, and breast implant–associated anaplastic large cell lymphoma. In addition, translocations and gene rearrangements such as those involving the 6p25.3 locus have started to inform diagnosis and classification of anaplastic large cell lymphoma and lymphomatoid papulosis. In this review, we will examine what is new in the diagnostic toolbox of cutaneous lymphoproliferative disorders.


Full Text
OUWB Medical Student Author

Objectives/Hypothesis: There has been growing recognition of the roles prescription drug misuse and diversion play in facilitating the ongoing opioid epidemic. Our objective was to evaluate opioid prescription patterns among practicing otolaryngologists. Study Design: Retrospective review of a CMS database. Methods: Medicare Part D beneficiary data (2015) were accessed for a list of otolaryngologists. Opioid prescription rates, amount, and supply were calculated. Factors including board certification, experience, gender, and location were obtained for the 9,068 unique otolaryngologists represented in this dataset. Results: In 2015, otolaryngologists wrote 133,779 opioid prescriptions for 922,806 days (6.9 days/per prescription). The majority was for hydrocodone-acetaminophen (64.0%). Most otolaryngologists (51.2%) prescribed ≤ 10 opioids; 6.1% offered > 50 opioid prescriptions. Men wrote more prescriptions on average. Opioid prescription rates were greatest in the Midwest (4.6%) and least in the Northeast (1.8%), and the highest/lowest rates were in Delaware (8.6%) and New York (1.3%). Midcareer (11 –20 years) otolaryngologists were most likely to write >50 prescriptions. The opioid prescription rate declined with greater experience. Conclusions: Opioid prescriptions written by otolaryngologists may play a significant role in the availability of these agents, as otolaryngologists wrote nearly 1 million days worth of opioids to
Medicare beneficiaries in 2015. Although the majority of otolaryngologists write fewer than 11 prescriptions annually, those writing more prescriptions also write lengthier courses. There is significant geographic variation in prescribing patterns, highlighting a lack of consensus, and midcareer otolaryngologists are more aggressive in offering opioids. These findings highlight an urgent need for strengthening educational resources aimed at minimizing unnecessary prescriptions.


Full Text

OUWB Medical Student Author

Background: Although the endoscopic approach has been increasingly utilized for a variety of sinonasal and skull base pathologies, there has been little inquiry into its adoption in the surgical management of orbital disease. Our objective was to evaluate nationwide temporal and geographic trends in approaches for orbital decompression. Methods: Data available from the Centers for Medicare and Medicaid Services (CMS) were evaluated, focusing on the use of open and endoscopic approaches for orbital decompression (CPT codes 67414, 67445, 31292, and 31293) among Medicare beneficiaries over a 10-year period. Regional data were also analyzed. Results: There were 8047 orbital decompressions billed to Medicare from 2007 to 2016. The number of external and endoscopic approaches increased by 73.0% and 29.2%, respectively, while the number of Medicare beneficiaries increased by 29.1%. Endoscopic decompression represented 23.5% of Medicare-billed orbital decompressions in 2016 (221 of 939), down from 29.2% in 2007 (171 of 586). The South had the greatest proportion of decompressions utilizing an endoscopic approach (30.2%). Conclusion: There has not been a clear movement toward the endoscopic approach for orbital decompression, with modest growth when compared with external approaches. Potential explanations include the specialty-exclusive nature of approaches, as well as a lack of consensus; the latter idea is further reinforced by geographic variation. High-quality prospective trials may clarify the role of endoscopic approaches in these patients.


Full Text

OUWB Medical Student Author

Background: Misuse and diversion of prescription opioids have been critical in facilitating the opioid epidemic. Our objective was to perform a systematic evidence-based review delineating perioperative regimens (including opioid alternatives) evaluated for endoscopic sinus surgery. Methods: PubMed/MEDLINE, Cochrane Library, and EmBase databases were evaluated for studies detailing analgesics employed after endoscopic sinus surgery. Studies were assessed for level of evidence. Bias risk was evaluated using the Cochrane Bias tool and GRADE criteria. Medication, administration, adverse effects, pain scores, and rescue analgesic consumption were evaluated. A summary of evidence detailing benefits, harm, and cost was prepared. Results: Thirty-two studies encompassing 1812 patients were included. The GRADE criteria determined the overall evidence to be of moderate quality. Perioperative acetaminophen had few adverse events and reduced immediate need for opioid rescue after sinus surgery; studies evaluating acetaminophen demonstrate a preponderance of benefit over harm. Nonsteroidal anti-inflammatory drugs (NSAIDs) also reduce postoperative opioid consumption, although a small portion of patients undergoing sinus surgery harbor the potential for NSAID intolerance. The aggregate level of evidence for studies evaluating NSAIDs was grade A, whereas the aggregate grade of evidence for several other agents was grade B. Conclusion: There is evidence supporting the use of NSAIDs and gabapentin for the control of pain after endoscopic sinus surgery. Acetaminophen, α-agonists, and local anesthetics are also viable options for postoperative analgesia. Familiarity with these data is essential to facilitate the use of opioid alternatives. Further large-scale, multi-institutional, randomized trials are needed to provide conclusive recommendations for these perioperative analgesics.

Swanberg SM, Mi M, Engwall K and Bulgarelli N (2018). "Community engagement at an emerging academic
The Oakland University William Beaumont School of Medicine's (OUWB) service-oriented mission and vision is reflected in all aspects of the school including its culture, curriculum, research, community engagement, and the OUWB Medical Library. Though starting informally, the OUWB Medical Library's outreach program has matured and now sustains a wide array of activities each year. This outreach program has blossomed into a three-pronged model that is inclusive of activities and endeavors engaging the institution and local community: integrate, partner, and create. Among its successes and challenges, the library's ongoing outreach efforts have showcased the value of libraries in promoting community health and meaningfully contributing to the institutional mission.


Full Text

Department of Ophthalmology

Purpose: To describe surgical outcomes and structural characteristics of intraocular lenses (IOLs) implanted with transconjunctival sutureless intrascleral (SIS) fixation in human eyes. Design: Retrospective interventional surgical case series involving live and cadaveric human eyes. Methods: In this study, we investigated the surgical outcomes and structural anatomy of secondary IOLs implanted with the SIS technique in human eyes. All cases involving SIS IOL fixation performed at a single academic center from January 1, 2012, through July 30, 2016, were reviewed to describe the surgical technique, common indications, clinical outcomes, and the rate of common operative complications. To investigate the structure of SIS-fixated IOLs in vivo, slit-lamp biomicroscopy, ultrasound biomicroscopy, and intraoperative endoscopy were analyzed to describe anatomical outcomes. The primary anatomical outcomes were the optic pupillary centration and location of haptic externalization. Results were correlated with cadaveric human eyes that underwent the SIS-IOL technique. Cadaveric eyes were imaged and analyzed using high-resolution photography for centration, stress measurements at the haptic-optic junction, and qualitative descriptors of IOL optic and haptic position. Results: A total of 122 consecutive patients who underwent IOL placement using SIS technique were included in the study with mean follow-up of 1.52 years (range, 0.4-4.5 years). The majority (75%) of patients received a new 3-piece IOL for primary aphakia or after IOL exchange. The other patients (25%) had a dislocated 3-piece IOL that was rescued using the SIS technique. Preoperative mean Snellen visual acuity was 20/633 (logarithm of the minimum angle of resolution = 1.501). At the final visit, the mean best-corrected visual acuity was 20/83 (logarithm of the minimum angle of resolution = 0.6243) and final mean spherical equivalent was -0.57 diopters. The most common complications were vitreous hemorrhage (22% of eyes), which resolved spontaneously in most cases, and cystoid macular edema. The rates of IOL dislocation, IOL decentration, haptic erosion, IOL tilting, iris capture, and endophthalmitis were low. Intraoperative endoscopy and ultrasound biomicroscopy demonstrated a securely fixated IOL and well-centered optic without iris or ciliary body touch. Structural study of cadaveric eyes confirmed IOL optic and haptic anatomy observed during live human surgery. The ab interno haptic insertion was the anterior pars plana, away from the iris, ciliary processes and ora serrata. The degree of haptic externalization was correlated with the degree of strain on the haptic-optic junction. The angle of the haptic-optic junction in SIS-fixated IOLs (33.97°) was not significantly different compared with overlaid native nonfixated IOL (32.93°) but increased slightly with degree of haptic tip externalization (36.26 and 39.16 for 2 and 3 mm haptic externalizations, respectively). Conclusion: In this comprehensive study, we demonstrate the surgical outcomes achieved with SIS fixation of IOLs. Surgical and postoperative complications do occur, albeit at a low rate, and can effectively be managed with excellent anatomical and visual outcomes. The structural and anatomical data in this study may help guide SIS placement and optimize long-term surgical results.


Full Text

Department of Diagnostic Radiology and Molecular Imaging

Various typical and atypical imaging findings for pulmonary sarcoidosis have been described in the literature. Ground-glass opacities are one of the atypical manifestations, reported as diffuse or patchy ill-defined opacities frequently associated with additional findings and interstitial nodules. We performed a literature review to determine if our case had previously been described. The literature describes cases of mass-like consolidations, but there are no reports of mass-like ground-glass opacities. The appearance of the ground-glass opacities in our case is unique, appearing as discrete well-defined mass-like ground-glass opacities in a peribronchovascular distribution without additional parenchymal findings typically seen in sarcoidosis.

Vitiligo is an acquired pigmentary skin of depigmentation occurring secondary to melanocyte destruction. Vitiligo and other leukodermas have a profound impact on quality of life. Current therapies include medical options, such as phototherapy, topical and systemic corticosteroids, topical calcineurin inhibitors, immunomodulators, and antioxidant, and surgical options. Surgical options provide melanocytic cells to previously depigmented areas and use either tissue grafting or cellular grafting methods. Topical treatments are often insufficient, and many of the current surgical procedures have shown variable response rates. In this review, we discuss the process of the cellular grafting melanocyte-keratinocyte transplantation procedure (MKTP) and critically analyze its efficacy and safety in the treatment of vitiligo and other leukodermas. PubMed was searched for studies (2001-2017) describing the use of MKTP in patients with vitiligo or other leukoderma. Articles or trials discussing the use of MKTP for these patients were selected for in-depth review. Clinically relevant results regarding efficacy and safety of MKTP in vitiligo and leukoderma patients were analyzed. Numerous trials and case series/reports have demonstrated tolerability and efficacy of MKTP with repigmentation for patients with refractory, stable vitiligo. However, the response rates have been variable, likely influenced by vitiligo type and affected areas. Future research and clinical reporting will provide more insight on which phenotypes may benefit from MKTP.


Bartonella henselae is a fastidious organism that causes cat scratch disease, commonly associated with fever and lymphadenopathy but, in rare instances, also results in culture-negative infectious endocarditis. We describe a patient who presented with flank pain, splenic infarct, and acute kidney injury with an active urinary sediment, initially suspicious for vasculitis, which was subsequently diagnosed as B. henselae endocarditis. Bartonella endocarditis may present with a crescentic glomerulonephritis (GN) and elevated PR3-ANCA antibody titers, mimicking ANCA-associated GN, with 54 cases reported in the literature. Unique to our case in this series is a positive PR3-ANCA antibody despite a negative IIF-ANCA. Thus, the presentation of Bartonella can mimic ANCA-associated GN, and renal biopsy showing immune complex deposition is critical for diagnosis and appropriate treatment.


Background: Appropriate use criteria (AUC) provide physicians guidance in test selection, and can affect health care delivery, reimbursement policy and physician decision-making. Objectives: The American Society of Dermatopathology, with input from the American Academy of Dermatology and the College of American Pathologists, sought to develop AUC in dermatopathology. Methods: The RAND/UCLA appropriateness methodology, which combines evidence-based medicine, clinical experience and expert judgment, was used to develop AUC in dermatopathology. Results: With the number of ratings predetermined at 3, AUC were developed for 211 clinical scenarios involving 12 ancillary studies. Consensus was reached for 188 (89%) clinical scenarios, with 93 (44%) considered "usually appropriate," 52 (25%) "rarely appropriate" and 43 (20%) "uncertain appropriateness." Limitations: The methodology requires a focus on appropriateness without comparison between tests and irrespective of cost. Conclusions: The ultimate decision of when to order specific test rests with the physician and is one where the expected benefit exceeds the negative consequences. This publication outlines the recommendations of appropriateness—AUC for 12 tests used in...

Purpose: The placement or repositioning of intraocular lenses (IOL) in the absence of capsular support can be difficult. The aim of this study was to evaluate the efficacy and safety of a novel surgical technique using flanged needleless sutureless intrascleral (SIS) fixation of a sulcus IOL. Methods: A retrospective chart review was performed for 52 patients who underwent pars plana vitrectomy with IOL repositioning, exchange, or secondary placement with flanged needleless SIS fixation. Trocar cannulas were used to make scleral tunnels instead of needles. Average follow-up was 6 months. Main outcome measures were best corrected visual acuity (BCVA), stable anatomic placement of IOL, and any intra- or post-operative complications. Results: The indications for SIS were dislocated crystalline lens (2 patients, 3.7%), aphakia (7, 13%), and pseudophakia with dislocated IOL (45, 83.3%). A total of 9 eyes (16.7%) underwent secondary IOL placement, 19 eyes (35.2%) underwent IOL exchange, and 26 (48.1%) underwent IOL repositioning. BCVA improved from pre-operative 0.93±0.74 logMAR (Snellen equivalent 20/170) to post-operative 0.34±0.35 logMAR (Snellen equivalent 20/44) (P < 0.001). Intra-operatively, one case of retinal tear, one case of serous choroidal effusion with a retinal tear, and one case of limited suprachoroidal hemorrhage were noted. The most common post-operative issues were transient IOP elevation (22.2%), CME (20.4%), reverse pupillary block (11.1%), and IOL tilt or decentration (11.1%). All patients with IOP elevation and CME responded to topical medications. Reverse pupillary block resolved after laser peripheral iridotomy. IOL tilt was mild and did not require reoperation. One eye with mild iris capture developed increased IOP at postoperative month 4, so the IOL was repositioned at the slit lamp with complete resolution of symptoms. There were no cases of endophthalmitis or retinal detachments. Of the 52 patients, 2 patients (3.8%) underwent reoperation for recurrent dislocation for a total of 54 surgeries. Conclusions: Our study demonstrated that a flanged needleless SIS fixation technique was effective with improved BCVA and minimal transient complications. Additionally, an intra-operative peripheral iridectomy may prevent the occurrence of reverse pupillary block. This combination offers a new approach in the surgical repair of dislocated lenses, especially in the absence of capsular support.

Full Text
Department of Foundational Medical Studies

This viewpoint provides clinical illustrations showing how taking parental permission seriously can help clinicians deliver better care to pediatric patients and addresses frustrations with parent requests for what may seem to be suboptimal interventions.


Request Form
OUWB Medical Student Author
Department of Ophthalmology

A 13-year-old female with a history of regressed retinopathy of prematurity presented with new-onset floaters after sustaining blunt force trauma to her left eye. Best-corrected visual acuity was 20/20 in both eyes (OU), with an intraocular pressure of 14 mm Hg and 15 mm Hg in the right eye (OD) and left eye (OS), respectively. Exam under anesthesia revealed an unremarkable anterior segment OU, including no hyphema or subluxated crystalline lens. Scleral depression OS demonstrated a retinal dialysis superotemporally (1-o'clock to 3-o'clock) and nasally (7-o'clock to 10-o'clock) associated with a prominent vitreous base avulsion but no subretinal fluid (Figure). Scleral depression OD was unremarkable. Both areas of retinal dialysis OS were treated with three rows of indirect green laser photocoagulation posterior to the edge of the dialysis.


Full Text
Department of Anesthesiology
Department of Emergency Medicine

Background: Syncope is a common chief complaint in the ED, and the electrocardiogram (ECG) is a routine diagnostic tool in the evaluation of syncope. We assessed whether increasingly prolonged QTc intervals are associated with composite 30-day serious outcomes in older adults presenting to the ED with syncope. Methods: This is a secondary analysis of a prospective, observational study at 11 EDs in adults 60 years or older who presented with syncope or near syncope. We excluded patients presenting without an ECG, measurement of QTc, non-sinus rhythm, bundle branch block or those without 30-day follow-up. We categorized QTc cutoffs into values of <451; 451–470; 471–500, and >500 ms. We determined the rate of composite 30-day serious outcomes including ED serious outcomes and 30-day arrhythmias not identified in ED. Results: The study cohort included 2609 patients. There were 1678 patients (64.3%) that had QTc intervals <451 ms; 544 (20.8%) were 451–470 ms; 302 (11.6%) were 471–500 ms, and 85 (3.3%) had intervals >500 ms. We determined the rate of composite 30-day serious outcomes including ED serious outcomes and 30-day arrhythmias not identified in ED. Results: The study cohort included 2609 patients. There were 1678 patients (64.3%) that had QTc intervals <451 ms; 544 (20.8%) were 451–470 ms; 302 (11.6%) were 471–500 ms, and 85 (3.3%) had intervals >500 ms. Composite 30-day serious outcomes was associated with increasingly prolonged QTc intervals (13.0%, 15.3%, 18.2%, 22.4%, p = 0.01), but this association did not persist in multivariate analysis. Conclusions: In a cohort of older patients presenting with syncope, increased QTc interval was a marker of but was not independently predictive of composite 30-day serious outcomes.


Request Form
Department of Ophthalmology

Background and Objective: Anti-vascular endothelial growth factor (VEGF) therapy is increasing in popularity for treatment of retinopathy of prematurity (ROP). Despite many technical benefits, issues remain prompting further investigation. Patients and Methods: Retrospective case report and literature review. Results: A 42-week-old postmenstrual age female with gestational age of 28 weeks and birth weight of 990 g presented with prominent progression of peripapillary purely tractional atypical stage 4A ROP in both eyes following
intravitreal bevacizumab therapy in the right eye only. Conclusion: The authors present the first reported case, to their knowledge, of a “crunch” phenomenon tractional retinal detachment from fellow eye administration of bevacizumab.


Objectives: Visualizing myocardium with near field ultrasound (NFUS) transducers in the tip of the catheter might provide an image of the evolving pathological lesion during energy delivery. Background: Radiofrequency (RF) catheter ablation has been effective in arrhythmia treatment, but no technology has allowed lesion formation to be visualized in real time in vivo. Methods: RF catheter ablations were performed in vivo with the goal to create transmural atrial lesions and large ventricular lesions. RF lesion formation was imaged in real time using M-mode, tissue Doppler, and strain rate information from the NFUS open irrigated RF ablation catheter incorporating 4 ultrasound transducers (1 axial and 3 radial), and growth kinetics were analyzed. Nineteen dogs underwent ablation in the right and left atria (n = 185), right ventricle (n = 67), and left ventricle (n = 66). Lesions were echolucent with tissue strain rate by NFUS. Results: Lesion growth frequently progressed from epicardium to endocardium in thin-walled tissue. The half time of lesion growth was 5.5 ± 2.8 s in thin-walled and 9.7 ± 4.3 s in thick-walled tissue. Latency of lesion onset was seen in 57% of lesions ranging from 1 to 63.8 s. Tissue edema (median 25% increased wall thickness) formed immediately upon lesion formation in 83%, and intramyocardial steam was seen in 71% of cases. Conclusions: NFUS was effective in imaging RF catheter ablation lesion formation in real time. It was useful in assessing the dynamics of lesion growth and could visualize impending steam pops. It may be a useful technology to improve both safety and efficacy of RF catheter ablation.


Purpose: The Michigan Opioid Safety Score (MOSS) combines health risk, respiratory rate, and sedation measurement to guide safe opioid administration. This study was designed to assess reliability and nursing
acceptance of the MOSS tool. Design: Cross-sectional survey. Methods: Nurses without prior exposure to the tool were asked to participate in an online survey. In part I, raters utilized the MOSS to answer questions based on four fictional case scenarios. In part II, anonymous opinion of the tool was queried. Finding: Participants correctly scored 58.1% of patient scenarios, while appropriate clinical action was 80.5%. The intraclass correlation coefficient was 0.83. In terms of opinion, a majority of raters agreed the tool positively impacted patient safety (59.2%), improved confidence in opioid therapy (59.2%), and was easy to use (53%). Conclusions: Participants interpreted case scenarios with excellent inter-rater reliability and had a generally positive opinion. These study findings suggest the MOSS is a reliable safety instrument.


Purpose: To investigate the intrafractional stability of the motion relationship between the diaphragm and tumor, as well as the feasibility of using diaphragm motion to estimate lung tumor motion. Methods: Eighty-five paired (pre and posttreatment) daily 4D-CBCT images were obtained from 20 lung cancer patients who underwent SBRT. Bony registration was performed between the pre- and post-CBCT images to exclude patient body movement. The end-exhalation phase image of the pre-CBCT image was selected as the reference image. Tumor positions were obtained for each phase image using contour-based translational alignments. Diaphragm positions were obtained by translational alignment of its apex position. A linear intrafraction model was constructed using regression analysis performed between the diaphragm and tumor positions manifested on the pretreatment 4D-CBCT images. By applying this model to posttreatment 4D-CBCT images, the tumor positions were estimated from posttreatment 4D-CBCT diaphragm positions and compared with measured values. A receiver operating characteristic (ROC) test was performed to determine a suitable indicator for predicting the estimate accuracy of the linear model. Results: Using the linear model, per-phase position, mean position, and excursion estimation errors were 1.12 ± 0.99 mm, 0.97 ± 0.88 mm, and 0.79 ± 0.67 mm, respectively. Intrafractional per-phase tumor position estimation error, mean position error, and excursion error were within 3 mm 95%, 96%, and 99% of the time, respectively. The residual sum of squares (RSS) determined from pretreatment images achieved the largest prediction power for the tumor position estimation error (discrepancy < 3 mm) with an Area Under ROC Curve (AUC) of 0.92 (P < 0.05). Conclusion: Utilizing the relationship between diaphragm and tumor positions on the pretreatment 4D-CBCT image, intrafractional tumor positions were estimated from intrafractional diaphragm positions. The estimation accuracy can be predicted using the RSS obtained from the pretreatment 4D-CBCT image.