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# Henry Ford Health System Publication List – September 2016

*This bibliography aims to recognize the scholarly activity and provide ease of access to journal articles, meeting abstracts, book chapters, books and other works published by Henry Ford Health System personnel. Searches were conducted in PubMed, Embase, Web of Science, and Google Scholar during the beginning of October, and then imported into EndNote for formatting.There are 147 unique citations listed this month. Because of various limitations, this does not represent an exhaustive list of all published works by Henry Ford Health System authors.*

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## Allergy and Immunology

Fujimura KE, **Sitarik AR**, **Havstad S**, Lin DL, Levan S, Fadrosh D, Panzer AR, LaMere B, Rackaityte E, Lukacs NW, **Wegienka G**, Boushey HA, Ownby DR, **Zoratti EM**, **Levin AM**, **Johnson CC**, and Lynch SV. Neonatal gut microbiota associates with childhood multisensitized atopy and T cell differentiation *Nat Med* 2016;PMID: 27618652. Full Text

Division of Gastroenterology, Department of Medicine, University of California, San Francisco, San Francisco, California, USA.
Department of Public Health Sciences, Henry Ford Health System, Detroit, Michigan, USA.
Department of Pathology, University of Michigan Medical School, Ann Arbor, Michigan, USA.
Pulmonary, Critical Care, Allergy and Sleep Medicine, Department of Medicine, University of California, San Francisco, San Francisco, California, USA.
Section of Allergy-Immunology, Augusta University, Augusta, Georgia, USA. .
Department of Internal Medicine, Division of Allergy and Immunology, Henry Ford Health System, Detroit, Michigan, USA.

Gut microbiota bacterial depletions and altered metabolic activity at 3 months are implicated in childhood atopy and asthma. We hypothesized that compositionally distinct human neonatal gut microbiota (NGM) exist, and are differentially related to relative risk (RR) of childhood atopy and asthma. Using stool samples (n = 298; aged 1-11 months) from a US birth cohort and 16S rRNA sequencing, neonates (median age, 35 d) were divisible into three microbiota composition states (NGM1-3). Each incurred a substantially different RR for multisensitized atopy at age 2 years and doctor-diagnosed asthma at age 4 years. The highest risk group, labeled NGM3, showed lower relative abundance of certain bacteria (for example, Bifidobacterium, Akkermansia and Faecalibacterium), higher relative abundance of particular fungi (Candida and Rhodotorula) and a distinct fecal metabolome enriched for pro-inflammatory metabolites. Ex vivo culture of human adult peripheral T cells with sterile fecal water from NGM3 subjects increased the proportion of CD4+ cells producing interleukin (IL)-4 and reduced the relative abundance of CD4+CD25+FOXP3+ cells. 12,13-DiHOME, enriched in NGM3 versus lower-risk NGM states, recapitulated the effect of NGM3 fecal water on relative CD4+CD25+FOXP3+ cell abundance. These findings suggest that neonatal gut microbiome dysbiosis might promote CD4+ T cell dysfunction associated with childhood atopy.

## Anesthesiology

**Loomba V**, **Upadhyay A**, and **Kaveeshvar H**. Radiofrequency ablation of the sphenopalatine ganglion using cone beam computed tomography for intractable cluster headache *Pain Physician* 2016; 19(7):E1093-1096. PMID: 27676681. Full Text

Henry Ford Hospital Dept. of Anesthesiology and Pain Medicine, Detroit, MI.

Percutaneous radiofrequency ablation (RFA) of the sphenopalatine ganglion (SPG) has been shown to be an effective modality of treatment for patients with intractable chronic cluster headaches (CHs). While the use of fluoroscopy for RFA of the SPG is common, to our knowledge there are no documented cases of procedures using cone beam computed tomography (CBCT) for image guidance. We present a case report of a patient suffering from chronic intractable CH with complete long-lasting relief after RFA of the SPG using CBCT. The case reaffirms the

potential efficacy of RFA of the SPG in a case of chronic cluster headache as well as the use of CBCT as a superior alternative to bi-plane fluoroscopy for image guidance in the management of chronic CH. KEY WORDS: Cone beam computed tomography, sphenopalatine ganglion block, cluster headache, interventional pain, autonomic cephalalgia, radiofrequency ablation.

Cardiology / Cardiovascular Research

Al-Mallah M, Qureshi W, Ahmed A, Blaha M, **Brawner C**, **Ehrman J**, and **Keteyian S**. Cardiorespiratory fitness predictes outcomes among patients with depression: The henry ford exercise testing (FIT) project *Eur Heart J* 2016; 37:37. PMID: Not assigned. Abstract

M. Al-Mallah, King Abdul Aziz Medical City, King Saud Bin Abdulaziz University for Health Sciences, King Abdullah International Medical Research, Riyadh, Saudi Arabia

Background: Cardiorespiratory fitness (CRF) is a strong protective factor for all - cause mortality. Hypothesis: We hypothesized that CRF is associated with lower risk of all-cause mortality and non - fatal myocardial infarction (MI) among patients with depression treated with an anti-depressant medication (ADM). Methods: We included 5,208 patients on ADM who completed a clinical exercise stress test between 1991 and 2009. Patients were followed for a mean duration of 11.5 years for all-cause mortality ascertained by a search of social security death index in April 2013 and non-fatal MI was ascertained by hospital and clinical documentation. CRF was estimated in metabolic equivalents (METs). Cox proportional hazards regression models were used to examine the relationship of CRF with all - cause mortality and MI after adjustments for age, sex, risk factors for coronary artery disease, medications (aspirin, β blockers and statins), reason referred for a stress test, and history of coronary artery disease. Results: Patients with ADM that achieved ≥10 METs (versus those that achieved ≤6 METs) were younger (46±10 vs. 61±12 years), more often males (70% vs. 30%), black (15% vs. 4%), hypertensive (68% vs. 32%), diabetics (84% vs. 16%), smokers (56% vs. 44%) and dyslipidemia (29% vs. 20%). In fully adjusted Cox regression model, CRF was associated with lower all - cause mortality [Hazard ratio (HR) per 1 MET increase in CRF, 95% Confidence Interval (95% CI) 0.82 (0.79-0.85); p<.0001)] and non-fatal MI [0.92 (0.87-0.97); p=0.004)]. A graded decreased risk of mortality was observed with increase in CRF (Table 1). Conclusions: CRF had a strong graded protective association with both all - cause mortality and non-fatal MI in patients with depression on ADM. These results highlight the potential importance of assessing fitness to identify risk, as well as promoting an active lifestyle. (Table Presented).

Cardiology / Cardiovascular Research

Arbit B, Sharma S, Clopton P, Mueller C, **Nowak R**, **McCord J**, Mockel M, Filippatos G, Daniels L, Di Somma S, and Maisel A. Influence of gender and copeptin levels on clinical outcomes in patients with acute heart failure *J Card Fail* 2016; 22:S29. PMID: Not assigned. Abstract

B. Arbit, UCSD, San Diego, United States

Background: Copeptin is a novel biomarker derived from the C-terminal fragment of arginine vasopressin precursor (AVP), also known as antidiuretic hormone. Copeptin is released in response to the same factors as AVP and is more readily isolated and measured than AVP. Some studies have suggested that it may be superior to BNP in predicting death in patients with acute heart failure (AHF). To our knowledge, we are presenting the first study of gender-related differences of copeptin in prediction of mortality, readmissions, and emergency department visits. Methods: Current anaylysis used data from the Biomarkers in Acute Heart Failure (BACH) trial. 1641 patients presenting to the ED with acute dyspnea were prospectively enrolled in the study. Patients with valid measurements of copeptin and sodium were included in the current analysis. Patients were followed for up to 90 days after initial evaluation for the end points of all-cause mortality, HF-related readmissions, and HF-related ED visits. For the prognostic evaluation of copeptin, we divided the cohort by gender and by copeptin quartiles (specific to each gender). We then performed Cox regression for the combined end-point of all-cause mortality, HFrelated readmissions, and HF-related ED visits. Results: 1641 subjects were enrolled, of which 568 were diagnosed with AHF. Of these, 557 patients (347 male, 210 female) had valid measurements of sodium and copeptin. There were 64 deaths, 149 death- or HFrelated readmission events, and 172 death- or HF-related readmission or HF related ED visit events. Patients with copeptin levels in the highest quartile (>61.4 pmol/L for men, >54.1 pmol/L for women) had significantly increased rates of the combined end-point, $\chi 2 = 19.4$, $P < .0001$. Interestingly, rates were very similar among men and women above the 75th percentile, but below, women had significantly less events. Conclusions: This is the first study of gender-related differences of copeptin in prediction of clinical endpoints. Accounting for gender, copeptin may be a valuable tool in risk stratification of patients with AHF. (Figure Presented).

Cardiology / Cardiovascular Research

**Brawner CA**, Girdano D, **Ehrman JK**, and **Keteyian SJ**. Association between phase 3 cardiac rehabilitation and clinical events *J Cardiopulm Rehabil Prev* 2016;PMID: 27676465. Full Text

Division of Cardiovascular Medicine, Henry Ford Hospital, Detroit, Michigan (Drs Brawner, Ehrman, and Keteyian); and College of Health Sciences, Walden University, Minneapolis, Minnesota (Drs Brawner and Girdano).

PURPOSE: There is an inverse relationship between phase 2 cardiac rehabilitation (CR) visits and all-cause mortality. Phase 3 CR is a maintenance exercise program for which clinical outcomes are uncertain. This retrospective study describes the association between phase 3 CR participation and clinical events among patients with ischemic heart disease after completion of phase 2 CR. METHODS: Patients who completed 12 visits of phase 2 CR as provided by their health insurance were categorized on the basis of their frequency of participation (ie, none, irregular, and regular) in phase 3 CR during the 8 weeks after phase 2 CR. Cox regression analysis was used to evaluate the association between phase 3 CR participation and risk for a composite outcome that included all-cause mortality, nonfatal myocardial infarction, or heart failure hospitalization. RESULTS: Among 2039 patients (32% women; age = 59 +/- 10 years) who completed phase 2 CR, 101 were regular and 129 were irregular participants of phase 3 CR. Over a median followup of 5.6 years, 556 (27%) patients experienced the outcome. Neither irregular nor regular participation in phase 3 CR was significantly associated with risk for the outcome in unadjusted (P = .671 and P = .396, respectively) or adjusted (P = .737 and P = .890, respectively) analyses. CONCLUSIONS: We did not observe an incremental clinical benefit from weekly participation in Phase 3 CR after completion of phase 2 CR among patients with ischemic heart disease. Additional research addressing the dose-response relationship between phase 2 and 3 CR and clinical outcomes is needed.

Cardiology / Cardiovascular Research

**Bryce K**, **Pehote M**, and **Lanfear D**. Cognitive functioning and post-LVAD outcomes: Influence of comorbidities and specific cognitive domains *J Card Fail* 2016; 22:S124. PMID: Not assigned. Abstract

K. Bryce, Henry Ford Hospital, Detroit, United States

Introduction: Left ventricular assist devices (LVAD) are accepted therapy for end stage heart failure, but optimal patient selection remains challenging. Our group and others recently showed that baseline cognitive impairment is associated with worse outcomes post LVAD. We investigated whether this was impacted overall comorbidity burden, and which dimensions of cognitive function were most critical. Methods: A retrospective review was conducted on 100 consecutive patients who received continuous flow LVADs over a three year period (2011 and 2014) who were administered The Montreal Cognitive Assessment (MoCA) at the time of their pre-surgical psychological evaluation. Those who did not survive to discharge were excluded. Demographic information, MoCA scores and patient outcomes were collected. The primary endpoint of interest was time to hospital readmission tested using Cox regression models adjusted for potential confounders (age, race, gender, indication, and INTERMACS category). Comorbidity burden was assessed using the Charlson index. Standard MoCA subscores for Executive function, Attention, Naming, Abstraction, Language, and Orientation were tested as categorical variables (dichotomized at the median). Results: Average age was 55.6 (±12.29), 22% were female (n = 22), 42% were non-white race (n = 42), and 69% were destination therapy (n = 69). Charlson index was higher in patients with worse baseline MoCA (mean 4.5 vs 3.6, P = .021), but this did not impact the association of MoCA score with time to readmission (Charlson p = NS, MoCA category P = .005 HR = 2.0). When each subscore was tested in regression models only Attention was associated with risk of readmission (HR 2.5, P = .029). Conclusions: Among patients receiving LVADs, baseline cognitive dysfunction is associated with a greater burden of comorbidities, but this did not account for the increased hospital readmission rates among cognitively impaired patients. The cognitive domain that appears most important to post-LVAD outcomes is Attention/Concentration; the mechanism involved is unclear and deserves further investigation.

Cardiology / Cardiovascular Research

**Frisoli TM**, Friedman H, and **O'Neill WW**. Rotational atherectomy of three overlapping stent layers *J Invasive Cardiol* 2016; 28(9):E77-79. PMID: 27591692. Full Text

Heart and Vascular Institute, Henry Ford Hospital, 2799 W. Grand Blvd, Detroit, MI 48202 USA. Tfrisol1@hfhs.org.

A patient was referred to us for Canadian Cardiovascular Society class III refractory angina. He was found to have in-stent restenosis within three layers of underexpanded stents implanted in 2004, 2011, and 2014. Rotational atherectomy safely yielded stent strut ablation (reduced to one layer), lesion expansion, and very good angiographic and physiologic results.

Cardiology / Cardiovascular Research

Hung RK, **Al-Mallah MH**, Whelton SP, Michos ED, Blumenthal RS, **Ehrman JK**, Brawner CA, Keteyian SJ, and Blaha MJ. Effect of beta-blocker therapy, maximal heart rate, and exercise capacity during stress testing on long-term survival (from the henry ford exercise testing project) *Am J Cardiol* 2016;PMID: 27670797. Full Text

Department of Cardiology, Johns Hopkins Ciccarone Center for the Prevention of Heart Disease, Baltimore, Maryland.
Department of Cardiology, King Saud bin Abdulaziz University for Health Sciences, King Abdullah International Medical Research Center, King Abdulaziz Cardiac Center, Ministry of National Guard, Health Affairs, Riyadh, Saudi Arabia; Department of Cardiology, Henry Ford Hospital, Detroit, Michigan.
Department of Cardiology, Henry Ford Hospital, Detroit, Michigan.
Department of Cardiology, King Saud bin Abdulaziz University for Health Sciences, King Abdullah International Medical Research Center, King Abdulaziz Cardiac Center, Ministry of National Guard, Health Affairs, Riyadh, Saudi Arabia.
Department of Cardiology, Johns Hopkins Ciccarone Center for the Prevention of Heart Disease, Baltimore, Maryland. Electronic address: mblaha1@jhmi.edu.

Whether lower heart rate thresholds (defined as the percentage of age-predicted maximal heart rate achieved, or ppMHR) should be used to determine chronotropic incompetence in patients on beta-blocker therapy (BBT) remains unclear. In this retrospective cohort study, we analyzed 64,549 adults without congestive heart failure or atrial fibrillation (54 +/- 13 years old, 46% women, 29% black) who underwent clinician-referred exercise stress testing at a single health care system in Detroit, Michigan from 1991 to 2009, with median follow-up of 10.6 years for all-cause mortality (interquartile range 7.7 to 14.7 years). Using Cox regression models, we assessed the effect of BBT, ppMHR, and estimated exercise capacity on mortality, with adjustment for demographic data, medical history, pertinent medications, and propensity to be on BBT. There were 9,259 deaths during follow-up. BBT was associated with an 8% lower adjusted achieved ppMHR (91% in no BBT vs 83% in BBT). ppMHR was inversely associated with all-cause mortality but with significant attenuation by BBT (per 10% ppMHR HR: no BBT: 0.80 [0.78 to 0.82] vs BBT: 0.89 [0.87 to 0.92]). Patients on BBT who achieved 65% ppMHR had a similar adjusted mortality rate as those not on BBT who achieved 85% ppMHR (p >0.05). Estimated exercise capacity further attenuated the prognostic value of ppMHR (per-10%-ppMHR HR: no BBT: 0.88 [0.86 to 0.90] vs BBT: 0.95 [0.93 to 0.98]). In conclusion, the prognostic value of ppMHR was significantly attenuated by BBT. For patients on BBT, a lower threshold of 65% ppMHR may be considered for determining worsened prognosis. Estimated exercise capacity further diminished the prognostic value of ppMHR particularly in patients on BBT.

Cardiology / Cardiovascular Research

Karacsonyi J, Karmpaliotis D, **Alaswad K**, Jaffer FA, Yeh RW, Patel M, Bahadorani J, Doing A, Ali ZA, Karatasakis A, Danek BA, Rangan BV, Alame AJ, Banerjee S, and Brilakis ES. Prevalence, indications and management of balloon uncrossable chronic total occlusions: Insights from a contemporary multicenter US registry *Catheter Cardiovasc Interv* 2016;PMID: 27650935. Full Text

VA North Texas Healthcare System and UT Southwestern Medical Center, Dallas, Texas.
Division of Invasive Cardiology, Second Department of Internal Medicine and Cardiology Center, University of Szeged, Szeged, Hungary.
Columbia University, New York, New York.
Henry Ford Hospital, Cardiology Department, Detroit, Michigan.
Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts.
Beth Israel Deaconess Medical Center, Boston, Massachusetts.
VA San Diego Healthcare System and University of California San Diego, San Diego, California.
Medical Center of the Rockies, Loveland, Colorado.
VA North Texas Healthcare System and UT Southwestern Medical Center, Dallas, Texas. esbrilakis@gmail.com.
Minnepolis Heart Institute, Minneapolis, Minnesota. esbrilakis@gmail.com.

BACKGROUND: Balloon uncrossable lesions can be challenging to treat, requiring specialized techniques and equipment. METHODS: We examined the prevalence, clinical and angiographic characteristics, management and procedural outcomes of balloon uncrossable lesions in a multicenter chronic total occlusion (CTO) percutaneous coronary intervention (PCI) registry. RESULTS: Between 2012 and 2016, 718 CTO PCIs (in which the occlusion was successfully crossed with a guidewire) were performed in 701 patients at 11 US centers. Mean age was 65.6 +/- 10 years and 84% of the patients were men. Balloon uncrossable lesions represented 9% of all CTOs. Balloon uncrossable CTOs had more moderate/severe calcification (82% vs. 52%, P < 0.0001), moderate/severe tortuosity (61% vs. 35% P < 0.0001) and higher J-CTO score (2.95 +/- 1.32 vs. 2.43 +/- 1.23, P = 0.005) as compared with the remaining lesions. Technical and procedural success was significantly lower for balloon uncrossable lesions (90.5%

vs. 98.3%, P < 0.0001 and 88.9% vs. 96.6% P = 0.004), respectively, but the incidence of major adverse events was similar (1.6% vs. 2.2%, P = 0.751). Balloon uncrossable lesions required longer procedure (208 [interquartile range: 135, 258] vs. 135 [94, 194] min, P < 0.0001) and fluoroscopy (77 [52, 100] vs. 45 min [27, 75], P < 0.0001) time. Techniques used to treat balloon uncrossable lesions included balloon-assisted microdissection (23%), excimer laser atherectomy (18%), and rotational atherectomy (16%). Excimer laser atherectomy and balloon-assisted microdissection were associated with the highest technical and procedural success rates. CONCLUSIONS: Balloon uncrossable CTOs are common, are associated with high rates of technical failure, and require specialized techniques for successful treatment.

Cardiology / Cardiovascular Research

Karatasakis A, Danek BA, Karmpaliotis D, **Alaswad K**, Jaffer FA, Yeh RW, Patel M, Bahadorani JN, Lombardi WL, Wyman RM, Grantham JA, Kandzari DE, Lembo NJ, Doing AH, Toma C, Moses JW, Kirtane AJ, Parikh MA, Ali ZA, Garcia S, Kalsaria P, Karacsonyi J, Alame AJ, Thompson CA, Banerjee S, and Brilakis ES. Comparison of various scores for predicting success of chronic total occlusion percutaneous coronary intervention *Int J Cardiol* 2016; 224:50-56. PMID: 27611917. Full Text

VA North Texas Health Care System and University of Texas Southwestern Medical Center, Dallas, TX, United States.
Columbia University, New York, NY, United States.
Henry Ford Hospital, Detroit, MI, United States.
Massachusetts General Hospital and Harvard Medical School, Boston, MA, United States.
Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA, United States.
VA San Diego Healthcare System and University of California San Diego, La Jolla, CA, United States.
University of Washington, Seattle, WA, United States.
Torrance Memorial Medical Center, Torrance, CA, United States.
St. Luke's Mid America Heart Institute, Kansas City, MO, United States.
Piedmont Heart Institute, Atlanta, GA, United States.
Medical Center of the Rockies, Loveland, CO, United States.
University of Pittsburgh Medical Center, Pittsburgh, PA, United States.
Minneapolis VA Health Care System and University of Minnesota, Minneapolis, MN, United States.
Boston Scientific, Natick, MA, United States.
VA North Texas Health Care System and University of Texas Southwestern Medical Center, Dallas, TX, United States. Electronic address: esbrilakis@gmail.com.

BACKGROUND: Various scoring systems have been developed to predict the technical outcome and procedural efficiency of chronic total occlusion (CTO) percutaneous coronary intervention (PCI). METHODS: We examined the predictive capacity of 3 CTO PCI scores (Clinical and Lesion-related [CL], Multicenter CTO registry in Japan [J-CTO] and Prospective Global Registry for the Study of Chronic Total Occlusion Intervention [PROGRESS CTO] scores) in 664 CTO PCIs performed between 2012 and 2016 at 13 US centers. RESULTS: Technical success was 88% and the retrograde approach was utilized in 41%. Mean CL, J-CTO and PROGRESS CTO scores were 3.9+/-1.9, 2.6+/-1.2 and 1.4+/-1.0, respectively. All scores were inversely associated with technical success (p<0.001 for all) and had moderate discriminatory capacity (area under the curve 0.691 for the CL score, 0.682 for the J-CTO score and 0.647 for the PROGRESS CTO score [p=non-significant for pairwise comparisons]). The difference in technical success between the minimum and maximum CL score strata was the highest (32%, vs. 15% for J-CTO and 18% for PROGRESS CTO scores). All scores tended to perform better in antegrade-only procedures and correlated significantly with procedure time and fluoroscopy dose; the CL score also correlated significantly with contrast utilization. CONCLUSIONS: CL, J-CTO and PROGRESS CTO scores perform moderately in predicting technical outcome of CTO PCI, with better performance for antegrade-only procedures. All scores correlate with procedure time and fluoroscopy dose, and the CL score also correlates with contrast utilization.

Cardiology / Cardiovascular Research

Khan JM, Rogers T, Schenke WH, Mazal JR, Faranesh AZ, **Greenbaum AB**, Babaliaros VC, Chen MY, and Lederman RJ. Intentional laceration of the anterior mitral valve leaflet to prevent left ventricular outflow tract obstruction during transcatheter mitral valve replacement: Pre-clinical findings *JACC Cardiovasc Interv* 2016; 9(17):1835-1843. PMID: 27609260. Full Text

Cardiovascular and Pulmonary Branch, Division of Intramural Research, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Maryland.
Center for Structural Heart Disease, Division of Cardiology, Henry Ford Health System, Detroit, Michigan.
Structural Heart and Valve Center, Emory University Hospital, Atlanta, Georgia.

Cardiovascular and Pulmonary Branch, Division of Intramural Research, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Maryland. Electronic address: lederman@nih.gov.

OBJECTIVES: The authors propose a novel transcatheter transection of the anterior mitral leaflet to prevent iatrogenic left ventricular outflow tract (LVOT) obstruction during transcatheter mitral valve replacement (TMVR). BACKGROUND: LVOT obstruction is a life-threatening complication of TMVR caused by septal displacement of the anterior mitral leaflet. METHODS: In vivo procedures in swine were guided by biplane x-ray fluoroscopy and intracardiac echocardiography. Retrograde transaortic 6-F guiding catheters straddled the anterior mitral leaflet. A stiff 0.014-inch guidewire with polymer jacket insulation was electrified and advanced from the LVOT, through the A2 leaflet base, into the left atrium. The wire was snared and externalized, forming a loop that was energized and withdrawn to lacerate the anterior mitral leaflet. RESULTS: The anterior mitral leaflet was successfully lacerated in 7 live and 1 post-mortem swine under heparinization. Lacerations extended to 89 +/- 19% of leaflet length and were located within 0.5 +/- 0.4 mm of leaflet centerline. The chordae were preserved and retracted the leaflet halves away from the LVOT. LVOT narrowing after benchtop TMVR was significantly reduced with intentional laceration of the anterior mitral leaflet to prevent LVOT obstruction than without (65 +/- 10% vs. 31 +/- 18% of pre-implantation diameter, $p < 0.01$). The technique caused mean blood pressure to fall (from 54 +/- 6 mm Hg to 30 +/- 4 mm Hg, $p < 0.01$), but blood pressure remained steady until planned euthanasia. No collateral tissue injury was identified on necropsy. CONCLUSIONS: Using simple catheter techniques, the anterior mitral valve leaflet was transected. Cautiously applied in patients, this strategy can prevent anterior mitral leaflet displacement and LVOT obstruction caused by TMVR.

Cardiology / Cardiovascular Research

**Michaels AT**, **Radjef R**, **She R**, **Liu B**, **Peterson E**, Pinto Y, **Williams K**, **Sabbah H**, and **Lanfear D**. Improving risk prediction in heart failure: Maggic + natriuretic peptides *J Card Fail* 2016; 22:S99. PMID: Not assigned. Abstract

A.T. Michaels, Henry Ford Hospital, Detroit, United States

Background: Risk stratification of patients with heart failure (HF) remains challenging but is a critical need. The MAGGIC score is a clinical risk model derived from meta-analysis of nearly 40k patients. Natriuretic peptides (NP) have consistently shown powerful risk prediction in HF patients, but the incremental value in addition to MAGGIC score is not known. Methods: In this single center study 4264 patients were analyzed from two cohorts; a prospective ambulatory registry of HF patients (n = 1314) who had baseline NTproBNP levels measured, and a retrospective cohort collected utilizing administrative data from hospital discharges for HF (January 1st, 2014 through July 30th, 2015; n = 2503) with clinical BNP levels measured at or near discharge. The hospital discharge cohort were all assigned NYHA class IV. The primary end-point was all cause mortality. Performance of the MAGGIC score and NP levels was assessed within each cohort utilizing Cox regression and receiver operating curves (ROC) analysis (MAGGIC alone vs. MAGGIC+NP) with the net reclassification improvement (NRI) also calculated. Results: The overall cohort had an average age of 71.2 years, was 47.8% females, and 41% self-identified African Americans. Median follow up was 1.52 years during which there were 1139 deaths (27%). The MAGGIC score was a strong predictor of outcome in both cohorts ($P < .001$). In ROC analysis of the ambulatory registry, NP significantly improved area under the curve (AUC) compared to MAGGIC alone from 0.74 to 0.79 ($P = .002$) and had a NRI of 0.354 (Figure). In contrast, within the hospital discharge cohort NP levels did not significantly add to MAGGIC score (AUC 0.681 vs. 0.676, NRI = 0.033, $P = .284$) (Figure). Conclusion: In our study, NP levels in the ambulatory setting significantly improved risk stratification provided by the MAGGIC score, but discharge NP levels did not improve MAGGIC prediction of posthospital survival. Overall risk stratification and particularly NP utility is much better in the ambulatory setting. (Figure Presented).

Cardiology / Cardiovascular Research

**Michaels AT**, **Radjef R**, **She R**, **Peterson E**, **Liu B**, and **Lanfear DE**. Predicting mortality at discharge following hospitalization for acute heart failure *J Card Fail* 2016; 22:S21-S22. PMID: Not assigned. Abstract

A.T. Michaels, Henry Ford Hospital, Detroit, United States

Background: Risk stratification for heart failure (HF) patients remains a critical need, particularly among those hospitalized where many clinical decisions are being made at discharge. Recently a robust risk model, the MAGGIC score, was derived from data on nearly 40k patients. This provides 1 year mortality estimates and is available as an online clinical tool. Whether it is useful to risk-stratify patients being discharged from the hospital is unknown. Methods: This single center study analyzed a total of 4264 patients from 2 cohorts; one utilizing administrative data from hospital discharges for HF (January 1st, 2014 through July 30th, 2015, n = 2503) and a prospective registry of ambulatory HF patients (n = 1761), both based in southeast Michigan. For the hospital discharge subjects, when

tabulating MAGGIC all patients were assigned NYHA class IV. The primary endpoint was all-cause mortality. Vital status was assessed utilizing system administrative data and the social security death master file. Performance of the MAGGIC score was evaluated within cohorts and compared across the two groups using Cox models stratified by cohort and then with an interaction term (MAGGIC∗Cohort). Calibration was assessed by comparing observed vs. MAGGICpredicted 1 year mortality. Results: Overall the study patients had an average age of 71.2 years, 47.8% were female and 41% were self-identified African Americans, and there were 1139 deaths (27%) over a median follow up of 1.52 years. The hospital discharge cohort was overall much higher risk than the ambulatory cohort (figure). The MAGGIC score was a strong predictor of outcomes in both groups (both P < .001). With a HR (per MAGGIC point) of 1.13 in the ambulatory registry and 1.10 in the hospital discharge patients. In ROC analysis MAGGIC showed an area under the curve (AUC) of 0.74, but an AUC in the hospital discharge cohort of 0.67. When modeled using an interaction term, MAGGIC did appear to be more predictive in the ambulatory group with an interaction coefficient of 0.03 (P = .004). Although calibration appeared suboptimal in both cohorts (Figure), with MAGGIC underestimating the true risk, this appeared similar in both cohorts. Discussion: The MAGGIC score is able to provide important prognostic information on patients being discharged from the hospital for HF, though the performance was somewhat inferior than in a comparable ambulatory cohort. MAGGIC underestimated risk in both ambulatory and hospital cohorts, suggesting calibration may need to be reassessed in more real-world patient data sets. (Figure Presented).

Cardiology / Cardiovascular Research

O'Neill BP, and **O'Neill WW**. Tricuspid valve intervention: New direction and new hope *J Am Coll Cardiol* 2016; 68(10):1034-1036. PMID: 27585508. Full Text

Department of Medicine, Division of Cardiology, Temple Heart and Vascular Institute, Philadelphia, Pennsylvania. Department of Medicine, Division of Cardiology, Henry Ford Hospital, Detroit, Michigan. Electronic address: Woneill1@hfhs.org.

Cardiology / Cardiovascular Research

**Radjef R**, **Michaels A**, **Peterson E**, **She R**, **Liu B**, **Williams K**, **Sabbah H**, and **Lanfear D**. Performance of maggic score in African Americans compared to whites *J Card Fail* 2016; 22:S101. PMID: Not assigned. Abstract

R. Radjef, Henry Ford Hospital, Detroit, United States

Background: Risk stratification is critical in Heart Failure (HF) care. The MAGGIC score is a validated tool derived from a large multi-study cohort of nearly 40,000 but very few of the patients self-identified as Black or of African Ancestry (less than 400). There is little data assessing MAGGIC score utility in African Americans (AA). Methods: This single center study analyzed a total of 4264 patients from 2 cohorts; one utilizing administrative data from hospital discharges for HF (January 1st, 2014 through July 30th, 2015, n = 2503) and a prospective registry of ambulatory HF patients (n = 1761), both based in southeast Michigan. Baseline characteristics were collected to tabulate MAGGIC score and test its risk stratification in selfidentified African Americans (AA) and whites. The primary endpoint was time to all-cause mortality. Death was detected using system records and the social security death master file. Cox models with MAGGIC score as the only variable stratified by race, and a combined model including MAGGIC, race, and MAGGIC∗race were tested. P < .05 was considered significant. Results: Overall, 1748 patients (41%) were AA, and a total of 1151 (27%) patients died during follow up. MAGGIC score was strongly and similarly predictive of survival in both race groups. Among AA, each MAGGIC point carried HR of 1.12 (95%CI 1.10, 1.14; P < .001) while in whites the HR was 1.13 (95%CI 1.12, 1.14; P < .001). Formal test of interaction of MAGGIC by race was not significant (P = .153). However, there was a difference in survival by race, with African Americans showing a survival advantage (HR = 0.72, P = .001) which appears to be isolated to the highest risk subgroup (Figure). Conclusion: These data support the utility of the MAGGIC score for risk stratification in African Americans who suffer from HF. However, there may still be residual differences in outcomes between AA and whites despite overall risk adjustment, particularly in highest risk subgroup. (Figure Presented).

Cardiology / Cardiovascular Research

**Sabbah HN**, **Gupta RC**, **Sing-Gupta V**, **Zhang K**, and **Xu J**. Long-term therapy with elamipretide normalizes ATP synthase activity in left ventricular myocardium of dogs with advanced heart failure *J Card Fail* 2016; 22:S23. PMID: Not assigned. Abstract

H.N. Sabbah, Henry Ford Hospital, Detroit, United States

Background: Adenosine triphosphate (ATP) is the “energy currency” of cardiomyocytes. ATP synthase is an “essential” enzyme that synthesizes ATP within the mitochondria from adenosine diphosphate (ADP) and inorganic phosphate (Pi) in the presence of energy. We showed that elamipretide (ELA) (MTP-131, BendaviaTM), a novel mitochondria-targeting tetrapeptide, improves LV function in dogs with heart failure (HF) and reduced ejection fraction (HFrEF) (EF~30%). We also showed that ELA normalizes maximum rate of ATP synthesis and limits excessive formation of reactive oxygen species (ROS) in mitochondria of cardiomyocytes from HFrEF dogs. This study tested the hypothesis that in dogs with HFrEF, ATP synthase activity (ATPSA) is reduced in LV myocardium and that chronic therapy with ELA normalizes ATPSA in LV of dogs with HFrEF. Methods: Studies were performed in LV tissue of 14 HF dogs randomized to 3 months therapy with subcutaneous injections of ELA (0.5 mg/kg once daily, n = 7) or saline (HF-Control, n = 7). LV tissue from 6 normal (NL) dogs was used for comparisons. Oligomycin-sensitive ATPSA was measured in isolated LV mitochondria as determined by oxidation of NADH to NAD monitored spectrophotometrically as a decrease in absorbance at 340 nm. In addition, LV myocardial protein levels of ATP synthase α and β subunits were measured in LV tissue homogenate by Western Blotting and bands quantified in densitometric units (du). Results: Data are shown in the Table. Compared to NL dogs, ATPSA and protein level of subunits α and β decreased significantly in HF-Control dogs. Chronic therapy with ELA normalizedATPSA but did not significantly increase protein levels of α and β subunits in treated dogs compared to HF-Controls. Conclusions: ATPSA and protein levels of α and β subunits are reduced in LV myocardium of dogs with chronic HF. Long-term therapy with ELA normalizes ATPSA but does not significantly improve protein level abundance of α and β subunits. The improvement in the ATPSA with ELA therapy is likely to have played a key role in improving the rate of ATP synthesis and consequently in improving LV function in dogs with HFrEF. (Table Presented).

Cardiology / Cardiovascular Research

Singh V, Rodriguez AP, Thakkar B, Patel NJ, Ghatak A, Badheka AO, Alfonso CE, de Marchena E, Sakhuja R, Inglessis-Azuaje I, Palacios I, Cohen MG, Elmariah S, and **O'Neill WW**. Comparison of outcomes of transcatheter aortic valve replacement plus percutaneous coronary intervention versus transcatheter aortic valve replacement alone in the United States *Am J Cardiol* 2016;PMID: 27665205. Full Text

Cardiology Division, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts. Electronic address: vikas.dr.singh@gmail.com.
Cardiovascular Division, University of Miami Miller School of Medicine, Miami, Florida.
Cardiovascular Division, Cleveland Clinic, Ohio.
Cardiology Department, Southwest Heart, Las Cruces, New Mexico.
Cardiovascular Division, The Everett Clinic, Everett, Washington.
Cardiology Division, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts.
Division of Cardiology, Henry Ford Hospital, Detroit, Michigan.

Transcatheter aortic valve replacement (TAVR) with percutaneous coronary intervention (PCI) has emerged as a less-invasive therapeutic option for high surgical risk patients with aortic stenosis and coronary artery disease. The aim of this study was to determine the outcomes of TAVR when performed with PCI during the same hospitalization. We identified patients using the International Classification of Diseases, Ninth Revision, Clinical Modification procedure codes from the Nationwide Inpatient Sample between the years 2011 and 2013. A total of 22,344 TAVRs were performed between 2011 and 2013. Of these, 21,736 (97.3%) were performed without PCI (TAVR group) while 608 (2.7%) along with PCI (TAVR + PCI group). Among the TAVR + PCI group, 69.7% of the patients had single-vessel, 22.2% had 2-vessel, and 1.6% had 3-vessel PCI. Drug-eluting stents were more commonly used than bare-metal stents (72% vs 28%). TAVR + PCI group witnessed significantly higher rates of mortality (10.7% vs 4.6%) and complications: vascular injury requiring surgery (8.2% vs 4.2%), cardiac (25.4% vs 18.6%), respiratory (24.6% vs 16.1%), and infectious (10.7% vs 3.3%), p <0.001% for all, compared with the TAVR group. The mean length of hospital stay and cost of hospitalization were also significantly higher in the TAVR + PCI group. The propensity score-matched analysis yielded similar results. In conclusion, performing PCI along with TAVR during the same hospital admission is associated with higher mortality, complications, and cost compared with TAVR alone. Patients would perhaps be better served by staged PCI before TAVR.

Cardiology / Cardiovascular Research

**Verma S**, Burkhoff D, and **O'Neill WW**. Avoiding hemodynamic collapse during high-risk percutaneous coronary intervention: Advanced hemodynamics of impella support *Catheter Cardiovasc Interv* 2016;PMID: 27658747. Full Text

Henry Ford Hospital, Division of Cardiology, Detroit, Michigan.
Division of Cardiology, Columbia University, New York, New York. Db59@columbia.edu.

The rate of performing primary percutaneous coronary intervention in patients with complex coronary artery disease is increasing. The use of percutaneous mechanical circulatory support devices provides critical periprocedural hemodynamic support. Mechanical support has increased the safety and efficacy of interventional procedures in this high-risk patient population. Predicting patient response to the selected intervention can be clinically challenging. Here we demonstrate a case where complete hemodynamic collapse during PCI was avoided by mechanical support provided by the Impella device. Further, we employ a comprehensive cardiovascular model to predict ventricular function and patient hemodynamics in response to the procedure. New computational tools may help interventionists visualize, understand, and predict the multifaceted hemodynamic aspects of these high risk procedures in individual patients.

Center for Health Policy and Health Services Research
Rundell SD, Sherman KJ, Heagerty PJ, Mock CN, Dettori NJ, Comstock BA, Avins AL, Nedeljkovic SS, **Nerenz DR**, and Jarvik JG. Predictors of persistent disability and back pain in older adults with a new episode of care for back pain *Pain Med* 2016;PMID: 27688311. Article Request Form

*Department of Rehabilitation Medicine Comparative Effectiveness, Cost, and Outcomes Research Center srundell@uw.edu.
Group Health Research Institute, Seattle, Washington.
Center for Biomedical Statistics.
Department of Epidemiology, University of Washington and Harborview Injury Prevention Research Center, Seattle, Washington.
Department of Health Services.
Division of Research, Kaiser Permanente Northern California, Oakland, CA.
**Department of Anesthesiology, Perioperative and Pain Medicine, Brigham and Women's Hospital, and Spine Unit, Harvard Vanguard Medical Associates, Boston, MA.
Henry Ford Hospital, Neuroscience Institute, Detroit, MI, USA.
Comparative Effectiveness, Cost, and Outcomes Research Center Department of Radiology, Neurological Surgery, Orthopedic Surgery and Sports Medicine, Health Services and Pharmacy, University of Washington, Seattle, Washington.

OBJECTIVE: To identify predictors of persistent disability and back pain in older adults. DESIGN: Prospective cohort study. SETTING: Back pain outcomes using longitudinal data registry. SUBJECTS: Five thousand two hundred twenty adults age 65 years and older with a new primary care visit for back pain. METHODS: Baseline measurements included: demographics, health, and back pain characteristics. We abstracted imaging findings from 348 radiology reports. The primary outcomes were the Roland-Morris Disability Questionnaire (RMDQ) and back pain intensity. We defined persistent disability as RMDQ of 4/24 or higher at both six and 12 months and persistent back pain as pain 3/10 or higher at both six and 12 months. RESULTS: There were 2,498 of 4,143 (60.3%) participants with persistent disability, and 2,099 of 4,144 (50.7%) had persistent back pain. Adjusted analyses showed the following characteristics most strongly predictive of persistent disability and persistent back pain: sex, race, worse baseline clinical characteristics of back pain, leg pain, back-related disability and duration of symptoms, smoking, anxiety symptoms, depressive symptoms, a history of falls, greater number of comorbidities, knee osteoarthritis, wide-spread pain syndromes, and an index diagnosis of lumbar spinal stenosis. Within the imaging data subset, central spinal stenosis was not associated with disability or pain. CONCLUSION: We found that many predictors in older adults were similar to those for younger populations.

Center for Health Policy and Health Services Research
Spradling PR, Xing J, **Rupp LB**, Moorman AC, **Gordon SC**, Teshale ET, **Lu M**, Boscarino JA, Schmidt MA, Trinacty CM, and Holmberg SD. Distribution of disease phase, treatment prescription and severe liver disease among 1598 patients with chronic hepatitis B in the Chronic Hepatitis Cohort Study, 2006-2013 *Aliment Pharmacol Ther* 2016;PMID: 27640985. Full Text

Division of Viral Hepatitis, National Centers for HIV, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention, Atlanta, GA, USA. pspradling@cdc.gov.
Division of Viral Hepatitis, National Centers for HIV, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention, Atlanta, GA, USA.
Henry Ford Health System, Detroit, MI, USA.
Center for Health Research, Geisinger Health System, Danville, PA, USA.
The Center for Health Research, Kaiser Permanente-Northwest, Portland, OR, USA.
The Center for Health Research, Kaiser Permanente-Hawaii, Honolulu, Hawaii.

BACKGROUND: Limited information exists regarding the distribution of disease phases, treatment prescription and severe liver disease among patients with chronic hepatitis B (CHB) in US general healthcare settings. AIM: To determine the distribution of disease phases, treatment prescription and severe liver disease among patients with CHB in general US healthcare settings. METHODS: We analysed demographic and clinical data collected during 2006-2013 from patients with confirmed CHB in the Chronic Hepatitis Cohort Study, an observational cohort study involving patients from healthcare organisations in Michigan, Pennsylvania, Oregon and Hawaii. CHB phases were classified according to American Association for the Study of Liver Disease guidelines. RESULTS: Of 1598 CHB patients with >/=12 months of follow-up (median 6.3 years), 457 (29%) were immune active during follow-up [11% hepatitis B e antigen (HBeAg)-positive, 16% HBeAg-negative, and 2% HBeAg status unknown], 10 (0.6%) were immune tolerant, 112 (7%) were inactive through the duration of follow-up and 886 (55%) were phase indeterminate. Patients with cirrhosis were identified within each group (among 21% of immune active, 3% of inactive and 9% of indeterminate phase patients) except among those with immune-tolerant CHB. Prescription of treatment was 59% among immune active patients and 84% among patients with cirrhosis and hepatitis B virus (HBV) DNA >2000 IU/mL. CONCLUSIONS: Approximately, one-third of the cohort had active disease during follow-up; 60% of eligible patients were prescribed treatment. Our findings underscore the importance of ascertainment of fibrosis status in addition to regular assessment of ALT and HBV DNA levels.

Dermatology

Boer B, **Tisack A**, and **Shwayder T**. Transient porphyrinemia in a neonate: A case report *Pediatr Dermatol* 2016;PMID: 27573700. Full Text

College of Human Medicine, Michigan State University, Grand Rapids, MI.
Department of Dermatology, Henry Ford Hospital, Detroit, MI.
Director of Pediatric Dermatology, Henry Ford Hospital, Detroit, MI.

We describe a neonate with anemia, thrombocytopenia, and hyperbilirubinemia secondary to hemolytic disease of the newborn. After phototherapy for hyperbilirubinemia, the neonate developed a photodistributed eruption with high serum and urine porphyrin levels. This transient porphyrinemia resolved at 1 month.

Dermatology

Cheng C, **Ozog D**, **Chaffins M**, Ginsberg D, and Krakowski A. Ablative fractional resurfacing for treatment of focal dermal hypoplasia in a pediatric patient with goltz syndrome *Lasers Surg Med* 2016; 48(4):428-428. PMID: Not assigned. Abstract

Dermatology

Eichenfield L, Call RS, Forsha D, Fowler J, Hebert AA, Spellman M, **Gold LFS**, Van Syoc M, Zane LT, and Tschen EH. Long-term safety of crisaborole topical ointment, 2%, in atopic dermatitis *J Invest Dermatol* 2016; 136(5):S49-S49. PMID: Not assigned. Abstract

Dermatology

Garzon MC, Epstein LG, Heyer GL, Frommelt PC, Orbach DB, Baylis AL, Blei F, Burrows PE, Chamlin SL, Chun RH, Hess CP, Joachim S, **Johnson K**, Kim W, Liang MG, Maheshwari M, McCoy GN, Metry DW, Monrad PA, Pope E, Powell J, **Shwayder TA**, Siegel DH, Tollefson MM, Vadivelu S, Lew SM, Frieden IJ, and Drolet BA. PHACE syndrome: Consensus-derived diagnosis and care recommendations *J Pediatr* 2016;PMID: 27659028. Full Text

Departments of Dermatology and Pediatrics, Columbia University, New York, NY.
Departments of Pediatrics and Neurology, The Ann and Robert H. Lurie Children's Hospital of Chicago, Northwestern University Feinberg School of Medicine, Chicago, IL.
Departments of Pediatrics and Neurology, Nationwide Children's Hospital, The Ohio State University, Columbus, OH.
Department of Pediatrics, Medical College of Wisconsin, Milwaukee, WI.
Division of Neurointerventional Radiology, Boston Children's Hospital, Boston, MA.
Department of Plastic Surgery, Nationwide Children's Hospital, Columbus, OH.
Department of Pediatrics/Hematology, Lenox Hill Hospital, Northwell Health, Great Neck, NY.
Department of Radiology, Medical College of Wisconsin, Milwaukee, WI.
Division of Pediatric Dermatology, The Ann and Robert H. Lurie Children's Hospital of Chicago, Chicago, IL.
Department of Otolaryngology, Medical College of Wisconsin, Milwaukee, WI.
Departments of Radiology and Neurology, University of California, San Francisco, San Francisco, CA.
Department of Dermatology, Medical College of Wisconsin, Milwaukee, WI.

Department of Dermatology, Henry Ford Hospital, Detroit, MI.
Division of Dermatology, Departments of Medicine and Pediatrics, Loyola University Medical Center, Maywood, IL.
Department of Dermatology, Harvard Medical School, Boston, MA.
Department of Dermatology, Texas Children's Baylor, Houston, TX.
Department of Neurology, Medical College of Wisconsin, Milwaukee, WI.
Section of Pediatric Dermatology, Hospital for Sick Children, University of Toronto, Toronto, Ontario, Canada.
Department of Dermatology, University of Montreal, Montreal, Quebec, Canada.
Department of Dermatology and Pediatrics, Mayo Clinic, Rochester, MN.
Department of Neurosurgery, Cincinnati Children's Hospital Medical Center, Cincinnati, OH.
Department of Neurosurgery, Medical College of Wisconsin, Milwaukee, WI.
Department of Dermatology, University of California, San Francisco, San Francisco, CA.
Departments of Dermatology and Pediatrics, Medical College of Wisconsin, Milwaukee, WI. Electronic address: bdrolet@mcw.edu.

Dermatology

**Jahnke MN**. Vascular Lesions *Pediatr Ann* 2016; 45(8):e299-305. PMID: 27517358. Article Request Form

Vascular lesions in childhood are comprised of vascular tumors and vascular malformations. Vascular tumors encompass neoplasms of the vascular system, of which infantile hemangiomas (IHs) are the most common. Vascular malformations, on the other hand, consist of lesions due to anomalous development of the vascular system, including the capillary, venous, arterial, and lymphatic systems. Capillary malformations represent the most frequent type of vascular malformation. IHs and vascular malformations tend to follow relatively predictable growth patterns in that IHs grow then involute during early childhood, whereas vascular malformations tend to exhibit little change. Both vascular tumors and vascular malformations can demonstrate a wide range of severity and potential associated complications necessitating specialist intervention when appropriate. Evaluation and treatment of the most common types of vascular lesions are discussed in this article. [Pediatr Ann. 2016;45(8):e299-e305.].

Dermatology

Kannan S, **Mehta D**, and **Ozog D**. Scalp closures with pulley sutures reduce time and cost compared to traditional layered technique-a prospective, randomized, observer-blinded study *Dermatol Surg* 2016;PMID: 27598452. Full Text

*Department of Dermatology, Henry Ford Hospital, Detroit, Michigan; daggerDivision of Dermatology, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, California.

BACKGROUND: Reconstruction of postsurgical scalp defects can be difficult and time-consuming using a conventional bilayered technique. A specialized closure using a pulley suture can assist in closing wounds under high tension and can decrease time and cost for the surgeon. OBJECTIVE: To determine if closing scalp defects with a single-layered closure using pulley sutures would result in decreased time but equivalent scar cosmesis compared to bilayered closures. MATERIALS AND METHODS: A total of 21 patients with postsurgical scalp defects were randomized to a bilayered or a pulley group, and time was measured for each closure. Scar appearance was assessed using the Patient and Observer Scar Assessment Scale at 2 weeks, 2 months, and 6 months postsurgery. Before and after photographs were also assessed by a blinded dermatologist using the visual analog scale. RESULTS: Compared to a bilayered closure, the pulley technique resulted in significantly reduced closure time ($p < .001$). Even though patient overall scores at 2 weeks and observer total score at 6 months were superior in the pulley group, the visual analog scale scores were similar between the 2 groups. CONCLUSION: Scalp reconstructions using a single layer of pulley sutures result in time and cost reduction and similar scar appearance compared to bilayered closures.

Dermatology

Levoska MA, **Jansen R**, **Jacobsen G**, **Jahnke M**, Hekman D, and **Eide M**. Decreasing pediatric skin biopsy rates of lesions that were pigmented in a large health system *J Invest Dermatol* 2016; 136(5):S36-S36. PMID: Not assigned. Abstract

Dermatology
**Madigan LM**, and **Lim HW**. Tanning beds: Impact on health, and recent regulations *Clin Dermatol* 2016; 34(5):640-648. PMID: 27638445. Full Text

Department of Dermatology, Henry Ford Hospital, Detroit, MI.
Chairman and Clarence. S. Livingood Chair, Department of Dermatology, Henry Ford Hospital, Detroit, MI. Electronic address: hlim1@hfhs.org.

As the use of indoor tanning beds gained popularity in the decades after their appearance in the market in the early 1970s, concerns arose regarding their use. Clinical research has revealed an association between indoor tanning and several health risks, including the subsequent occurrence of melanoma and nonmelanoma skin cancers, the development of psychologic dependence, and a tendency toward other high-risk health behaviors. In the face of mounting evidence, legislation has been passed, which includes the restriction of access to tanning beds by minors in 42 states and the District of Columbia, and the recent reclassification by the Food and Drug Administration, which now categorizes tanning beds as class II devices and worthy of restrictions and oversight. Early evidence suggests that these labors are resulting in cultural change, although continued efforts are necessary to limit further exposure and better inform the public of the dangers associated with indoor tanning use.

Dermatology
**Madigan LM**, Treyger G, and **Kohen LL**. Compliance with serial dermoscopic monitoring: An academic perspective *J Am Acad Dermatol* 2016;PMID: 27665211. Full Text

Department of Dermatology, Henry Ford Hospital, Detroit, Michigan.
Michigan State University College of Osteopathic Medicine, East Lansing, Michigan.
Department of Dermatology, Henry Ford Hospital, Detroit, Michigan. Electronic address: lkohen1@hfhs.org.

BACKGROUND: For even seasoned practitioners, early melanomas can be difficult to distinguish from melanocytic nevi. Although serial digital dermoscopy is considered by many to be the gold standard for monitoring patients at high risk, poor compliance can seriously alter efficacy. In 2014, a concerning compliance rate of 25% was reported from a single, private clinic. Information is currently limited regarding the determinants of compliance and whether patients at high risk return at an acceptable rate. OBJECTIVE: We sought to determine the compliance rate within the pigmented lesions clinic at our academic institution and identify demographic variables that may influence adherence. METHODS: A retrospective review was conducted using 120 patient charts. RESULTS: An overall compliance rate of 87.5% was observed with 63.3% of patients returning within 1 month of the recommended interval. The most notable risk factor for noncompliance was patient age between 20 and 29 years. Factors promoting adherence include a personal history of melanoma, greater than 5 serially monitored nevi, and a personal history of atypical nevi. LIMITATIONS: The external validity is limited and the sample size is small. CONCLUSION: These findings contradict concerns that adherence to serial monitoring is unacceptably poor and demonstrate that compliance is highest for patients with the greatest inherent risk.

Dermatology
**Modh A**, **McHargue CA**, **Lim H**, and **Siddiqui F**. Single-fraction radiation therapy provides highly effective palliation for cutaneous t-cell lymphoma *Int J Radiat Oncol Biol Phys* 2016; 96(2s):E492. PMID: 27674835. Full Text

Henry Ford Health System, Detroit, MI.

Dermatology
Paul C, **Gold LS**, Cambazard F, Kalb RE, Lowson D, Moller AH, and Griffiths CEM. More rapid improvement in quality of life with fixed-combination calcipotriene plus betamethasone dipropionate aerosol foam vs. topical suspension (PSO-ABLE study in patients with psoriasis vulgaris) *Br J Dermatol* 2016; 175:213-214. PMID: Not assigned. Abstract

Dermatology
**Porto DA**, **Powers M**, **Patel D**, **Chaffins M**, and **Shwayder TA**. Lymphoplasmacytic plaque in children: A demonstrative case of an emerging clinicopathologic entity *Pediatr Dermatol* 2016;PMID: 27573871. Full Text

Department of Dermatology, Henry Ford Health System, Detroit, MI.

Lymphoplasmacytic plaque in children is a rare but increasingly reported clinicopathologic entity characterized by extratruncal erythematous solitary plaques, most often in children and Caucasian girls, that are thought to be a reactive or pseudolymphomatous process. We report a demonstrative case of lymphoplasmacytic plaque in a 3-year-old girl and discuss the clinical and pathologic experience with this entity.

Dermatology
**Pritchett EN**, Doyle A, Shaver CM, Miller B, Abdelmalek M, Cusack CA, Malat GE, and Chung CL. Nonmelanoma skin cancer in nonwhite organ transplant recipients *JAMA Dermatol* 2016;PMID: 27653769. Full Text

Department of Dermatology, Henry Ford Hospital, Detroit, Michigan.
Department of Internal Medicine, Drexel University, Philadelphia, Pennsylvania.
Department of Dermatology, Drexel University, Philadelphia, Pennsylvania.
Department of Surgery, Drexel University, Philadelphia, Pennsylvania.

Importance: Organ transplant recipients have a higher incidence of skin cancer. This risk is magnified over time and with continued exposure to immunosuppression. Skin cancer in nonwhite patients is associated with greater morbidity and mortality owing to diagnosis at a more advanced stage, which suggests that nonwhite organ transplant recipients are at even higher risk. Objective: To describe demographic and clinical factors and the incidence of skin cancer in nonwhite organ transplant recipients. Design, Setting, and Participants: We performed a retrospective medical record review of patients who were organ transplant recipients (154 were white and 259 nonwhite [black, Asian, Hispanic, Pacific Islander]) seen from November 1, 2011, to April 18, 2016 at an academic referral center. Main Outcomes and Measures: Variables were analyzed and compared between racial groups, including sex, age, race/ethnicity, Fitzpatrick type, type and location of skin cancer, type of organ transplanted, time to diagnosis of skin cancer after transplantation, and history of condyloma acuminata and/or verruca vulgaris. Results: Most of the 413 patients (62.7%) evaluated were nonwhite organ transplant recipients; 264 were men, and 149 were women. Their mean (SD) age was 60.09 (13.59) years. Nineteen skin cancers were identified in 15 patients (5.8%) representing 3 racial/ethnic groups: black (6 patients), Asian (5), and Hispanic (4). All squamous cell carcinomas in blacks were diagnosed in the in situ stage, located on sun-protected sites, and occurred in patients whose lesions tested positive for human papilloma virus (HPV) and/or who endorsed a history of condyloma acuminata or verruca vulgaris. Most skin cancers in Asians were located on sun-exposed areas and occurred in individuals who emigrated from equatorial locations. Conclusions and Relevance: Nonwhite organ transplant recipients are at risk for developing skin cancer posttransplantation. Follow-up in a specialized transplant dermatology center and baseline total-body skin examination should be part of posttransplantation care in all organ transplant recipients, including nonwhite patients. A thorough inspection of the groin and genitalia is imperative in black organ transplant recipients. History of HPV infection, particularly in black organ transplant recipients, and sun exposure/emigration history in Asian organ transplant recipients should be documented. Vigilant photoprotection may be of lesser importance in the prevention of skin cancer in black organ transplant recipients. Risk factors for nonwhite organ transplant recipients differ between races/ethnicities and warrant further study in efforts to better counsel and prevent skin cancer in these patients.

Dermatology
**Riyaz F**, and **Ozog D**. A review of confocal microscopy for inflammatory skin disorders *Lasers Surg Med* 2016; 48:34-34. PMID: Not assigned. Abstract

Dermatology
**Wu D**, **Bi X**, **Qu L**, **Han L**, **Yin C**, **Deng J**, Dong Z, **Mi QS**, and **Zhou L**. miRNA miR-17-92 cluster is differentially regulated in the imiqumod-treated skin but is not required for imiqumod-induced psoriasis-like dermatitis in mice *Exp Dermatol* 2016;PMID: 27579777. Full Text

Henry Ford Immunology Program, Henry Ford Health System, Detroit, MI.
Department of Dermatology, Henry Ford Health System, Detroit, MI.
Department of Dermatology, Guangdong provincial Hospital of Chinese Medicine, Guanghzou, P. R. China, 510120.
Department of Cellular Biology and Anatomy, Augusta University, Augusta, GA.
Department of Immunology and Microbiology, Wayne State University, Detroit, MI, USA.
Department of Internal Medicine, Henry Ford Health System, Detroit, MI.

Dermatology
**Zhang X**, Gu J, **Zhou L**, and **Mi QS**. TIM-4 is expressed on invariant NKT cells but dispensable for their development and function *Oncotarget* 2016;PMID: 27662666. Full Text

Henry Ford Immunology Program, Henry Ford Health System, Detroit, MI, USA.
Department of Dermatology, Henry Ford Health System, Detroit, MI, USA.
Department of Dermatology, Changhai Hospital, Second Military Medical University, Shanghai, China.
Department of Internal Medicine, Henry Ford Health System, Detroit, MI, USA.
Department of Immunology and Microbiology, Wayne State University School of Medicine, MI, USA.

T cell immunoglobulin and mucin-4 (TIM-4), mainly expressed on antigen presenting cells, plays a versatile role in immunoregulation. CD1d-restricted invariant natural killer T (iNKT) cells are potent cells involved in the diverse immune responses. It was recently reported that recombinant TIM-4 (rTIM-4) alone enhanced cytokine production in NKT hybridoma, DN32.D3 cells. Hence, we hypothesized that TIM-4 might regulate iNKT cell biology, especially their function of cytokine secretion. For the first time, we identified that TIM-4 was expressed in thymus iNKT cells, and its expression increased upon iNKT cell migration to the secondary lymphoid organs, especially in lymph nodes. Using TIM-4-deficient mice, we found that lack of TIM-4 did not disturb iNKT cell development, maturation, peripheral homeostasis and cytokine secretion. Moreover, TIM-4 deficiency did not alter the polarization of iNKT sublineages, including NKT1, NKT2 and NKT17. Finally, the mixed bone marrow transfer experiments further confirmed normal iNKT cell development and function from TIM-4-deficient bone marrow. In conclusion, our data suggest that TIM-4 is expressed on iNKT cells but dispensable for their development and function.

Diagnostic Radiology

**Spain J**, and **Rheinboldt M**. MDCT of pelvic inflammatory disease: a review of the pathophysiology, gamut of imaging findings, and treatment *Emerg Radiol* 2016;PMID: 27646971. Full Text

Department of Diagnostic Radiology, Division of Emergency Radiology, Henry Ford Hospital, Detroit, MI, USA.
Department of Diagnostic Radiology, Division of Emergency Radiology, Henry Ford Hospital, Detroit, MI, USA.
matthewr@rad.hfh.edu.

Representing an ascending, sexually spread pyogenic infection of the female genital tract, pelvic inflammatory disease (PID) is a commonly encountered cause for emergency visits and hospitalizations among young and adult female patients. Though gynecologic evaluation and sonography constitute the mainstay of diagnosis, multidetector CT imaging of the abdomen and pelvis is not uncommonly performed, often as the initial imaging modality, due to the frequently vague and indeterminate clinical presentation. As such, knowledge and attenuation to the often subtle early imaging features of PID afford the radiologist a critical chance to direct and expedite appropriate pathways of patient care, minimizing the risk for secondary complications, including infertility, ectopic pregnancy, and enteric adhesions. In this paper, we will review the pathophysiology, clinical presentation, early and late imaging features of PID as well as potential secondary complications and treatment options. Additionally, we will discuss published data metrics on CT performance regarding sensitivity and specificity for diagnosis as well as potential imaging differential diagnostic considerations.

Emergency Medicine

Arbit B, Sharma S, Clopton P, Mueller C, **Nowak R**, **McCord J**, Mockel M, Filippatos G, Daniels L, Di Somma S, and Maisel A. Influence of gender and copeptin levels on clinical outcomes in patients with acute heart failure *J Card Fail* 2016; 22:S29. PMID: Not assigned. Abstract

B. Arbit, UCSD, San Diego, United States

Background: Copeptin is a novel biomarker derived from the C-terminal fragment of arginine vasopressin precursor (AVP), also known as antidiuretic hormone. Copeptin is released in response to the same factors as AVP and is more readily isolated and measured than AVP. Some studies have suggested that it may be superior to BNP in predicting death in patients with acute heart failure (AHF). To our knowledge, we are presenting the first study of gender-related differences of copeptin in prediction of mortality, readmissions, and emergency department visits. Methods: Current anaylysis used data from the Biomarkers in Acute Heart Failure (BACH) trial. 1641 patients presenting to the ED with acute dyspnea were prospectively enrolled in the study. Patients with valid measurements of copeptin and sodium were included in the current analysis. Patients were followed for up to 90 days after initial evaluation for the end points of all-cause mortality, HF-related readmissions, and HF-related ED visits. For the prognostic evaluation of copeptin, we divided the cohort by gender and by copeptin quartiles (specific to each gender). We then performed Cox regression for the combined end-point of all-cause mortality, HFrelated readmissions, and HF-related ED visits. Results: 1641 subjects were enrolled, of which 568 were diagnosed with AHF. Of these, 557 patients (347 male, 210 female) had valid measurements of sodium and copeptin. There were 64 deaths, 149 death- or HFrelated readmission events, and 172 death- or HF-related readmission or HF related ED visit events. Patients with copeptin levels in the highest quartile (>61.4 pmol/L for men, >54.1 pmol/L for women) had significantly increased rates of the

combined end-point, $\chi 2 = 19.4$, $P < .0001$. Interestingly, rates were very similar among men and women above the 75th percentile, but below, women had significantly less events. Conclusions: This is the first study of gender-related differences of copeptin in prediction of clinical endpoints. Accounting for gender, copeptin may be a valuable tool in risk stratification of patients with AHF. (Figure Presented).

Emergency Medicine
**Goodwin M**, **Ito K**, **Gupta AH**, and **Rivers EP**. Protocolized care for early shock resuscitation *Curr Opin Crit Care* 2016; 22(5):416-423. PMID: 27583584. Full Text

aDepartment of SurgerybDepartment of Emergency Medicine, Henry Ford Hospital, Wayne State University, Detroit, Michigan, USA.

PURPOSE OF REVIEW: Protocolized care for early shock resuscitation (PCESR) has been intensely examined over the last decade. The purpose is to review the pathophysiologic basis, historical origin, clinical applications, components and outcome implications of PCESR. RECENT FINDINGS: PCESR is a multifaceted systems-based approach that includes early detection of high-risk patients and interventions to rapidly reverse hemodynamic perturbations that result in global or regional tissue hypoxia. It has been applied to perioperative surgery, trauma, cardiology (heart failure and acute myocardial infarction), pulmonary embolus, cardiac arrest, undifferentiated shock, postoperative cardiac surgery and pediatric septic shock. When this approach is used for adult septic shock, in particular, it is associated with a mortality reduction from 46.5 to less than 30% over the last 2 decades. Challenges to these findings are seen when repeated trials contain enrollment, diagnostic and therapeutic methodological differences. SUMMARY: PCESR is more than a hemodynamic optimization procedure. It also provides an educational framework for the less experienced and objective recognition of clinical improvement or deterioration. It further minimizes practices' variation and provides objective measures that can be audited, evaluated and amendable to continuous quality improvement. As a result, morbidity and mortality are improved.

Emergency Medicine
Linnstaedt SD, Hu J, Liu AY, Soward AC, Bollen KA, Wang HE, Hendry PL, **Zimny E**, **Lewandowski C**, Velilla MA, Damiron K, Pearson C, Domeier R, Kaushik S, Feldman J, Rosenberg M, Jones J, Swor R, Rathlev N, and McLean SA. Methodology of AA CRASH: a prospective observational study evaluating the incidence and pathogenesis of adverse post-traumatic sequelae in African-Americans experiencing motor vehicle collision *BMJ Open* 2016; 6(9):e012222. PMID: 27601501. Full Text

TRYUMPH Research Program Department of Anesthesiology, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA.
Department of Psychology and Neuroscience, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA Department of Sociology, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA.
Department of Emergency Medicine, University of Alabama at Birmingham, Birmingham, Alabama, USA.
Department of Emergency Medicine, University of Florida College of Medicine, Jacksonville, Florida, USA.
Department of Emergency Medicine, Henry Ford Hospital, Detroit, Michigan, USA.
Department of Emergency Medicine, Sinai Grace Hospital, Detroit, Michigan, USA.
Department of Emergency Medicine, Albert Einstein Medical Center, Philadelphia, Pennsylvania, USA.
Department of Emergency Medicine, Detroit Receiving, Detroit, Michigan, USA.
Department of Emergency Medicine, St Joseph Mercy Health System, Ypsilanti, Michigan, USA.
Department of Emergency Medicine, MedStar Washington Hospital Center, Washington District of Columbia, USA.
Department of Emergency Medicine, Boston Medical Center, Boston, Massachusetts, USA.
Department of Emergency Medicine, St Joseph's Regional Medical Center, Paterson, New Jersey, USA.
Department of Emergency Medicine, Spectrum Health Butterworth Campus, Grand Rapids, Michigan, USA.
Department of Emergency Medicine, William Beaumont Hospital, Royal Oak, Massachusetts, USA.
Department of Emergency Medicine, Baystate Health, Springfield, Massachusetts, USA.
TRYUMPH Research Program Department of Anesthesiology, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA Department of Emergency Medicine, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA.

INTRODUCTION: A motor vehicle collision (MVC) is one of the most common life-threatening events experienced by individuals living in the USA. While most individuals recover following MVC, a significant proportion of individuals develop adverse post-traumatic sequelae such as post-traumatic stress disorder or persistent musculoskeletal pain. Adverse post-traumatic sequelae are common, morbid and costly public health problems in the USA and other industrialised countries. The pathogenesis of these disorders following MVC remains poorly understood. In the USA, available data suggest that African-Americans experience an increased burden of adverse post-traumatic sequelae

after MVC compared to European Americans, but to date no studies examining the pathogenesis of these disorders among African-Americans experiencing MVC have been performed. METHODS AND ANALYSIS: The African-American CRASH (AA CRASH) study is an NIH-funded, multicentre, prospective study that enrols African-Americans (n=900) who present to the emergency department (ED) within 24 hours of MVC. Participants are enrolled at 13 ED sites in the USA. Individuals who are admitted to the hospital or who report a fracture or tissue injury are excluded. Participants complete a detailed ED interview that includes an assessment of crash history, current post-traumatic symptoms and health status prior to the MVC. Blood samples are also collected in the ED using PAXgene DNA and PAXgene RNA tubes. Serial mixed-mode assessments 6 weeks, 6 months and 1 year after MVC include an assessment of adverse sequelae, general health status and health service utilisation. The results from this study will provide insights into the incidence and pathogenesis of persistent pain and other post-traumatic sequelae in African-Americans experiencing MVC. ETHICS AND DISSEMINATION: AA CRASH has ethics approval in the USA, and the results will be published in a peer-reviewed journal.

Emergency Medicine

Maisel AS, Wettersten N, van Veldhuisen DJ, Mueller C, Filippatos G, **Nowak R**, Hogan C, Kontos MC, Cannon CM, Muller GA, Birkhahn R, Clopton P, Taub P, Vilke GM, McDonald K, Mahon N, Nunez J, Briguori C, Passino C, and Murray PT. Neutrophil gelatinase-associated lipocalin for acute kidney injury during acute heart failure hospitalizations: The AKINESIS study *J Am Coll Cardiol* 2016; 68(13):1420-1431. PMID: 27659464. Full Text

Division of Cardiovascular Medicine, Veterans Affairs Medical Center, San Diego, La Jolla, California; Division of Cardiovascular Medicine, University of California, San Diego, La Jolla, California. Electronic address: amaisel@ucsd.edu.
Division of Cardiovascular Medicine, University of California, San Diego, La Jolla, California.
Department of Cardiology, University Medical Center Groningen, University of Groningen, Groningen, the Netherlands.
Department of Cardiology, University Hospital Basel, Basel, Switzerland.
Department of Cardiology, Athens University Hospital Attikon, University of Athens, Athens, Greece.
Department of Emergency Medicine, Henry Ford Hospital System, Detroit, Michigan.
Division of Emergency Medicine and Acute Care Surgical Services, VCU Medical Center, Virginia Commonwealth University, Richmond, Virginia.
Division of Cardiology, VCU Medical Center, Virginia Commonwealth University, Richmond, Virginia.
Department of Emergency Medicine, University of Kansas Hospital, Kansas City, Kansas.
Department of Nephrology and Rheumatology, University Medical Center Gottingen, University of Gottingen, Gottingen, Germany.
Department of Emergency Medicine, New York Methodist, Brooklyn, New York.
Division of Cardiovascular Medicine, Veterans Affairs Medical Center, San Diego, La Jolla, California.
Departement of Emergency Medicine, University of California, San Diego, La Jolla, California.
Department of Cardiology, St. Vincent's University Hospital, Dublin, Ireland; Department of Nephrology, Mater Misericordaie University Hospital, University College Dublin, Dublin, Ireland.
Department of Nephrology, Mater Misericordaie University Hospital, University College Dublin, Dublin, Ireland; Department of Cardiology, Mater Misericordaie University Hospital, Dublin, Ireland.
Department of Cardiology, Hospital Clinico Universitario Valencia, University of Valencia, Valencia, Spain.
Department of Cardiology, Clinica Mediterranea, Naples, Italy.
Department of Cardiology and Cardiovascular Medicine, Fondazione Gabriele Monasterio, Pisa, Italy.
Department of Nephrology, Mater Misericordaie University Hospital, University College Dublin, Dublin, Ireland.

BACKGROUND: Worsening renal function (WRF) often occurs during acute heart failure (AHF) and can portend adverse outcomes; therefore, early identification may help mitigate risk. Neutrophil gelatinase-associated lipocalin (NGAL) is a novel renal biomarker that may predict WRF in certain disorders, but its value in AHF is unknown. OBJECTIVES: This study sought to determine whether NGAL is superior to creatinine for prediction and/or prognosis of WRF in hospitalized patients with AHF treated with intravenous diuretic agents. METHODS: This was a multicenter, prospective cohort study enrolling patients presenting with AHF requiring intravenous diuretic agents. The primary outcome was whether plasma NGAL could predict the development of WRF, defined as a sustained increase in plasma creatinine of 0.5 mg/dl or >/=50% above first value or initiation of acute renal-replacement therapy, within the first 5 days of hospitalization. The main secondary outcome was in-hospital adverse events. RESULTS: We enrolled 927 subjects (mean age, 68.5 years; 62% men). The primary outcome occurred in 72 subjects (7.8%). Peak NGAL was more predictive than the first NGAL, but neither added significant diagnostic utility over the first creatinine (areas under the curve: 0.656, 0.647, and 0.652, respectively). There were 235 adverse events in 144 subjects. The first NGAL was a better predictor than peak NGAL, but similar to the first creatinine (areas under the curve: 0.691, 0.653, and 0.686, respectively). In a post hoc analysis of subjects with an estimated glomerular filtration rate <60 ml/min/1.73 m(2), a first NGAL <150 ng/ml indicated a low likelihood of adverse events.

CONCLUSIONS: Plasma NGAL was not superior to creatinine for the prediction of WRF or adverse in-hospital outcomes. The use of plasma NGAL to diagnose acute kidney injury in AHF cannot be recommended at this time. (Acute Kidney Injury Neutrophil Gelatinase-Associated Lipocalin [N-GAL] Evaluation of Symptomatic Heart Failure Study [AKINESIS]; NCT01291836).

Emergency Medicine

**Miller JB**, **Lewandowski C**, Wira CR, **Taylor A**, **Burmeister C**, and Welch R. Volume of plasma expansion and functional outcomes in stroke *Neurocrit Care* 2016;PMID: 27629275. Full Text

Department of Emergency Medicine, Henry Ford Hospital, 2799 W Grand Blvd, Detroit, MI, 48202, USA. jmiller6@hfhs.org.
Department of Internal Medicine, Henry Ford Hospital, Detroit, MI, USA. jmiller6@hfhs.org.
Wayne State University, Detroit, MI, USA. jmiller6@hfhs.org.
Department of Emergency Medicine, Henry Ford Hospital, 2799 W Grand Blvd, Detroit, MI, 48202, USA.
Wayne State University, Detroit, MI, USA.
Department of Emergency Medicine, Yale University School of Medicine, New Haven, CT, USA.
Department of Public Health Sciences, Henry Ford Hospital, Detroit, MI, USA.
Department of Emergency Medicine, Wayne State University, Detroit, MI, USA.

BACKGROUND: Plasma expansion in acute ischemic stroke has potential to improve cerebral perfusion, but the long-term effects on functional outcome are mixed in prior trials. The goal of this study was to evaluate how the magnitude of plasma expansion affects neurological recovery in acute stroke. METHODS: This was a secondary analysis of data from the Albumin in Acute Stroke Part 2 trial investigating the relationship between the magnitude of overall intravenous volume infusion (crystalloid and colloid) to clinical outcome. The data were inclusive of 841 patients with a mean age of 64 years and a median National Institutes of Health Stroke Scale (NIHSS) of 11. In a multivariable-adjusted logistic regression model, this analysis tested the volume of plasma expansion over the first 48 h of hospitalization as a predictor of favorable outcome, defined as either a modified Rankin Scale score of 0 or 1 or a NIHSS score of 0 or 1 at 90 days. This model included all study patients, irrespective of albumin or isotonic saline treatment. RESULTS: Patients that received higher volumes of plasma expansion more frequently had large vessel ischemic stroke and higher NIHSS scores. The multivariable-adjusted model revealed that there was decreased odds of a favorable outcome for every 250 ml additional volume plasma expansion over the first 48 h (OR 0.91, 95 % CI, 0.88-0.94). CONCLUSIONS: The present study demonstrates an association between greater volume of plasma expansion and worse neurological recovery.

Emergency Medicine

**Miller JB**, Merck LH, Wira CR, Meurer WJ, Schrock JW, Nomura JT, Siket MS, Madsen TE, Wright DW, Panagos PD, and **Lewandowski C**. The advanced reperfusion era: Implications for emergency systems of ischemic stroke care *Ann Emerg Med* 2016;PMID: 27600649. Full Text

Department of Emergency Medicine, Henry Ford Hospital and Wayne State University, Detroit, MI; Department of Internal Medicine, Henry Ford Hospital and Wayne State University, Detroit, MI. Electronic address: jmiller6@hfhs.org.
Department of Emergency Medicine and the Department of Diagnostic Imaging, The Warren Alpert Medical School of Brown University, Providence, RI.
Department of Emergency Medicine and the Department of Neurology, Yale School of Medicine, New Haven, CT.
Department of Emergency Medicine and the Department of Neurology, University of Michigan, Ann Arbor, MI.
Department of Emergency Medicine, MetroHealth Medical Center, Case Western Reserve University, Cleveland, OH.
Department of Emergency Medicine and the Department of Neurosciences, Christiana Care Health System, Newark, DE.
Department of Emergency Medicine, The Warren Alpert Medical School of Brown University, Providence, RI.
Department of Emergency Medicine, Emory University School of Medicine and Grady Memorial Hospital, Atlanta, GA.
Department of Emergency Medicine and the Department of Neurology, Washington University, St Louis, MO.
Department of Emergency Medicine, Henry Ford Hospital and Wayne State University, Detroit, MI.

Large vessel ischemic stroke is a leading cause of morbidity and mortality throughout the world. Recent advances in endovascular stroke treatment are changing the treatment paradigm for these patients. This concepts article summarizes the time-dependent nature of stroke care and evaluates the recent advancements in endovascular treatment. These advancements have significant implications for out-of-hospital, hospital, and regional systems of stroke care. Emergency medicine clinicians have a central role in implementing these systems that will ensure timely treatment of patients and selection of those who may benefit from endovascular care.

Emergency Medicine

**Nowak RM**, Reed BP, Nanayakkara P, DiSomma S, **Moyer ML**, Millis S, and Levy P. Presenting hemodynamic phenotypes in ED patients with confirmed sepsis *Am J Emerg Med* 2016;PMID: 27613360. Full Text

Department of Emergency Medicine, Henry Ford Health System, Detroit, MI, USA. Electronic address: rnowak1@hfhs.org.
Department of Biostatistics, Wayne State University, Detroit, MI, USA. Electronic address: bpreed@med.wayne.edu.
Section of Acute Medicine, Department of Internal Medicine, VU Medical Center, Amsterdam, Netherlands. Electronic address: P.Nanayakkara@vumc.nl.
Department of Medical-Surgery Sciences and Translational Medicine, University Sapienza, Rome, Italy. Electronic address: Salvatore.Disomma@uniroma1.it.
Department of Emergency Medicine, Henry Ford Health System, Detroit, MI, USA. Electronic address: mmoyer1@hfhs.org.
Department of Biostatistics, Wayne State University, Detroit, MI, USA. Electronic address: smillis@med.wayne.edu.
Departments of Emergency Medicine and Physiology and Cardiovascular Research Institute, Wayne State University, Detroit, MI, USA. Electronic address: plevy@med.wayne.edu.

OBJECTIVES: To derive distinct clusters of septic emergency department (ED) patients based on their presenting noninvasive hemodynamic (HD) measurements and to determine if any clinical parameters could identify these groups. METHODS: Prospective, observational, convenience study of individuals with confirmed systemic infection. Presenting, pretreatment noninvasive HD parameters were compiled using Nexfin (Bmeye/Edwards LifeSciences) from 127 cases. Based on normalized parameters, k-means clustering was performed to identify a set of variables providing the greatest level of intercluster discrimination and intracluster cohesion. RESULTS: Our best HD clustering model used 2 parameters: the cardiac index (CI [L/min per square meter]) and systemic vascular resistance index (SVRI [dynes.s/cm5 per square meter]). Using this model, 3 different patient clusters were identified. Cluster 1 had high CI with normal SVRI (CI, 4.03 +/- 0.61; SVRI, 1655.20 +/- 348.08); cluster 2 low CI with increased vascular tone (CI, 2.50 +/- 0.50; SVRI, 2600.83 +/- 576.81); and cluster 3 very low CI with markedly elevated SVRI (CI, 1.37 +/- 0.81; SVRI, 5951.49 +/- 1480.16). Cluster 1 patients had the lowest 30-day overall mortality. Among clinically relevant variables available during the initial patient evaluation in the ED age, heart rate and temperature were significantly different across the 3 clusters. CONCLUSIONS: Emergency department patients with confirmed sepsis had 3 distinct cluster groupings based on their presenting noninvasively derived CI and SVRI. Further clinical studies evaluating the effect of early cluster-specific therapeutic interventions are needed to determine if there are outcome benefits of ED HD phenotyping in these patients.

Endocrinology

Khan AA, Hanley DA, Rizzoli R, Bollerslev J, Young JE, Rejnmark L, Thakker R, D'Amour P, Paul T, Van Uum S, Shrayyef MZ, Goltzman D, Kaiser S, Cusano NE, Bouillon R, Mosekilde L, Kung AW, **Rao SD**, Bhadada SK, Clarke BL, Liu J, Duh Q, Lewiecki EM, Bandeira F, Eastell R, Marcocci C, Silverberg SJ, Udelsman R, Davison KS, Potts JT, Jr., Brandi ML, and Bilezikian JP. Primary hyperparathyroidism: review and recommendations on evaluation, diagnosis, and management. A Canadian and international consensus *Osteoporos Int* 2016;PMID: 27613721. Full Text

McMaster University, Hamilton, Canada. Aliya@mcmaster.ca.
Bone Research and Education Center, 223-3075 Hospital Gate, Oakville, ON, Canada. Aliya@mcmaster.ca.
University of Calgary, Calgary, Canada.
Division of Bone Diseases, Geneva University Hospitals and Faculty of Medicine, Geneva, Switzerland.
University of Oslo, Oslo, Norway.
McMaster University, Hamilton, Canada.
Department of Endocrinology and Internal Medicine, Aarhus University Hospital, Aarhus, Denmark.
University of Oxford, Oxford, UK.
CHUM, Montreal, Canada.
Western University, London, ON, Canada.
Division of Endocrinology, University of Toronto, Mississauga, ON, Canada.
McGill University, Montreal, Canada.
Dalhousie University, Halifax, Canada.
Columbia University College of Physicians and Surgeons, New York, NY, USA.
KU, Leuven, Belgium.
University of Aarhus, Aarhus, Denmark.
University of Hong Kong, Hong Kong, China.
Henry Ford Hospital, Detroit, MI, USA.
Postgraduate Institute of Medical Education and Research, Chandigarth, India.

Mayo Clinic, Rochester, MN, USA.
Rui-Jin Hospital, Shanghai Jiao-Tong University School of Medicine, Shanghai, China.
University of California, San Francisco, CA, USA.
New Mexico Clinical Research and Osteoporosis Center, University of New Mexico School of Medicine, Albuquerque, NM, USA.
Division of Endocrinology, Diabetes and Metabolic Bone Diseases, Agamenon Magalhaes Hospital, Brazilian Ministry of Health, University of Pernambuco Medical School, Recife, Brazil.
Department of Human Metabolism, University of Sheffield, Sheffield, UK.
Department for Clinical and Experimental Medicine, University of Pisa, Endocrine Unit 2, University Hospital of Pisa, Pisa, Italy.
Division of Endocrinology, Columbia University College of Physicians and Surgeons, New York, NY, USA.
Department of Surgery, Yale University School of Medicine, New Haven, CT, USA.
University of Victoria, Victoria, BC, Canada.
Massachusetts General Hospital, Harvard University, Boston, MA, USA.
University of Florence, Florence, Italy.

The purpose of this review is to assess the most recent evidence in the management of primary hyperparathyroidism (PHPT) and provide updated recommendations for its evaluation, diagnosis and treatment. A Medline search of "Hyperparathyroidism. Primary" was conducted and the literature with the highest levels of evidence were reviewed and used to formulate recommendations. PHPT is a common endocrine disorder usually discovered by routine biochemical screening. PHPT is defined as hypercalcemia with increased or inappropriately normal plasma parathyroid hormone (PTH). It is most commonly seen after the age of 50 years, with women predominating by three to fourfold. In countries with routine multichannel screening, PHPT is identified earlier and may be asymptomatic. Where biochemical testing is not routine, PHPT is more likely to present with skeletal complications, or nephrolithiasis. Parathyroidectomy (PTx) is indicated for those with symptomatic disease. For asymptomatic patients, recent guidelines have recommended criteria for surgery, however PTx can also be considered in those who do not meet criteria, and prefer surgery. Non-surgical therapies are available when surgery is not appropriate. This review presents the current state of the art in the diagnosis and management of PHPT and updates the Canadian Position paper on PHPT. An overview of the impact of PHPT on the skeleton and other target organs is presented with international consensus. Differences in the international presentation of this condition are also summarized.

Gastroenterology
Elmunzer BJ, and **Piraka CR**. EUS-guided methylene blue injection to facilitate pancreatic duct access after unsuccessful ERCP *Gastroenterology* 2016;PMID: 27639800. Full Text

Division of Gastroenterology & Hepatology, Medical University of South Carolina, Charleston, SC, USA. Electronic address: Elmunzer@musc.edu.
Division of Gastroenterology, Henry Ford Health System, Detroit, MI, USA.

Gastroenterology
Fischer M, Kao D, Kelly C, Kuchipudi A, **Jafri SM**, **Blumenkehl M**, Rex D, Mellow M, **Kaur N**, Sokol H, Cook G, Hamilton MJ, Phelps E, Sipe B, Xu H, and Allegretti JR. Fecal microbiota transplantation is safe and efficacious for recurrent or refractory clostridium difficile infection in patients with inflammatory bowel disease *Inflamm Bowel Dis* 2016; 22(10):2402-2409. PMID: 27580384. Full Text

*Indiana University, Indianapolis, Indiana; daggerUniversity of Alberta, Edmonton, Alberta, Canada; double daggerLifespan Women's Medicine Collaborative and the Alpert Medical School of Brown University, Providence, Rhode Island; section signHenry Ford Hospital, Detroit, Michigan; ||Integris Digestive Health Center, Oklahoma City, Oklahoma; paragraph signHospital Saint-Antoine, Paris, France; **Brigham and Women's Hospital, Boston Massachusetts; and daggerdaggerCommunity Hospital, Anderson, Indiana.

BACKGROUND: New treatments are needed as Clostridium difficile infection (CDI) is becoming increasingly formidable. Fecal microbiota transplantation (FMT) has a 90% success rate in the treatment of recurrent CDI. However, evidence regarding its safety, efficacy, and effect on disease activity in patients with inflammatory bowel disease (IBD) is lacking. METHODS: This cohort study used data from 8 national and international academic centers. Patients with established IBD who underwent FMT for recurrent CDI were followed for a minimum of 3 months. The primary outcome was CDI recurrence at 3 months after FMT. The secondary outcomes were (1) IBD activity and severity at 3 months based on the judgment of the treating physician, endoscopic findings, and clinical disease activity scores; and (2) safety. RESULTS: Sixty-seven patients were included in the analysis. Thirty-five (52%) had Crohn's disease, 31 (46%) ulcerative colitis, and one indeterminate colitis with 43 (64%) patients on an

immunosuppressive agent at the time of FMT. The initial FMT was successful in 53 (79%) patients. After the FMT, IBD disease activity was reported as improved in 25 (37%), no change in 20 (30%), and worse in 9 (13%) patients. Serious adverse events included colectomy (1.4%), hospitalization for CDI (2.9%), hospitalization for IBD flare (2.9%), small bowel obstruction (1.4%), CMV colitis (1.4%), and pancreatitis (1.4%). DISCUSSION: The overall CDI cure rates were high, with a large percentage of patients experiencing clinical improvement of their IBD after FMT. A minority of patients developed an IBD flare. No severe adverse events directly attributable to FMT were found in this largest reported series of recurrent or refractory CDI patients with concurrent IBD.

Gastroenterology
**Jinjuvadia R**, Antaki F, Lohia P, and Liangpunsakul S. The association between nonalcoholic fatty liver disease and metabolic abnormalities in the United States population *J Clin Gastroenterol* 2016;PMID: 27580477. Full Text

*Department of Internal Medicine, Division of Gastroenterology and Hepatology, Henry Ford Hospital daggerJohn D. Dingell VA Medical Center double daggerDepartment of Medicine, Division of Gastroenterology, Wayne State University section signDetroit Medical Center, Detroit, MI parallelDepartment of Medicine, Division of Gastroenterology and Hepatology, Indiana University Medical Center paragraph signRoudebush Veterans Administration Medical Center, Indianapolis, IN.

BACKGROUND: Prevalence of nonalcoholic fatty liver disease (NAFLD) and rate of advanced fibrosis among individuals with metabolic syndrome (MetS) and its individual metabolic abnormalities needs better understanding in the United States population. We aim to study these by using a large United States population database, the Third National Health and Nutrition Examination Survey (NHANES III). METHODS: A total of 11,674 individuals were included in our study cohort. NAFLD was defined as presence of moderate to severe hepatic steatosis on liver ultrasound in absence of viral hepatitis, significant alcohol use, elevated transferrin level, and medication use leading to hepatic steatosis. Advanced fibrosis among those with NAFLD was determined using noninvasive method, the NAFLD fibrosis score. MetS was defined based on the National Cholesterol Education Program Adult Treatment Panel III definition. RESULTS: The prevalence of NAFLD among included study cohort was 18.2% (95% confidence interval, 16.5-19.9). Individuals with metabolic abnormalities demonstrated higher prevalence (MetS, 43.2%; increased waist circumference, 31.2%; impaired fasting glucose/diabetes, 41.2%; high triglyceride level, 34.7%; low high-density lipoprotein, 27.8%; high blood pressure, 29.2%). The individuals with MetS had significantly higher NAFLD prevalence compared with controls (adjusted odds ratio, 11.5; 95% confidence interval, 8.9-14.7). The severity of hepatic steatosis was also noted to increase with higher number of metabolic abnormalities. Among individual metabolic abnormalities, increased waist circumference, impaired fasting glucose/diabetes, high triglyceride, and low high-density lipoprotein levels were found to be independently associated with NAFLD. Individuals with impaired fasting glucose/diabetes and those with 5 metabolic abnormalities had higher rate of advanced fibrosis (18.6% and 30.3%, respectively). Prevalence of NAFLD among individuals without any metabolic abnormality was 6.1%. CONCLUSION: Prevalence of NAFLD and rate of advanced fibrosis are significantly high among individuals with metabolic abnormalities.

Gastroenterology
Spradling PR, Xing J, **Rupp LB**, Moorman AC, **Gordon SC**, Teshale ET, **Lu M**, Boscarino JA, Schmidt MA, Trinacty CM, and Holmberg SD. Distribution of disease phase, treatment prescription and severe liver disease among 1598 patients with chronic hepatitis B in the Chronic Hepatitis Cohort Study, 2006-2013 *Aliment Pharmacol Ther* 2016;PMID: 27640985. Full Text

Division of Viral Hepatitis, National Centers for HIV, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention, Atlanta, GA, USA. pspradling@cdc.gov.
Division of Viral Hepatitis, National Centers for HIV, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention, Atlanta, GA, USA.
Henry Ford Health System, Detroit, MI, USA.
Center for Health Research, Geisinger Health System, Danville, PA, USA.
The Center for Health Research, Kaiser Permanente-Northwest, Portland, OR, USA.
The Center for Health Research, Kaiser Permanente-Hawaii, Honolulu, Hawaii.

BACKGROUND: Limited information exists regarding the distribution of disease phases, treatment prescription and severe liver disease among patients with chronic hepatitis B (CHB) in US general healthcare settings. AIM: To determine the distribution of disease phases, treatment prescription and severe liver disease among patients with CHB in general US healthcare settings. METHODS: We analysed demographic and clinical data collected during 2006-2013 from patients with confirmed CHB in the Chronic Hepatitis Cohort Study, an observational cohort study involving patients from healthcare organisations in Michigan, Pennsylvania, Oregon and Hawaii. CHB phases were

classified according to American Association for the Study of Liver Disease guidelines. RESULTS: Of 1598 CHB patients with >/=12 months of follow-up (median 6.3 years), 457 (29%) were immune active during follow-up [11% hepatitis B e antigen (HBeAg)-positive, 16% HBeAg-negative, and 2% HBeAg status unknown], 10 (0.6%) were immune tolerant, 112 (7%) were inactive through the duration of follow-up and 886 (55%) were phase indeterminate. Patients with cirrhosis were identified within each group (among 21% of immune active, 3% of inactive and 9% of indeterminate phase patients) except among those with immune-tolerant CHB. Prescription of treatment was 59% among immune active patients and 84% among patients with cirrhosis and hepatitis B virus (HBV) DNA >2000 IU/mL. CONCLUSIONS: Approximately, one-third of the cohort had active disease during follow-up; 60% of eligible patients were prescribed treatment. Our findings underscore the importance of ascertainment of fibrosis status in addition to regular assessment of ALT and HBV DNA levels.

Global Health Initiative

**Kaljee LM**, Kilgore P, **Prentiss T**, **Lamerato L**, **Moreno D**, **Arshad S**, and **Zervos M**. 'You need to be an advocate for yourself': Factors associated with decision-making regarding influenza and pneumococcal vaccine use among U.S. older adults from within a large metropolitan health system *Hum Vaccin Immunother* 2016:0. PMID: 27625007. Article Request Form

a Global Health Initiative, Henry Ford Health System , 2799 West Grand Blvd., CFP # 202 Detroit , MI USA 48202.
b Eugene Applebaum School of Pharmacy and Health Sciences, Wayne State University , Detroit , MI USA.
c Henry Ford Health System, Public Health Sciences and Research , Detroit , MI USA.
d Division of Infectious Disease, Henry Ford Health System , 2799 West Grand Blvd., CFP #302 Detroit , MI USA 48202.

In the United States, influenza and pneumonia account significantly to emergency room use and hospitalization of adults >65 years. The Centers for Disease Control and Prevention recommends use of the annual influenza vaccine and two pneumococcal vaccines for older adults to decrease risks of morbidity and mortality. However, actual vaccine up-take is estimated at 61.3% for pneumococcal vaccines and 65% for influenza vaccine in the 2013-2014 season. Vaccine up-take is affected by multiple socio-cultural and economic factors including general healthcare access and utilization, social networks and norms, communication with health providers and health information sources, as well as perceptions related to vaccines and targeted diseases. In this study, eight focus group discussions (total N = 48) were conducted with adults 65+ years living in urban and suburban communities in the Detroit Metropolitan Area. The research objective was to increase understanding of barriers and facilitators to vaccine up-take in this age cohort within the context of general healthcare availability and accessibility, social networks, information sources, and personal perceptions of diseases and vaccines. The data suggest the need to integrate broader health care service experiences, concepts of knowledge of one's own well-being and vulnerabilities, and self-advocacy as factors associated with older adults' vaccine-use decisions. These data also support recognition of multiple levels of vaccine acceptance which can be disease specific. Implications include potential for increasing vaccine up-take through general improvement in health care delivery and services, as well as specific vaccine-focused patient and provider education programs.

Hematology, Oncology and the Josephine Ford Cancer Institute

Apolo AB, Infante JR, Hamid O, Patel MR, **Wang D**, Kelly K, Mega AE, Britten CD, Mita AC, Ravaud A, Cuillerot JM, von Heydebreck A, and Gulley JL. Safety, clinical activity, and PD-L1 expression of avelumab (MSB0010718C), an anti-PD-L1 antibody, in patients with metastatic urothelial carcinoma from the JAVELIN Solid Tumor phase Ib trial *J Clin Oncol* 2016; 34(2)PMID: Not assigned. Abstract

Hematology, Oncology and the Josephine Ford Cancer Institute

Geary M, **Kachalsky E**, Pennick L, Johnson M, Hatcher N, Rosenblatt K, Dunn L, and Stolfi A. Perceived ideal roles of hemophilia treatment center social workers in the United States and barriers to those roles *Haemophilia* 2016; 22:113-113. PMID: Not assigned. Abstract

Introduction & Objectives: The multidisciplinary team approach has long been the model of healthcare delivery by hemophilia treatment centers (HTCs) across the United States. Working with physicians and nurses, hemophilia social workers (SWs) have been the primary provider of psychosocial services. However, minimal research appears to have been done on the actual roles of SWs and the perceived “ideal” roles of SWs in HTCs. Objectives include: 1. Identifying the perceived “ideal” role responsibilities that HTC SWs feel are the most important for adult and pediatric patients and their families. 2. Determining correlations between and barriers to the ideal roles that SWs feel should be practiced and those that are actually practiced.

Materials and Methods: In 2015, a group of HTC SWs received the National Hemophilia Foundation Social Work Award of Excellence grant to create an online survey to determine the roles of SWs. The SW role was divided into 6 categories of
responsibilities: counseling, grants/research, case management, financial and insurance, outreach/programs, and administration. SWs were asked to identify the "ideal" role responsibilities that they determined to be the most important/beneficial for the adult patients, pediatric patients and families. Results: Results are currently being analyzed from the 80 submitted surveys (54% response rate). By soliciting the "ideal" role responsibilities from the HTC SWs themselves and comparing them with the work that is actually done by the SWs, further correlations will be made to determine whether HTC SWs are performing the roles they feel are the most important for patients and families. Barriers to the practice of these "ideal" roles will be examined from responses to questions related to job resources such as training, supervision and budgeted hours. Conclusion: Results of the analyses will yield whether SWs are performing the roles that they themselves perceive to be the most important and beneficial to the patients and families with whom they work. This may be an impetus for the examination of SW roles and the elimination of barriers to those roles in the future.

Hematology, Oncology and the Josephine Ford Cancer Institute

Geary M, **Kachalsky E**, Pennick L, Rosenblatt K, Hatcher N, Johnson M, Dunn L, and Stolfi A. Social work caseloads in hemophilia treatment centers in the United States *Haemophilia* 2016; 22:117-117. PMID: Not assigned. Abstract

Introduction & Objectives: Hemophilia treatment centers (HTCs) were established and funded to primarily meet the medical and psychosocial needs of persons with hemophilia in the United States. However, over the years, the scope of care has grown to include various bleeding disorders such as von Willebrand disease. More recently, many HTCs have included persons with clotting disorders in their practices. As HTCs expanded their specialty care, the caseloads of HTC social workers (SWs) increased and diversified. It appears that little research has been done to describe and quantify these caseloads. Objectives include: 1. Quantifying the caseloads of SWs in United States HTCs. 2. Determining the makeup of bleeding and clotting disorder patients in HTC SW caseloads. Materials and Methods: A group of HTC SWs developed and administered a confidential online survey for SWs, funded by a grant from the National Hemophilia Foundation's Social Work Award of Excellence in 2015. Although the primary research focus was the SW role, investigators were interested in measuring the number and type of patients in caseloads. Questions about these variables and possible related determinants were asked. Results: Eighty SWs responded from the total sample of 147 subjects who were invited to take the survey. Data is currently being gathered and analyzed. These results will serve to quantify caseloads and will be examined relative to budgeted hours worked. Other possible determinants such as geographic region and HTC size will be analyzed. Caseloads will also be studied in order to provide graphical compositions by diagnosis: hemophilia, von Willebrand, other bleeding disorders and clotting disorders. Conclusion: It is important to determine and monitor the number of patients in HTC SW caseloads in order to ensure that adequate psychosocial services can be provided to the growing populations served by HTCs in the United States. SWs should also be aware of the makeup of their caseloads so that specialized training can be obtained and appropriate resources can be targeted to the varied populations.

Hematology, Oncology and the Josephine Ford Cancer Institute

Johnson M, **Kachalsky E**, Geary M, Pennick L, Dunn L, Hatcher N, Stolfi A, and Rosenblatt K. The role of the Hemophilia Treatment Center (HTC) social worker in the United States *Haemophilia* 2016; 22:117-117. PMID: Not assigned. Abstract

Introduction & Objectives: Social Workers (SWs) have been active members of the multidisciplinary teams at Hemophilia Treatment Centers (HTCs) for many years. However, their roles may differ greatly from Center to Center. SWs advocate for
patients, provide a variety of psychosocial and case management services, are a primary source of information and referral, and may provide counseling and therapy to patients and families, as well as consultation to staff. Despite being a vital HTC member, little research about the HTC SW role has been done. Since many SWs work in isolation, it is important to define the job tasks they undertake and identify the variables which influence their roles. This study could provide important data for the development of evidence-based standards of practice for HTC SWs. This would greatly benefit new or isolated HTC SWs, and could enhance patient expectations and satisfaction. Objectives include: Describing the various role tasks of the HTC SW, and; identifying the influences on the HTC SW role. Materials and Methods: An on-line survey was developed by a group of HTC SWs who received the National Hemophilia Foundation's Social Work Excellence grant award. The survey was emailed to 147 HTC SWs and 80 were completed and returned for a 54% response rate. Responses are in the process of being analyzed as aggregate data. These findings will allow HTC SWs to develop and evaluate their roles, and to discuss establishing standards of practice to meet the needs of SW professionals and their patients. Results: This poster or panel presentation will provide information about the survey results in an attempt to define job tasks and roles performed by HTC SWs at the

present time. The data will also identify the factors that shape these roles and include the priorities of SWs in these positions. Conclusion: The results will be important in providing a framework to establish future standards of practice for HTC SWs in the United States, with further discussion occurring among SWs in HTCs around the world.

Hematology, Oncology and the Josephine Ford Cancer Institute
Kuriakose J, John J, Hanagavadi S, Balar M, Pillai V, and **Kuriakose P**. Impact of twinning between HTC's: Incremental gain with longitudinal experience *Haemophilia* 2016; 22:54-54. PMID: Not assigned. Abstract

Introduction and Objectives: Although the role of twinning between HTC's has been adequately established, and often leads to a fruitful, long term relationship between the two concerned twins, it is not clear if changing one of the twinning partners at the end of a formal twinning period will allow for an entire set of new goals, as opposed to be a repetition of the earlier twinning endeavor. Materials and Methods: Henry Ford Health System, Detroit, USA, twinned with two centers in India (KHS Davangere, and CMC Ludhiana), and is now looking to twin with a third center (Aluva HTC). The goals of twinning with KHS Davangere were to help streamline patient registration, provide input into basic clinical patient care, coordinate educational updates and lectures, and provide factor support. With CMC Ludhiana, the goals were to help in the creation of a comprehensive HTC, focus on establishment of a specialty lab, exchange educational discourse, provide factor support, and create a referral center in the end. With Aluva HTC, the need appears to be for guidance in strategic planning and education. Results: Twinning with KHS (2006–2009) led to creation of a robust patient data base, establishment of ongoing clinics & camps, and a dedicated focus on reliable factor procurement. In coordination with CMC Ludhiana (2012–2015), a comprehensive clinic model was set up, patient registration was expanded, a specialty lab was created, medical students and other clinicians were included in educational learning and updates. Also, the HTC collaborated with the state government to become a center for spearheading the development of other hemophilia care centers. Both these twinning programs were recognized as Twins of the Year in 2013. Regarding the Aluva HTC, a customized plan to help reach their sought for goals is currently being arranged. Conclusions: Twinning between HTC's can span different partners, and each separate twinning program can both establish, and reach, their specific desired goals. In fact, experience gained in the prior twinning programs can be harnessed for helping other centers as potential, future twins.

Hematology, Oncology and the Josephine Ford Cancer Institute
Malik D, **Kuriakose P**, **Ivins DB**, and **Church J**. Single center clinical and pharmacokinetic experience with long-acting recombinant factor VIII (rFVIIIFx) and IX (rFIXFc) *Haemophilia* 2016; 22:101-101. PMID: Not assigned. Abstract

Introduction and Objectives: With the FDA approval of long-acting recombinant factor VIII (rFVIIIFc, Eloctate) and IX (rFIXFc, Alprolix) in 2014, patients with Hemophilia A and B, respectively, were provided a wider range of options for the prevention of bleeding episodes. Because these are still relatively new medications to treat two relatively rare diseases, clinical experience is limited. As a comprehensive Hemophilia Treatment Center, we aim to describe our experience with these newly approved medications. Materials and Methods: While initiating treatment with rFVIIIFc or rFIXFc, the respective factor activity levels were monitored. Samples were drawn at baseline and then at intervals of 1 hour, 24 hours, 48 hours, and trough (for rFVIIIFc), and
baseline, 1 hour, 24 hours, 48 hours, 96 hours, and trough (for rFIXFc). If available, the patients' bleeding logs were reviewed both before initiation of long-acting factor replacement, as well as while on therapy. However, no adjustments to dose and/or
frequency of long acting factor replacement was made based on the noted individual pharmacokinetics. Results: Five patients with either Hemophilia A (4) or B (1) were started on therapy with rFVIIIFc or rFIXFc, respectively, at our institution. Of these 5 patients, 3 (all Hemophilia A) remain on their long-acting factor replacement. One Hemophilia A patient felt that he had begun to experience a higher bleed rate than when he was on his standard acting rFVIII prophylaxis. The only Hemophilia B patient of rFIXFc, too, felt that he was experiencing more bleeds with his therapy. Both these patients switched back to their respective original standard acting recombinant factor products. Conclusions: In our experience with the use of rFVIIIFc and rFIXFc, appropriate factor recovery was obtained. Additionally, 3 of 5 patients reported less clinically significant bleeding episodes while on long-acting factor replacement, compared to their previous treatment regimens. However, two patients discontinued their treatment due to concerns about inadequate protection with acting factor replacement. In general, rFVIIIFc and rFIXFc have shown to be effective in bleeding prophylaxis in our patients with Hemophilia A and B.

Hematology, Oncology and the Josephine Ford Cancer Institute
Rand KA, Song C, Dean E, Serie DJ, Curtin K, Sheng X, Hu D, Huff CA, Bernal-Mizrachi L, Tomasson MH, Ailwadhi S, Singhal S, Pawlish KS, Peters ES, CH BL, Stram A, Van Den Berg DJ, Edlund CK, Conti DV, Zimmerman TM, Hwang AE, Huntsman S, Graff JJ, Nooka A, Kong Y, Pregja SL, Berndt SI, Blot WJ, Carpten JD, Casey G, Chu LW,

Diver WR, Stevens VL, Lieber MR, Goodman PJ, Hennis AJ, Hsing AW, Mehta J, Kittles RA, Kolb S, Klein EA, Leske CM, Murphy AB, Nemesure B, **Neslund-Dudas C**, Strom SS, Vij R, **Rybicki BA**, Stanford JL, Signorello L, Witte JS, Ambrosone CB, Bhatti P, John EM, Bernstein L, Zheng W, Olshan AF, Hu JJ, Ziegler RG, Nyante SJ, Bandera EV, Birmann BM, Ingles SA, Press MF, Atanackovic D, Glenn M, Cannon-Albright L, Jones B, Tricot G, Martin TG, Kumar SK, Wolf JL, Deming SL, Rothman N, Brooks-Wilson A, Rajkumar SV, Kolonel LN, Chanock SJ, Slager SL, Severson RK, **Janakirman N**, Terebelo HJ, Brown EE, De Roos AJ, Mohrbacher A, Colditz GA, Giles GG, Spinelli JJ, Chiu BC, Munshi NC, Anderson KC, Levy J, Zonder JA, Orlowski RZ, Lonial S, Camp NJ, Vachon CM, Ziv E, Stram DO, Hazelett DJ, and Cozen W. A meta-analysis of multiple myeloma risk regions in African and European ancestry populations identifies putatively functional loci *Cancer Epidemiol Biomarkers Prev* 2016;PMID: 27587788.
Article Request Form

Department of Preventive Medicine, University of Southern California.
Preventive Medicine, Keck School of Medicine of USC and Norris Comprehensive Cancer Center, University of Southern California.
Sutter Health.
Health Sciences Research, Mayo Clinic.
Human Genetics, University of Utah.
Keck School of Medicine, USC.
Division of General Internal Medicine, University of California at San Francisco.
Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University School of Medicine.
Hematology and Medical Oncology, Winship Cancer Institute of Emory University.
Department of Medicine, Washington University.
Mayo Clinic.
Robert H. Lurie Cancer Center, Northwestern University.
Cancer Epidemiology Services, New Jersey Department of Health & Senior Services.
Dept. of Epidemiology, Louisiana School of Public Health.
Karmanos Cancer Institute, Wayne State University School of Medicine.
Genomic Health, Inc.
Keck School of Medicine at USC and Norris Comprehensive Cancer Center, University of Southern California.
Department of Preventive Medicine, Norris Comprehensive Cancer Center, Keck School of Medicine, University of Southern California.
Medical Oncology, University of Chicago.
University of Southern California Keck School of Medicine.
Rutgers-Robert Wood Johnson Medical School, Rutgers State University of New Jersey.
Hematology and Medical Oncology, Emory University School of Medicine.
Keck School of Medicine of USC and Norris Comprehensive Cancer Center, University of Southern California.
Cancer Epidemiology and Genetics, National Cancer Institute.
Division of Epidemiology, Department of Medicine, Vanderbilt University School of Medicine.
Keck School of Medicine, Norris Comprehensive Cancer Center, University of Southern California, Los Angeles, California, USA.
Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health.
Epidemiology Research Program, American Cancer Society.
Keck School of Medicine of USC, University of Southern California.
Southwest Oncology Group Statistical Center.
Stony Brook University.
Department of Research, Cancer Prevention Institute of California.
Northwestern University School of Medicine.
Surgery, University of Arizona.
Division of Public Health Sciences, Fred Hutchinson Cancer Research Center.
Glickman Urological and Kidney Institute, Cleveland Clinic.
State University of New York at Stony Brook.
Feinberg School of Medicine, Department of Urology, Northwestern University.
Stony Brook University Medical Center.
Department of Public Health Sciences, Henry Ford Health System.
epidemiology, U.T MD Anderson Cancer Center.
Department of Medicine, Washington University in Saint Louis School of Medicine.
Department of Epidemiology, Harvard School of Public Health.
Epidemiology and Biostatistics, UCSF.
Cancer Prevention and Control, Roswell Park Cancer Institute.
Fred Hutchinson Cancer Research Center.
Department of Epidemiology, Cancer Prevention Institute of California.
Population Sciences/Cancer Etiology, City of Hope.

Department of Epidemiology, University of North Carolina at Chapel Hill.
Public Health Sciences, University of Miami Leonard Miller School of Medicine.
Division of Cancer Epidemiology and Genetics, Hormonal and Reproductive Epidemiology Branch, National Cancer Institute.
Department of Radiology, University of North Carolina at Chapel Hill.
Population Science, Rutgers Cancer Institute of New Jersey.
Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School.
Department of Preventive Medicine, USC.
Pathology, University of Southern California.
Hematology and Hematologic Malignancies, Huntsman Cancer Institute.
Hematology-Oncology, University of Utah.
Division of Genetic Epidemiology, Department of Medicine, University of Utah School of Medicine.
Medicine, University of Utah.
The Univeristy of Iowa.
Oncology, UCSF Medical Center.
Hematology, Mayo Clinic.
University of California at San Francisco.
Vanderbilt Epidemiology Center, Vanderbilt.
National Cancer Institute.
Michael Smith Genome Sciences Centre, BC Cancer Agency.
Hematologic research, Mayo Clinic Rochester.
University of Hawaii.
Division of Cancer Epidemiology and Genetics, National Cancer Institute; National Institute of Health.
Department of Health Sciences Research, Mayo Clinic.
Department of Family Meidicne and Public Health Sciences, Wayne State University.
Henry Ford Hospital.
Providence Hospital.
Pathology, UAB.
Department of Environmental and Occupational Health, Drexel University School of Public Health.
Oncology, University of Southern California.
Division of Public Health Sciences, Department of Surgery, Washington University School of Medicine and Alvin J. Siteman Cancer Center.
Cancer Epidemiology Centre, Cancer Council Victoria.
Cancer Control Research, BC Cancer Agency.
University of Chicago.
Jerome Lipper Multiple Myeloma Center,Department of Medical Oncology, Dana-Farber Cancer Insitute.
Jerome Lipper Multiple Myeloma Center,Department of Medical Oncology, Dana-Farber Cancer Institute.
MMRF, Multiple Myeloma Research Consortuim.
Department of Oncology, Karmanos Cancer Center, Wayne State University.
Lymphoma/Myeloma, The University of Texas MD Anderson Cancer Center.
Hematology and Medical Oncology, Winship Cancer Institute, Emory University.
Department of Health Sciences Research, Division of Epidemiology, Mayo Clinic.
Division of General Internal Medicine, University of California, San Francisco.
University of Southern California.
Cedars-Sinai Medical Center.
Preventive Medicine, Keck School of Medicine of USC and Norris Comprehensive Cancer Center, University of Southern California wcozen@usc.edu.

BACKGROUND: Genome-wide association studies (GWAS) in European populations have identified genetic risk variants associated with multiple myeloma (MM). METHODS: We performed association testing of common variation in eight regions in 1,264 MM patients and 1,479 controls of European ancestry (EA) and 1,305 MM patients and 7,078 controls of African ancestry (AA) and conducted a meta-analysis to localize the signals, with epigenetic annotation used to predict functionality. RESULTS: We found that variants in 7p15.3, 17p11.2, 22q13.1 were statistically significantly ($p<0.05$) associated with MM risk in AAs and EAs and the variant in 3p22.1 was associated in EAs only. In a combined AA-EA meta-analysis, variation in five regions (2p23.3, 3p22.1, 7p15.3, 17p11.2, 22q13.1) was statistically signficantly associated with MM risk. In 3p22.1, the correlated variants clustered within the gene body of ULK4. Correlated variants in 7p15.3 clustered around an enhancer at the 3' end of the CDCA7L transcription termination site. A missense variant at 17p11.2 (rs34562254, Pro251Leu, OR=1.32, p=2.93x10-7) in TNFRSF13B, encodes a lymphocyte-specific protein in the tumor necrosis factor receptor family that interacts with the NF-kappaB pathway. SNPs correlated with the index signal in 22q13.1 cluster around the promoter and enhancer regions of CBX7. CONCLUSIONS: We found that reported MM susceptibility regions contain risk variants important across

populations supporting the use of multiple racial/ethnic groups with different underlying genetic architecture to enhance the localization and identification of putatively functional alleles. IMPACT: A subset of reported risk loci for multiple myeloma have consistent affects across populations and are likely to be functional.

Hematology, Oncology and the Josephine Ford Cancer Institute
Sabry OM, Goeger DE, **Valeriote FA**, and Gerwick WH. Cytotoxic halogenated monoterpenes from Plocamium cartilagineum *Nat Prod Res* 2016:1-7. PMID: 27627578. Article Request Form

a College of Pharmacy , Oregon State University , Corvallis , OR , USA.
b Faculty of Pharmacy , Cairo University , Cairo , Egypt.
c Division of Hematology and Oncology Department of Internal Medicine , Henry Ford Hospital , Detroit , MI , USA.
d Center for Marine Biotechnology and Biomedicine , Scripps Institution of Oceanography, University of California , San Diego , CA , USA.

As a result of our efforts to identify bioactive agents from marine algae, we have isolated and identified one new halogenated monoterpene 1 [(-)-(5E,7Z)-348-trichloro-7-dichloromethyl-3-methyl-157-octatriene] in addition to three known compounds (2, 3 and 4) from the red alga Plocamium cartilagineum collected by hand from the eastern coast of South Africa. Compound 1 was found to be active as a cytotoxic agent in human lung cancer (NCI-H460) and mouse neuro-2a cell lines (IC50 4 mug/mL). Two of these compounds (3 and 4) were found to have cytotoxic activity in other cell line assays, especially against human leukaemia and human colon cancers (IC50 1.3 mug/mL). None of these metabolites were active as sodium channel blockers or activators. All structures were determined by spectroscopic methods (UV, IR, LRMS, HRMS, 1D NMR and 2D NMR). 1D and 2D NOE experiments were carried out on these compounds to confirm the geometry of the double bonds.

Hematology, Oncology and the Josephine Ford Cancer Institute
Schwartz AG, Lusk CM, Wenzlaff AS, Watza D, Pandolfi S, Mantha L, Cote ML, Soubani AO, Walworth G, Wozniak A, **Neslund-Dudas C**, **Ardisana AA**, **Flynn MJ**, **Song T**, **Spizarny DL**, **Kvale PA**, **Chapman RA**, and Gadgeel SM. Risk of lung cancer associated with COPD phenotype based on quantitative image analysis *Cancer Epidemiol Biomarkers Prev* 2016; 25(9):1341-1347. PMID: 27383774. Article Request Form

Karmanos Cancer Institute, Detroit, Michigan. Department of Oncology, Wayne State University School of Medicine, Detroit, Michigan. schwarta@karmanos.org.
Karmanos Cancer Institute, Detroit, Michigan. Department of Oncology, Wayne State University School of Medicine, Detroit, Michigan.
Department of Oncology, Wayne State University School of Medicine, Detroit, Michigan.
Karmanos Cancer Institute, Detroit, Michigan.
Karmanos Cancer Institute, Detroit, Michigan. Department of Internal Medicine, Wayne State University School of Medicine, Detroit, Michigan.
Department of Radiology, Karmanos Cancer Institute, Detroit, Michigan.
Department of Public Health Sciences, Henry Ford Health System, Detroit, Michigan. Josephine Ford Cancer Institute, Henry Ford Health System, Detroit, Michigan.
Josephine Ford Cancer Institute, Henry Ford Health System, Detroit, Michigan. Department of Radiology, Henry Ford Health System, Detroit, Michigan.
Josephine Ford Cancer Institute, Henry Ford Health System, Detroit, Michigan. Department of Pulmonary and Critical Care Medicine, Henry Ford Health System, Detroit, Michigan.
Josephine Ford Cancer Institute, Henry Ford Health System, Detroit, Michigan. Department of Hematology/Oncology, Henry Ford Health System, Detroit, Michigan.

BACKGROUND: Chronic obstructive pulmonary disease (COPD) is a risk factor for lung cancer. This study evaluates alternative measures of COPD based on spirometry and quantitative image analysis to better define a phenotype that predicts lung cancer risk. METHODS: A total of 341 lung cancer cases and 752 volunteer controls, ages 21 to 89 years, participated in a structured interview, standardized CT scan, and spirometry. Logistic regression, adjusted for age, race, gender, pack-years, and inspiratory and expiratory total lung volume, was used to estimate the odds of lung cancer associated with FEV1/FVC, percent voxels less than -950 Hounsfield units on the inspiratory scan (HUI) and percent voxels less than -856 HU on expiratory scan (HUE). RESULTS: The odds of lung cancer were increased 1.4- to 3.1-fold among those with COPD compared with those without, regardless of assessment method; however, in multivariable modeling, only percent voxels <-856 HUE as a continuous measure of air trapping [OR = 1.04; 95% confidence interval (CI), 1.03-1.06] and FEV1/FVC < 0.70 (OR = 1.71; 95% CI, 1.21-2.41) were independent predictors of lung cancer risk. Nearly 10% of lung cancer cases were negative on all objective measures of COPD. CONCLUSION: Measures of air trapping using quantitative imaging, in addition to FEV1/FVC, can identify individuals

at high risk of lung cancer and should be considered as supplementary measures at the time of screening for lung cancer. IMPACT: Quantitative measures of air trapping based on imaging provide additional information for the identification of high-risk groups who might benefit the most from lung cancer screening. Cancer Epidemiol Biomarkers Prev; 25(9); 1341-7.

Hypertension and Vascular Research
**Ortiz PA**. k+-mediated regulation of distal convoluted tubule na/cl cotransporter phosphorylation during angiotensin II-induced hypertension *Hypertension* 2016; 68(4):853-854. PMID: 27600180. Full Text

From the Hypertension and Vascular Research Division, Department of Internal medicine, Henry Ford Hospital, Detroit, MI. portiz1@hfhs.org.

Hypertension and Vascular Research
**Romero C**, **Monu S**, **Cabral G**, **Knight R**, and **Carretero O**. OS 21-02 Connecting tubule-glomerular feedback (ctgf) in renal hemodynamics and blood pressure regulation after unilateral nephrectomy (unx) *J Hypertens* 2016; 34 Suppl 1:e235. PMID: 27643022. Full Text

1Hypertension and Vascular Research Division, Henry Ford Hospital, Detroit (MI), U.S.A. 2MRI core, Department of Neurology, Henry Ford Hospital, Detroit (MI), U.S.A.

OBJECTIVE: Renal hemodynamics is critical for regulation of glomerular filtration (GFR), sodium excretion and blood pressure (BP), and it depends on myogenic response, tubuloglomerular feedback (TGF) and connecting tubule-glomerular feedback (CTGF). CTGF dilates afferent arteriole in response to high sodium in connecting tubule (CNT), counteracting and resetting TGF; and increasing the plasma flow and glomerular pressure favoring sodium excretion. CTGF is initiated by epithelial sodium channel (ENaC) activation in CNT and inhibited by ENaC blocker Benzamil. Unilateral nephrectomy (UNx) is accompanied by TGF resetting, increase in renal blood flow (RBF) and single nephron GFR in the remnant kidney, without any changes in systemic BP. We evaluated CTGF role in BP regulation and TGF resetting after UNx. DESIGN AND METHOD: UNx was performed on Sprague-Dawley rats and 24 h later TGF was evaluated in vivo by renal micropuncture using stop flow pressure (Psf) techniques. CTGF was evaluated by intratubularly adding Benzamil during the TGF response. Another set of animals received chronic kidney infusion of Benzamil that started 1 week before UNx. Renal blood flow (RBF) was measured by arterial spin labeling-MRI 24 h before and 24 h after the UNx. Direct BP measurement was performed before and 3 weeks after the UNx. RESULTS: After UNx, TGF resetting was observed (delta-Psf 8 +/- 1 vs. 1 +/- 1 mmHg $p < 0.05$, Sham vs. Unx) and that was inhibited by Benzamil. RBF increased after the UNx in comparison to sham and this increase was inhibited by chronic infusion of Benzamil (Sham: 305 +/- 59; UNx: 456 +/- 34; UNx + Benzamil 346 +/- 64 ml/min/100 g tissue $p < 0.002$). Mean BP values were not different between the vehicle or Benzamil infused rats before the UNx, however 3 weeks after the UNx, Benzamil infused rats showed higher mean BP values than vehicle (88 +/- 0.3 vs. 97 +/- 4 mmHg, $p < 0.01$). CONCLUSIONS: CTGF participates in TGF resetting and BP regulation after UNx. CTGF impairment could be a potential cause of hypertension.

Immunology
**Wu D**, **Bi X**, **Qu L**, **Han L**, **Yin C**, **Deng J**, Dong Z, **Mi QS**, and **Zhou L**. miRNA miR-17-92 cluster is differentially regulated in the imiqumod-treated skin but is not required for imiqumod-induced psoriasis-like dermatitis in mice *Exp Dermatol* 2016;PMID: 27579777. Full Text

Henry Ford Immunology Program, Henry Ford Health System, Detroit, MI.
Department of Dermatology, Henry Ford Health System, Detroit, MI.
Department of Dermatology, Guangdong provincial Hospital of Chinese Medicine, Guanghzou, P. R. China, 510120.
Department of Cellular Biology and Anatomy, Augusta University, Augusta, GA.
Department of Immunology and Microbiology, Wayne State University, Detroit, MI, USA.
Department of Internal Medicine, Henry Ford Health System, Detroit, MI.

Infectious Diseases
**Kaljee LM**, Kilgore P, **Prentiss T**, **Lamerato L**, **Moreno D**, **Arshad S**, and **Zervos M**. 'You need to be an advocate for yourself': Factors associated with decision-making regarding influenza and pneumococcal vaccine use among U.S. older adults from within a large metropolitan health system *Hum Vaccin Immunother* 2016:0. PMID: 27625007. Article Request Form

a Global Health Initiative, Henry Ford Health System , 2799 West Grand Blvd., CFP # 202 Detroit , MI USA 48202.
b Eugene Applebaum School of Pharmacy and Health Sciences, Wayne State University , Detroit , MI USA.
c Henry Ford Health System, Public Health Sciences and Research , Detroit , MI USA.
d Division of Infectious Disease, Henry Ford Health System , 2799 West Grand Blvd., CFP #302 Detroit , MI USA 48202.

In the United States, influenza and pneumonia account significantly to emergency room use and hospitalization of adults >65 years. The Centers for Disease Control and Prevention recommends use of the annual influenza vaccine and two pneumococcal vaccines for older adults to decrease risks of morbidity and mortality. However, actual vaccine up-take is estimated at 61.3% for pneumococcal vaccines and 65% for influenza vaccine in the 2013-2014 season. Vaccine up-take is affected by multiple socio-cultural and economic factors including general healthcare access and utilization, social networks and norms, communication with health providers and health information sources, as well as perceptions related to vaccines and targeted diseases. In this study, eight focus group discussions (total N = 48) were conducted with adults 65+ years living in urban and suburban communities in the Detroit Metropolitan Area. The research objective was to increase understanding of barriers and facilitators to vaccine up-take in this age cohort within the context of general healthcare availability and accessibility, social networks, information sources, and personal perceptions of diseases and vaccines. The data suggest the need to integrate broader health care service experiences, concepts of knowledge of one's own well-being and vulnerabilities, and self-advocacy as factors associated with older adults' vaccine-use decisions. These data also support recognition of multiple levels of vaccine acceptance which can be disease specific. Implications include potential for increasing vaccine up-take through general improvement in health care delivery and services, as well as specific vaccine-focused patient and provider education programs.

Infectious Diseases

**Reyes K**, **Bardossy AC**, and **Zervos M**. Vancomycin-resistant enterococci: Epidemiology, infection prevention, and control *Infect Dis Clin North Am* 2016;PMID: 27660091. Full Text

Infection Prevention and Control, Division of Infectious Disease, Henry Ford Hospital, Henry Ford Health System, 2799 West Grand Boulevard, CFP 302, Detroit, MI 48202, USA. Electronic address: kreyes1@hfhs.org.
Division of Infectious Disease, Henry Ford Health System, 2799 West Grand Boulevard, CFP 302, Detroit, MI 48202, USA.
Division of Infectious Disease, Henry Ford Health System, 2799 West Grand Boulevard, CFP 302, Detroit, MI 48202, USA; Wayne State University School of Medicine, Detroit, MI, USA.

Vancomycin-resistant enterococci (VRE) infections have acquired prominence as a leading cause of health care-associated infections. Understanding VRE epidemiology, transmission modes in health care settings, risk factors for colonization, and infection is essential to prevention and control of VRE infections. Infection control strategies are pivotal in management of VRE infections and should be based on patient characteristics, hospital needs, and available resources. Hand hygiene is basic to decrease acquisition of VRE. The effectiveness of surveillance and contact precautions is variable and controversial in endemic settings, but important during VRE outbreak investigations and control. Environmental cleaning, chlorhexidine bathing, and antimicrobial stewardship are vital in VRE prevention and control.

Infectious Diseases

Singh N, Sifri CD, Silveira FP, Miller R, Gregg KS, Huprikar S, Lease ED, Zimmer A, Dummer JS, Spak CW, Koval C, Banach DB, Shroff M, Le J, Ostrander D, Avery R, Eid A, Razonable RR, Montero J, Blumberg E, Alynbiawi A, Morris MI, Randall HB, **Alangaden G**, Tessier J, Cacciarelli TV, Wagener MM, and Sun HY. Unique characteristics of cryptococcosis identified after death in patients with liver cirrhosis: comparison with concurrent cohort diagnosed antemortem *Med Mycol* 2016;PMID: 27601609. Article Request Form

University of Pittsburgh, Pittsburgh, PA nis5@pitt.edu.
University of Virginia, Charlottesville, VA.
University of Pittsburgh, Pittsburgh, PA.
University of Iowa, Iowa City, IA; Duke University Medical Center, Durham, NC.
University of Michigan, Ann Arbor, MI.
Icahn School of Medicine at Mount Sinai, New York, NY.
University of Washington, Seattle, WA.
Vanderbilt University, Nashville, TN.
Baylor Health System, Dallas, TX.
Cleveland Clinic, Cleveland, OH.

Yale School of Medicine, New Haven, CT; University of Connecticut School of Medicine, Farmington, CT.
University of Texas Southwestern Medical Center, Dallas, TX.
Johns Hopkins University, Baltimore, MD.
University of Kansas, Kansas City, KS.
Mayo Clinic, Rochester, MN.
University of South Florida, Tampa, FL.
University of Pennsylvania, Philadelphia, PA.
UCSF, Fresno Branch, San Francisco, CA.
University of Miami, Miller School of Medicine, Miami, FL.
St. Luke's Hospital, Kansas City, MO.
Henry Ford Hospital, Detroit, MI.
Virginia Commonwealth University, Richmond, VA.
Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan Department of Internal Medicine, National Taiwan University College of Medicine, Taipei, Taiwan.

Characteristics of cirrhosis-associated cryptococcosis first diagnosed after death are not fully known. In a multicenter study, data generated as standard of care was systematically collected in 113 consecutive patients with cirrhosis and cryptococcosis followed for 80 patient-years. The diagnosis of cryptococcosis was first established after death in 15.9% (18/113) of the patients. Compared to cases diagnosed while alive, these patients had higher MELD score (33 vs. 22, P = .029) and higher rate of cryptococcemia (75.0% vs. 41.9%, P = .027). Cases diagnosed after death, in comparison to those diagnosed during life were more likely to present with shock (OR 3.42, 95% CI 1.18-9.90, P = .023), require mechanical ventilation at admission (OR 8.5, 95% CI 2.74-26.38, P = .001), less likely to undergo testing for serum cryptococcal antigen (OR 0.07, 95% CI 0.02-0.21, P < .001) and have positive antigen when the test was performed (OR 0.07, 95% CI 0.01-0.60, P = .016). In a subset of cirrhotic patients with advanced liver disease cryptococcosis was first recognized after death. These patients had the characteristics of presenting with fulminant fungemia, were less likely to have positive serum cryptococcal antigen and posed a diagnostic challenge for care providers.

Internal Medicine
Barnes GD, Kurlander J, Haymart B, **Kaatz S**, Saini S, and Froehlich JB. Bridging anticoagulation before colonoscopy: Results of a multispecialty clinician survey *JAMA Cardiol* 2016;PMID: 27627046. Full Text

Frankel Cardiovascular Center, Department of Internal Medicine, University of Michigan, Ann Arbor2Institute for Healthcare Policy and Innovation, University of Michigan, Ann Arbor.
Institute for Healthcare Policy and Innovation, University of Michigan, Ann Arbor3Division of Gastroenterology, Department of Internal Medicine, University of Michigan, Ann Arbor4VA Ann Arbor Center for Clinical Management Research, Ann Arbor, Michigan.
Frankel Cardiovascular Center, Department of Internal Medicine, University of Michigan, Ann Arbor.
Department of Internal Medicine, Henry Ford Hospital, Ann Arbor, Michigan.

Internal Medicine
**Jinjuvadia R**, Antaki F, Lohia P, and Liangpunsakul S. The association between nonalcoholic fatty liver disease and metabolic abnormalities in the United States population *J Clin Gastroenterol* 2016;PMID: 27580477. Full Text

*Department of Internal Medicine, Division of Gastroenterology and Hepatology, Henry Ford Hospital daggerJohn D. Dingell VA Medical Center double daggerDepartment of Medicine, Division of Gastroenterology, Wayne State University section signDetroit Medical Center, Detroit, MI parallelDepartment of Medicine, Division of Gastroenterology and Hepatology, Indiana University Medical Center paragraph signRoudebush Veterans Administration Medical Center, Indianapolis, IN.

BACKGROUND: Prevalence of nonalcoholic fatty liver disease (NAFLD) and rate of advanced fibrosis among individuals with metabolic syndrome (MetS) and its individual metabolic abnormalities needs better understanding in the United States population. We aim to study these by using a large United States population database, the Third National Health and Nutrition Examination Survey (NHANES III). METHODS: A total of 11,674 individuals were included in our study cohort. NAFLD was defined as presence of moderate to severe hepatic steatosis on liver ultrasound in absence of viral hepatitis, significant alcohol use, elevated transferrin level, and medication use leading to hepatic steatosis. Advanced fibrosis among those with NAFLD was determined using noninvasive method, the NAFLD fibrosis score. MetS was defined based on the National Cholesterol Education Program Adult Treatment Panel III definition. RESULTS: The prevalence of NAFLD among included study cohort was 18.2% (95% confidence interval, 16.5-19.9). Individuals with metabolic abnormalities demonstrated higher prevalence (MetS, 43.2%;

increased waist circumference, 31.2%; impaired fasting glucose/diabetes, 41.2%; high triglyceride level, 34.7%; low high-density lipoprotein, 27.8%; high blood pressure, 29.2%). The individuals with MetS had significantly higher NAFLD prevalence compared with controls (adjusted odds ratio, 11.5; 95% confidence interval, 8.9-14.7). The severity of hepatic steatosis was also noted to increase with higher number of metabolic abnormalities. Among individual metabolic abnormalities, increased waist circumference, impaired fasting glucose/diabetes, high triglyceride, and low high-density lipoprotein levels were found to be independently associated with NAFLD. Individuals with impaired fasting glucose/diabetes and those with 5 metabolic abnormalities had higher rate of advanced fibrosis (18.6% and 30.3%, respectively). Prevalence of NAFLD among individuals without any metabolic abnormality was 6.1%. CONCLUSION: Prevalence of NAFLD and rate of advanced fibrosis are significantly high among individuals with metabolic abnormalities.

Internal Medicine
Mendiratta-Lala M, **Park H**, **Kolicaj N**, **Mendiratta V**, and **Bassi D**. Small intrahepatic peripheral cholangiocarcinomas as mimics of hepatocellular carcinoma in multiphasic CT *Abdom Radiol (NY)* 2016;PMID: 27590067. Article Request Form

School of Medicine, University of Michigan, 1500 East Medical Center Drive, UH B2 A209R, Ann Arbor, MI, 48109, USA. mmendira@med.umich.edu.
Henry Ford Hospital, 2799 West Grand Blvd, Detroit, MI, 48202, USA.

PURPOSE: Liver transplant guidelines for diagnosing hepatocellular carcinoma (HCC) do not mandate pathologic confirmation; instead, 'classic' imaging features alone are deemed satisfactory. Intrahepatic peripheral mass forming cholangiocarcinoma (IHPMCC) is a relative contraindication for transplantation due to high rate of recurrence and poor prognosis. This study examines the imaging findings of IHPMCC, to aid in the identification and differentiation from potentially confounding cases of HCC. METHODS: After IRB approval, 43 tissue-proven cases of IHPMCC on multiphase CT were retrospectively reviewed by 2 fellowship-trained radiologists. Tumor size, presence of cirrhosis, tumor capsule, vascular invasion, tumor markers, and enhancement pattern were assessed. A grading system was assigned as determined by enhancement pattern to background liver on arterial, portal venous, and equilibrium phases, ranging from typical HCC to typical IHPMCC enhancement pattern. RESULTS: Analysis based on our grading system shows 5 (11.6%) tumors demonstrating grade 1-2 enhancement, 9 (21%) grade 3-4 enhancement, and 29 (67.4%) grade 5 enhancement. Kruskal-Wallis test comparing CA19-9 between the five groups, Wilcoxin rank-sum test comparing tumor markers with presence or absence of tumor capsule, vascular invasion and cirrhosis, and nonparametric Pearson's correlation coefficient comparing tumor markers to tumor size were not statistically significant ($p > 0.05$). CONCLUSION: Typical enhancement pattern of IHPMCC consisting of arterial phase hypoenhancement with progressive, centripetal-delayed enhancement is present in the majority of cases (68%). Five cases (11.7%) showed enhancement features potentially mimicking HCC, all of which are under 3.5 cm in size. Thus, small hyperenhancing lesions in a cirrhotic liver should be carefully scrutinized in light of differing therapy options from HCC, particularly in transplant situations.

Internal Medicine
**Michaels AT**, **Radjef R**, **She R**, **Liu B**, **Peterson E**, Pinto Y, **Williams K**, **Sabbah H**, and **Lanfear D**. Improving risk prediction in heart failure: Maggic + natriuretic peptides *J Card Fail* 2016; 22:S99. PMID: Not assigned. Abstract

A.T. Michaels, Henry Ford Hospital, Detroit, United States

Background: Risk stratification of patients with heart failure (HF) remains challenging but is a critical need. The MAGGIC score is a clinical risk model derived from meta-analysis of nearly 40k patients. Natriuretic peptides (NP) have consistently shown powerful risk prediction in HF patients, but the incremental value in addition to MAGGIC score is not known. Methods: In this single center study 4264 patients were analyzed from two cohorts; a prospective ambulatory registry of HF patients (n = 1314) who had baseline NTproBNP levels measured, and a retrospective cohort collected utilizing administrative data from hospital discharges for HF (January 1st, 2014 through July 30th, 2015; n = 2503) with clinical BNP levels measured at or near discharge. The hospital discharge cohort were all assigned NYHA class IV. The primary end-point was all cause mortality. Performance of the MAGGIC score and NP levels was assessed within each cohort utilizing Cox regression and receiver operating curves (ROC) analysis (MAGGIC alone vs. MAGGIC+NP) with the net reclassification improvement (NRI) also calculated. Results: The overall cohort had an average age of 71.2 years, was 47.8% females, and 41% self-identified African Americans. Median follow up was 1.52 years during which there were 1139 deaths (27%). The MAGGIC score was a strong predictor of outcome in both cohorts ($P < .001$). In ROC analysis of the ambulatory registry, NP significantly improved area under the curve (AUC) compared to MAGGIC alone from 0.74 to 0.79 ($P = .002$) and had a NRI of 0.354 (Figure). In contrast, within the hospital discharge cohort NP levels did not significantly add to MAGGIC score (AUC

0.681 vs. 0.676, NRI = 0.033, P = .284) (Figure). Conclusion: In our study, NP levels in the ambulatory setting significantly improved risk stratification provided by the MAGGIC score, but discharge NP levels did not improve MAGGIC prediction of posthospital survival. Overall risk stratification and particularly NP utility is much better in the ambulatory setting. (Figure Presented).

Internal Medicine
**Michaels AT**, **Radjef R**, **She R**, **Peterson E**, **Liu B**, and **Lanfear DE**. Predicting mortality at discharge following hospitalization for acute heart failure *J Card Fail* 2016; 22:S21-S22. PMID: Not assigned. Abstract

A.T. Michaels, Henry Ford Hospital, Detroit, United States

Background: Risk stratification for heart failure (HF) patients remains a critical need, particularly among those hospitalized where many clinical decisions are being made at discharge. Recently a robust risk model, the MAGGIC score, was derived from data on nearly 40k patients. This provides 1 year mortality estimates and is available as an online clinical tool. Whether it is useful to risk-stratify patients being discharged from the hospital is unknown. Methods: This single center study analyzed a total of 4264 patients from 2 cohorts; one utilizing administrative data from hospital discharges for HF (January 1st, 2014 through July 30th, 2015, n = 2503) and a prospective registry of ambulatory HF patients (n = 1761), both based in southeast Michigan. For the hospital discharge subjects, when tabulating MAGGIC all patients were assigned NYHA class IV. The primary endpoint was all-cause mortality. Vital status was assessed utilizing system administrative data and the social security death master file. Performance of the MAGGIC score was evaluated within cohorts and compared across the two groups using Cox models stratified by cohort and then with an interaction term (MAGGIC∗Cohort). Calibration was assessed by comparing observed vs. MAGGICpredicted 1 year mortality. Results: Overall the study patients had an average age of 71.2 years, 47.8% were female and 41% were self-identified African Americans, and there were 1139 deaths (27%) over a median follow up of 1.52 years. The hospital discharge cohort was overall much higher risk than the ambulatory cohort (figure). The MAGGIC score was a strong predictor of outcomes in both groups (both P < .001). With a HR (per MAGGIC point) of 1.13 in the ambulatory registry and 1.10 in the hospital discharge patients. In ROC analysis MAGGIC showed an area under the curve (AUC) of 0.74, but an AUC in the hospital discharge cohort of 0.67. When modeled using an interaction term, MAGGIC did appear to be more predictive in the ambulatory group with an interaction coefficient of 0.03 (P = .004). Although calibration appeared suboptimal in both cohorts (Figure), with MAGGIC underestimating the true risk, this appeared similar in both cohorts. Discussion: The MAGGIC score is able to provide important prognostic information on patients being discharged from the hospital for HF, though the performance was somewhat inferior than in a comparable ambulatory cohort. MAGGIC underestimated risk in both ambulatory and hospital cohorts, suggesting calibration may need to be reassessed in more real-world patient data sets. (Figure Presented).

Internal Medicine
Milling TJ, Jr., and **Kaatz S**. Preclinical and clinical data for factor xa and "universal" reversal agents *Am J Med* 2016;PMID: 27575436. Full Text

Departments of Neurology and Surgery and Perioperative Care, Seton Dell Medical School Stroke Institute Austin, Tex.
Division of Hospital Medicine, Henry Ford Hospital, Detroit, MI. Electronic address: skaatz1@hfhs.org.

Oral Factor Xa (FXa) inhibitors, a growing class of direct-acting anticoagulants, are frequently used to prevent stroke and systemic embolism in patients with atrial fibrillation and to prevent and treat venous thromboembolism. These drugs reduce the risk of clotting at the expense of increasing the risk of bleeding, and currently they have no specific reversal agent. However, andexanet alfa, a recombinant modified FXa decoy molecule, is in a late-phase clinical trial in bleeding patients, and ciraparantag, a small molecule that appears to reverse many anticoagulants including the FXa inhibitors, is in development. This review summarizes the published data to date on both drugs, which have the potential to change the management approach to patients with FXa inhibitor-associated major hemorrhage.

Internal Medicine
**Ortiz PA**. k+-mediated regulation of distal convoluted tubule na/cl cotransporter phosphorylation during angiotensin II-induced hypertension *Hypertension* 2016; 68(4):853-854. PMID: 27600180. Full Text

From the Hypertension and Vascular Research Division, Department of Internal medicine, Henry Ford Hospital, Detroit, MI. portiz1@hfhs.org.

Internal Medicine
**Radjef R**, **Michaels A**, **Peterson E**, **She R**, **Liu B**, **Williams K**, **Sabbah H**, and **Lanfear D**. Performance of maggic score in African Americans compared to whites *J Card Fail* 2016; 22:S101. PMID: Not assigned. Abstract

R. Radjef, Henry Ford Hospital, Detroit, United States

Background: Risk stratification is critical in Heart Failure (HF) care. The MAGGIC score is a validated tool derived from a large multi-study cohort of nearly 40,000 but very few of the patients self-identified as Black or of African Ancestry (less than 400). There is little data assessing MAGGIC score utility in African Americans (AA). Methods: This single center study analyzed a total of 4264 patients from 2 cohorts; one utilizing administrative data from hospital discharges for HF (January 1st, 2014 through July 30th, 2015, n = 2503) and a prospective registry of ambulatory HF patients (n = 1761), both based in southeast Michigan. Baseline characteristics were collected to tabulate MAGGIC score and test its risk stratification in selfidentified African Americans (AA) and whites. The primary endpoint was time to all-cause mortality. Death was detected using system records and the social security death master file. Cox models with MAGGIC score as the only variable stratified by race, and a combined model including MAGGIC, race, and MAGGIC∗race were tested. P < .05 was considered significant. Results: Overall, 1748 patients (41%) were AA, and a total of 1151 (27%) patients died during follow up. MAGGIC score was strongly and similarly predictive of survival in both race groups. Among AA, each MAGGIC point carried HR of 1.12 (95%CI 1.10, 1.14; P < .001) while in whites the HR was 1.13 (95%CI 1.12, 1.14; P < .001). Formal test of interaction of MAGGIC by race was not significant (P = .153). However, there was a difference in survival by race, with African Americans showing a survival advantage (HR = 0.72, P = .001) which appears to be isolated to the highest risk subgroup (Figure). Conclusion: These data support the utility of the MAGGIC score for risk stratification in African Americans who suffer from HF. However, there may still be residual differences in outcomes between AA and whites despite overall risk adjustment, particularly in highest risk subgroup. (Figure Presented).

Internal Medicine
Sabry OM, Goeger DE, **Valeriote FA**, and Gerwick WH. Cytotoxic halogenated monoterpenes from Plocamium cartilagineum *Nat Prod Res* 2016:1-7. PMID: 27627578. Article Request Form

a College of Pharmacy , Oregon State University , Corvallis , OR , USA.
b Faculty of Pharmacy , Cairo University , Cairo , Egypt.
c Division of Hematology and Oncology Department of Internal Medicine , Henry Ford Hospital , Detroit , MI , USA.
d Center for Marine Biotechnology and Biomedicine , Scripps Institution of Oceanography, University of California , San Diego , CA , USA.

As a result of our efforts to identify bioactive agents from marine algae, we have isolated and identified one new halogenated monoterpene 1 [(-)-(5E,7Z)-348-trichloro-7-dichloromethyl-3-methyl-157-octatriene] in addition to three known compounds (2, 3 and 4) from the red alga Plocamium cartilagineum collected by hand from the eastern coast of South Africa. Compound 1 was found to be active as a cytotoxic agent in human lung cancer (NCI-H460) and mouse neuro-2a cell lines (IC50 4 mug/mL). Two of these compounds (3 and 4) were found to have cytotoxic activity in other cell line assays, especially against human leukaemia and human colon cancers (IC50 1.3 mug/mL). None of these metabolites were active as sodium channel blockers or activators. All structures were determined by spectroscopic methods (UV, IR, LRMS, HRMS, 1D NMR and 2D NMR). 1D and 2D NOE experiments were carried out on these compounds to confirm the geometry of the double bonds.

Internal Medicine
**Wu D**, **Bi X**, **Qu L**, **Han L**, **Yin C**, **Deng J**, Dong Z, **Mi QS**, and **Zhou L**. miRNA miR-17-92 cluster is differentially regulated in the imiqumod-treated skin but is not required for imiqumod-induced psoriasis-like dermatitis in mice *Exp Dermatol* 2016;PMID: 27579777. Full Text

Henry Ford Immunology Program, Henry Ford Health System, Detroit, MI.
Department of Dermatology, Henry Ford Health System, Detroit, MI.
Department of Dermatology, Guangdong provincial Hospital of Chinese Medicine, Guanghzou, P. R. China, 510120.
Department of Cellular Biology and Anatomy, Augusta University, Augusta, GA.
Department of Immunology and Microbiology, Wayne State University, Detroit, MI, USA.
Department of Internal Medicine, Henry Ford Health System, Detroit, MI.

Internal Medicine
**Zhang X**, Gu J, **Zhou L**, and **Mi QS**. TIM-4 is expressed on invariant NKT cells but dispensable for their development and function *Oncotarget* 2016;PMID: 27662666. Full Text

Henry Ford Immunology Program, Henry Ford Health System, Detroit, MI, USA.
Department of Dermatology, Henry Ford Health System, Detroit, MI, USA.
Department of Dermatology, Changhai Hospital, Second Military Medical University, Shanghai, China.
Department of Internal Medicine, Henry Ford Health System, Detroit, MI, USA.
Department of Immunology and Microbiology, Wayne State University School of Medicine, MI, USA.

T cell immunoglobulin and mucin-4 (TIM-4), mainly expressed on antigen presenting cells, plays a versatile role in immunoregulation. CD1d-restricted invariant natural killer T (iNKT) cells are potent cells involved in the diverse immune responses. It was recently reported that recombinant TIM-4 (rTIM-4) alone enhanced cytokine production in NKT hybridoma, DN32.D3 cells. Hence, we hypothesized that TIM-4 might regulate iNKT cell biology, especially their function of cytokine secretion. For the first time, we identified that TIM-4 was expressed in thymus iNKT cells, and its expression increased upon iNKT cell migration to the secondary lymphoid organs, especially in lymph nodes. Using TIM-4-deficient mice, we found that lack of TIM-4 did not disturb iNKT cell development, maturation, peripheral homeostasis and cytokine secretion. Moreover, TIM-4 deficiency did not alter the polarization of iNKT sublineages, including NKT1, NKT2 and NKT17. Finally, the mixed bone marrow transfer experiments further confirmed normal iNKT cell development and function from TIM-4-deficient bone marrow. In conclusion, our data suggest that TIM-4 is expressed on iNKT cells but dispensable for their development and function.

Nephrology
Jalal D, McFadden M, Dwyer JP, **Umanath K**, Aguilar E, Yagil Y, Greco B, Sika M, Lewis JB, Greene T, and Goral S. Adherence rates to ferric citrate as compared to active control in patients with end stage kidney disease on dialysis *Hemodial Int* 2016;PMID: 27615161. Full Text

University of Colorado, Aurora, Colorado, USA. diana.jalal@ucdenver.edu.
University of Utah, Salt Lake, Utah, USA.
Vanderbilt University School of Medicine, Nashville, Tennessee, USA.
Henry Ford Hospital, Detroit, Michigan, USA.
Louisiana State University Health Center, New Orleans, Louisiana, USA.
Ben-Gurion University of the Negev, Beer Sheba and Barzilai University Medical Center, Ashkelon, Israel.
Baystate Medical Center, Springfield, Massachusetts, USA.
University of Pennsylvania, Philadelphia, Pennsylvania, USA.

Introduction Oral phosphate binders are the main stay of treatment of hyperphosphatemia. Adherence rates to ferric citrate, a recently approved phosphate binder, are unknown. Methods We conducted a post-hoc analysis to evaluate whether adherence rates were different for ferric citrate vs. active control in 412 subjects with end stage kidney disease (ESKD) who were randomized to ferric citrate vs. active control (sevelamer carbonate and/or calcium acetate). Adherence was defined as percent of actual number of pills taken to total number of pills prescribed. Findings There were no significant differences in baseline characteristics including gender, race/ethnicity, and age between the ferric citrate and active control groups. Baseline phosphorus, calcium, and parathyroid hormone levels were similar. Mean (SD) adherence was 81.4% (17.4) and 81.7% (15.9) in the ferric citrate and active control groups, respectively (P = 0.88). Adherence remained similar between both groups after adjusting for gender, race/ethnicity, age, cardiovascular disease (CVD), and diabetic nephropathy (mean [95% CI]: 81.4% [78.2, 84.6] and 81.5% [77.7, 85.2] for ferric citrate and active control, respectively). Gender, race/ethnicity, age, and diagnosis of diabetic nephropathy did not influence adherence to the prescribed phosphate binder. Subjects with CVD had lower adherence rates to phosphate binder; this was significant only in the active control group. Discussion Adherence rates to the phosphate binder, ferric citrate, were similar to adherence rates to active control. Similar adherence rates to ferric citrate are notable since tolerance to active control was an entry criteria and the study was open label. Gender, race/ethnicity, nor age influenced adherence.

Nephrology
**Matzumura M**, **Arias-Stella J, 3rd**, and **Novak JE**. Erdheim-chester disease: A rare presentation of a rare disease *J Investig Med High Impact Case Rep* 2016; 4(3):2324709616663233. PMID: 27606325. Full Text

Detroit Medical Center/Wayne State University, Detroit, MI, USA.
Henry Ford Hospital, Detroit, MI, USA.

Erdheim-Chester disease (ECD) is a rare, xanthogranulomatous, non-Langerhans cell histiocytosis with frequent systemic involvement. Although the diagnosis is based on characteristic histological and radiological findings, its identification can be challenging because of its heterogeneous presentation. Osteosclerosis of long bones, often associated with bone pain, is the most common initial manifestation, followed by extraskeletal manifestations in approximately 50% of cases. There is no standard treatment for ECD, although recommendations have been made on the basis of small studies. A systematic approach to the diagnosis of ECD is important, because its manifestations may be life-threatening and may require specific management. We report an atypical presentation of ECD, with early cardiac, renal, and central nervous system involvement, and only late skeletal manifestations.

Nephrology

Rocco MV, Chapman A, Chertow GM, Cohen D, Chen J, Cutler JA, Diamond MJ, Freedman BI, Hawfield A, Judd E, Killeen AA, Kirchner K, Lewis CE, Pajewski NM, Wall BM, and **Yee J**. Chronic kidney disease classification in systolic blood pressure intervention trial: Comparison using modification of diet in renal disease and ckd-epidemiology collaboration definitions *Am J Nephrol* 2016; 44(2):130-140. PMID: 27513312. Article Request Form

Wake Forest School of Medicine, Winston-Salem, N.C., USA.

BACKGROUND: Interventional trials have used either the Modification of Diet in Renal Disease (MDRD) or chronic kidney disease (CKD)-Epidemiology Collaboration (CKD-EPI) equation for determination of estimated glomerular filtration rate (eGFR) to define whether participants have stages 3-5 CKD. The equation used to calculate eGFR may influence the number and characteristics of participants designated as having CKD. METHODS: We examined the classification of CKD at baseline using both equations in the Systolic Blood Pressure Intervention Trial (SPRINT). eGFR was calculated at baseline using fasting serum creatinine values from a central laboratory. RESULTS: Among 9,308 participants with baseline CKD classification using the 4-variable MDRD equation specified in the SPRINT protocol, 681 (7.3%) participants were reclassified to a less advanced CKD stage (higher eGFR) and 346 (3.7%) were reclassified to a more advanced CKD stage (lower eGFR) when the CKD-EPI equation was used to calculate eGFR. For eGFRs <90 ml/min/1.73 m2, participants <75 years were more likely to be reclassified to a less advanced CKD stage; this reclassification was more likely to occur in non-blacks rather than blacks. Participants aged >/=75 years were more likely to be reclassified to a more advanced than a less advanced CKD stage, regardless of baseline CKD stage. Reclassification of baseline CKD status (eGFR <60 ml/min/1.73 m2) occurred in 3% of participants. CONCLUSIONS: Use of the MDRD equation led to a higher percentage of participants being classified as having CKD stages 3-4. Younger and non-black participants were more likely to be reclassified as not having CKD using the CKD-EPI equation.

Nephrology

Townsend RR, Chang TI, Cohen DL, Cushman WC, Evans GW, Glasser SP, Haley WE, Olney C, Oparil S, Del Pinto R, Pisoni R, Taylor AA, **Umanath K**, Wright JT, Jr., and Yeboah J. Orthostatic changes in systolic blood pressure among SPRINT participants at baseline *J Am Soc Hypertens* 2016;PMID: 27665708. Full Text

Department of Medicine, Perelman School of Medicine, University of Pennsylvania, Philadelphia PA, USA. Electronic address: townsend@upenn.edu.
Department of Medicine, Stanford University School of Medicine, Palo Alto, CA, USA.
Department of Medicine, Perelman School of Medicine, University of Pennsylvania, Philadelphia PA, USA.
Preventive Medicine Section and Medical Service, Veterans Affairs Medical Center, Memphis, TN, USA.
Department of Biostatistical Sciences, Wake Forest School of Medicine, Winston-Salem, NC, USA.
Department of Preventive Medicine, University of Alabama at Birmingham, Birmingham, AL, USA.
Division of Nephrology and Hypertension, Mayo Clinic, Jacksonville, FL, USA.
James A Haley Veterans Hospital, 13000 Bruce B. Downs Blvd, Tampa, FL, USA.
Department of Medicine, University of Alabama at Birmingham, Birmingham AL, USA.
Division of Internal Medicine, Department of Life, Health and Environmental Sciences, San Salvatore Hospital, University of L'Aquila, L'Aquila, Italy.
Department of Medicine, Medical University of South Carolina, Charleston, SC, USA.
Medical Care Line, Michael E. DeBakey VA Medical Center, Baylor College of Medicine, Houston, TX, USA.
Division of Nephrology and Hypertension, Henry Ford Hospital, Detroit, MI, USA.
Department of Medicine, Case Western Reserve University, Cleveland, OH, USA.
Heart and Vascular Center of Excellence, Wake Forest University School of Medicine, Winston-Salem, NC, USA.

Orthostatic changes in systolic blood pressure (SBP) impact cardiovascular outcomes. In this study, we aimed to determine the pattern of orthostatic systolic pressure changes in participants enrolled in the SBP Intervention Trial (SPRINT) at their baseline visit before randomization and sought to understand clinical factors predictive of these

changes. Of the 9323 participants enrolled in SPRINT, 8662 had complete data for these analyses. The SBP after 1 minute of standing was subtracted from the mean value of the three preceding seated SBP values. At the baseline visit, medical history, medications, anthropometric measures, and standard laboratory testing were undertaken. The mean age of SPRINT participants was 68 years, two-thirds were male, with 30% black, 11% Hispanic, and 55% Caucasian. The spectrum of SBP changes on standing demonstrated that increases in SBP were as common as declines, and about 5% of participants had an increase, and 5% had a decrease of >20 mm Hg in SBP upon standing. Female sex, taller height, more advanced kidney disease, current smoking, and several drug classes were associated with larger declines in BP upon standing, while black race, higher blood levels of glucose and sodium, and heavier weight were associated with more positive values of the change in BP upon standing. Our cross-sectional results show a significant spectrum of orthostatic SBP changes, reflecting known (eg, age) and less well-known (eg, kidney function) relationships that may be important considerations in determining the optimal target blood pressure in long-term outcomes of older hypertensive patients.

Nephrology

Wish JB, Charytan C, Chertow GM, Kalantar-Zadeh K, Kliger AS, Rubin RJ, **Yee J**, and Fishbane S. Introduction of biosimilar therapeutics into nephrology practice in the united states: Report of a scientific workshop sponsored by the national kidney foundation *Am J Kidney Dis* 2016;PMID: 27599628. Full Text

Indiana University Health, Indianapolis, IN. Electronic address: jaywish@earthlink.net.
New York Presbyterian-Queens, Queens, NY.
Stanford University, Stanford, CA.
University of California-Irvine, Orange, CA.
Yale New Haven Health System, New Haven, CT.
Georgetown University, Washington, DC.
Henry Ford Hospital, Detroit, MI.
Hofstra Northwell School of Medicine, Great Neck, NY.

Biosimilars are biologic medicines highly similar to the reference product with no meaningful clinical differences in terms of safety, purity, and potency. All biologic medicines are produced by living cells, resulting in an inherent heterogeneity in their higher order structures and post-translational modifications. In 2010, the US Congress enacted legislation to streamline the approval process for biosimilars of products losing patent protection, with the goal of decreasing costs and improving patient access to therapeutically important but expensive biologic agents. In 2015, the US Food and Drug Administration approved the first biosimilar agent through this pathway. Approval of additional biosimilar agents in the United States, including those used by nephrologists, is anticipated. Given the relative lack of knowledge regarding biosimilars and their approval process and a lack of trust by the nephrology community regarding their safety and efficacy, the National Kidney Foundation conducted a symposium, Introduction of Biosimilar Therapeutics Into Nephrology Practice in the U.S., September 17 to 18, 2015. Issues related to manufacturing, the regulatory approval process, interchangeability, substitution/switching, nomenclature, and clinician and patient awareness and acceptance were examined. This report summarizes the main discussions at the symposium, highlights several controversies, and makes recommendations related to public policy, professional and patient education, and research needs.

Neurology

Dehkordi AN, Kamali-Asl A, **Ewing JR**, and **Bagher-Ebadian H**. An adaptive model for direct estimation of extravascular-extracellular space in dynamic contrast-enhanced magnetic resonance imaging studies *Int J Radiat Oncol Biol Phys* 2016; 96(2s):E644. PMID: 27675247. Full Text Abstract

Shahid Beheshti University, Tehran, Iran (Islamic Republic of Korea); Henry Ford Hospital, Detroit, MI.
Shahid Beheshti University, Tehran, Iran (Islamic Republic of Korea).
Henry Ford Hospital, Detroit, MI; Oakland University, Rochester, MI.
Oakland University, Rochester, MI; Henry Ford Health System, Detroit, MI.

Neurology

Harms PW, Hocker TL, Zhao L, Chan MP, Andea AA, Wang M, Harms KL, Wang ML, **Carskadon S**, **Palanisamy N**, and Fullen DR. Loss of p16 expression and copy number changes of CDKN2A in a spectrum of spitzoid melanocytic lesions *Hum Pathol* 2016;PMID: 27569296. Full Text

Department of Pathology, University of Michigan Health System, Ann Arbor, MI, 48109, USA; Department of Dermatology, University of Michigan Health System, Ann Arbor, MI, 48109, USA. Electronic address: paulharm@med.umich.edu.
Department of Pathology, University of Michigan Health System, Ann Arbor, MI, 48109, USA.
Department of Biostatistics, University of Michigan Health System, Ann Arbor, MI, 48109, USA.
Department of Pathology, University of Michigan Health System, Ann Arbor, MI, 48109, USA; Department of Dermatology, University of Michigan Health System, Ann Arbor, MI, 48109, USA.
Department of Dermatology, University of Michigan Health System, Ann Arbor, MI, 48109, USA.
Vattikutti Urology Institute, Department of Urology, Henry Ford Health System, Detroit, MI, 48202, USA.

Spitzoid melanocytic lesions, including Spitz nevi (benign), spitzoid melanoma (malignant), and borderline atypical Spitz tumors (ASTs), frequently present challenges for accurate diagnosis and prognosis. Evaluation for loss of the tumor suppressor p16, encoded by CDKN2A gene on chromosome 9p21.3, has been proposed to be useful for evaluation of spitzoid melanocytic lesions. However, reports on the utility of p16 immunohistochemistry for spitzoid lesions have been conflicting, and few studies have directly compared p16 immunohistochemistry with fluorescence in situ hybridization (FISH) for CDKN2A genomic status. We analyzed a spectrum of benign (n=24), borderline (n=27), and malignant (n=19) spitzoid lesions for p16 protein expression by immunohistochemistry and CDKN2A copy number by FISH. Immunohistochemistry was evaluated by two scoring methods: h-score and two-tiered score (positive or negative for p16 loss). By immunohistochemistry, loss of p16 expression was not observed in Spitz nevi (0/24), but was seen in ASTs (7/27, 26%) and spitzoid melanomas (3/19, 16%). By h-score, p16 expression was significantly higher in Spitz nevi relative to ASTs or spitzoid melanomas. Similarly, copy number aberrations of CDKN2A by FISH were absent in Spitz nevi, but were found in 2/21 (9.5%) ASTs and 4/12 (33%) spitzoid melanomas. Our findings from this large cohort suggest p16 aberrations are highly specific for borderline and malignant spitzoid neoplasms relative to Spitz nevi. Similar to ASTs, p16 loss in spitzoid melanomas may occur in the presence or absence of genomic CDKN2A loss.

Neurology

Kokeny P, Cheng YC, Liu S, Xie H, and **Jiang Q**. Quantifications of in vivo labeled stem cells based on measurements of magnetic moments *Magn Reson Imaging* 2016;PMID: 27594530. Full Text

Department of Radiology, Wayne State University, Detroit, MI 48201. Electronic address: kokenymri@gmail.com.
Department of Radiology, Wayne State University, Detroit, MI 48201. Electronic address: yxc16@wayne.edu.
The MRI Institute for Biomedical Research, 761 Lucerne Avenue, Waterloo, ON, Canada.
Department of Physics, Wayne State University, Detroit, MI 48201.
Department of Neurology, Henry Ford Health System, Detroit, MI 48202.

Cells labeled by super paramagnetic iron-oxide (SPIO) nanoparticles are more easily seen in gradient echo MR images, but it has not been shown that the amount of nanoparticles or the number of cells can be directly quantified from MR images. This work utilizes a previously developed and improved Complex Image Summation around a Spherical or Cylindrical Object (CISSCO) method to quantify the magnetic moments of several clusters of SPIO nanoparticle labeled cells from archived rat brain images. With the knowledge of mass magnetization of the cell labeling agent and cell iron uptake, the number of cells in each nanoparticle cluster can be determined. Using a high pass filter with a reasonable size has little effect on each measured magnetic moment from the CISSCO method. These procedures and quantitative results may help improve the efficacy of cell-based treatments in vivo.

Neurology

**Mahajan A**, and **Sidiropoulos C**. Myoclonus dystonia: A report of two rare mutations *Mov Disord* 2016; 31:S191. PMID: Not assigned. Abstract

A. Mahajan, Detroit, United States

Objective: To present the results of genetic analysis of three patients who presented to our clinic with Myoclonus Dystonia. Background: Myoclonus Dystonia (MD) is a rare autosomal dominant movement disorder characterized by myoclonic jerks and dystonia, often first seen in patients in their childhood and early adolescence. Most reported mutations are located in the E-sarcoglycan (SGCE) gene in chromosome 7. Allele specific methylation is primarily responsible for paternal imprinting. A number of mutations of the SGCE gene have been reported in literature. We present two siblings with genetically confirmed MD and a 709C>T mutation and another patient with a c.463+5del in the SGCE gene. Methods: Samples were collected from 3 patients who presented to the Movement disorders clinic at Henry Ford West Bloomfield Hospital, Michigan with prominent myoclonus. Analysis was performed by PCR amplification of highly purified genomic DNA, followed by automated bi-directional DNA sequencing of the coding

region (12 exons, 1386 bp) of the SGCE gene. In exons where one of the strands was not informative for confirmation, uni-directional sequencing with alternative dye chemistry was used for confirmation. Further, a minimum of 20 bases of intronic DNA surrounding each exon were also sequenced. Results: Mutation 1: Analysis of two patients' SGCE gene identified a C>T transition at nucleotide 709 and codon 237. The amino acid change identified was arginine>OPA (Stop codon). Mutation 2: Analysis of the patient's SGCE gene identified a 1 bp c.463+5del. Conclusions: The first mutation has been reported in the literature and has been associated with the development or predisposition to developing myoclonus dystonia. However, to the best of our knowledge, this is the first one to be reported in North America. The second mutation has never been reported before. Patients who present with pure myoclonus to Movement Disorders Centers should be offered genetic screening for SGCE mutations.

Neurology
**Romero C**, **Monu S**, **Cabral G**, **Knight R**, and **Carretero O**. OS 21-02 Connecting tubule-glomerular feedback (ctgf) in renal hemodynamics and blood pressure regulation after unilateral nephrectomy (unx) *J Hypertens* 2016; 34 Suppl 1:e235. PMID: 27643022. Full Text

1Hypertension and Vascular Research Division, Henry Ford Hospital, Detroit (MI), U.S.A. 2MRI core, Department of Neurology, Henry Ford Hospital, Detroit (MI), U.S.A.

OBJECTIVE: Renal hemodynamics is critical for regulation of glomerular filtration (GFR), sodium excretion and blood pressure (BP), and it depends on myogenic response, tubuloglomerular feedback (TGF) and connecting tubule-glomerular feedback (CTGF). CTGF dilates afferent arteriole in response to high sodium in connecting tubule (CNT), counteracting and resetting TGF; and increasing the plasma flow and glomerular pressure favoring sodium excretion. CTGF is initiated by epithelial sodium channel (ENaC) activation in CNT and inhibited by ENaC blocker Benzamil. Unilateral nephrectomy (UNx) is accompanied by TGF resetting, increase in renal blood flow (RBF) and single nephron GFR in the remnant kidney, without any changes in systemic BP. We evaluated CTGF role in BP regulation and TGF resetting after UNx. DESIGN AND METHOD: UNx was performed on Sprague-Dawley rats and 24 h later TGF was evaluated in vivo by renal micropuncture using stop flow pressure (Psf) techniques. CTGF was evaluated by intratubularly adding Benzamil during the TGF response. Another set of animals received chronic kidney infusion of Benzamil that started 1 week before UNx. Renal blood flow (RBF) was measured by arterial spin labeling-MRI 24 h before and 24 h after the UNx. Direct BP measurement was performed before and 3 weeks after the UNx. RESULTS: After UNx, TGF resetting was observed (delta-Psf 8 +/- 1 vs. 1 +/- 1 mmHg $p < 0.05$, Sham vs. Unx) and that was inhibited by Benzamil. RBF increased after the UNx in comparison to sham and this increase was inhibited by chronic infusion of Benzamil (Sham: 305 +/- 59; UNx: 456 +/- 34; UNx + Benzamil 346 +/- 64 ml/min/100 g tissue $p < 0.002$). Mean BP values were not different between the vehicle or Benzamil infused rats before the UNx, however 3 weeks after the UNx, Benzamil infused rats showed higher mean BP values than vehicle (88 +/- 0.3 vs. 97 +/- 4 mmHg, $p < 0.01$). CONCLUSIONS: CTGF participates in TGF resetting and BP regulation after UNx. CTGF impairment could be a potential cause of hypertension.

Neurology
Vithanarachchi SM, Foley CD, Trimpin S, **Ewing JR**, Ali MM, and Allen MJ. Myelin-targeted, texaphyrin-based multimodal imaging agent for magnetic resonance and optical imaging *Contrast Media Mol Imaging* 2016;PMID: 27596704. Full Text

Department of Chemistry, Wayne State University, 5101 Cass Avenue, Detroit, MI, 48202, MI, USA.
Department of Chemistry, University of Colombo, Colombo 03, Sri Lanka.
Department of Neurology, Henry Ford Hospital, Detroit, MI, 48202, USA.
Department of Chemistry, Wayne State University, 5101 Cass Avenue, Detroit, MI, 48202, MI, USA.
mallen@chem.wayne.edu.

Reliable methods of imaging myelin are essential to investigate the causes of demyelination and to study drugs that promote remyelination. Myelin-specific compounds can be developed into imaging probes to detect myelin with various imaging techniques. The development of multimodal myelin-specific imaging probes enables the use of orthogonal imaging techniques to accurately visualize myelin content and validate experimental results. Here, we describe the synthesis and application of multimodal myelin-specific imaging agents for light microscopy and magnetic resonance imaging. The imaging agents were synthesized by incorporating the structural features of luxol fast blue MBS, a myelin-specific histological stain, into texaphyrins coordinated to GdIII . These new complexes demonstrated absorption of visible light, emission of near-IR light, and relaxivity values greater than clinically approved contrast agents for magnetic resonance imaging. These properties enable the use of optical imaging and magnetic resonance imaging for visualization of myelin. We performed section- and en block-staining of ex vivo mouse brains to investigate the specificity for myelin of the new compounds. Images obtained from light microscopy

and magnetic resonance imaging demonstrate that our complexes are retained in white matter structures and enable detection of myelin. Copyright (c) 2016 John Wiley & Sons, Ltd.

Neurology

**Wasade VS**, Balki I, **Bowyer SM**, **Gaddam S**, **Mohammadi-Nejad AR**, **Nazem-Zadeh MR**, **Soltanian-Zadeh H**, **Zillgitt A**, and **Spanaki-Varelas M**. Controllable yawning expressed as focal seizures of frontal lobe epilepsy *Epilepsy Behav Case Rep* 2016; 6:61-63. PMID: 27668178. Full Text

Department of Neurology, Henry Ford Health System, Detroit, MI 48202, USA.
University of Toronto, Ontario M5S 1A1, Canada.
Department of Radiology (Image Analysis Laboratory), Henry Ford Health System, Detroit, MI 48202, USA; Control and Intelligent Processing Center of Excellence (CIPCE), School of Electrical and Computer Engineering, University of Tehran, Tehran 14395-515, Iran.
Department of Radiology (Image Analysis Laboratory), Henry Ford Health System, Detroit, MI 48202, USA.

Excessive yawning was described in some neurological conditions as part of periictal or ictal manifestations of epilepsy, most commonly temporal lobe. We present the first case of controllable yawning as a primary seizure semiology with dominant frontal lobe involvement in a 20-year-old man. Video electroencephalography recorded 8 yawning episodes accompanied with right arm movement correlating with rhythmic diffuse theta range activity with left hemispheric predominance. Magnetoencephalography coherence source imaging was consistent with persistent neuronal networks with areas of high coherence reliably present over the left lateral orbitofrontal region. Epileptogenic areas may have widespread networks involving the dominant frontal lobe in unique symptomatogenic areas.

Neuropsychology

Goldenberg PC, Adler BJ, Parrott A, Anixt J, Mason K, **Phillips J**, Cooper DS, Ware SM, and Marino BS. High burden of genetic conditions diagnosed in a cardiac neurodevelopmental clinic *Cardiol Young* 2016:1-8. PMID: 27641144.
Article Request Form

1Divison of Medical Genetics,Massachusetts General Hospital,Boston,Massachusetts,United States of America.
2The Heart Institute,Cincinnati Children's Hospital Medical Center,Cincinnati, Ohio,United States of America.
3Division of Cardiology,Cincinnati Children's Hospital Medical Center Cincinnati,Ohio,United States of America.
4Division of Developmental and Behavioral Pediatrics,Cincinnati Children's Hospital,Cincinnati,Ohio,United States of America.
5Division of Neuropsychology,Henry Ford Hospital,Detroit,Michigan,United States of America.
6Departments of Pediatrics and Medical and Molecular Genetics,Indiana University School of Medicine,Indianapolis,Indiana,United States of America.
7Division of Cardiology,Lurie Children's Hospital,Chicago,Illinois,United States of America.

BACKGROUND: There is a known high prevalence of genetic and clinical syndrome diagnoses in the paediatric cardiac population. These disorders often have multisystem effects, which may have an important impact on neurodevelopmental outcomes. Taken together, these facts suggest that patients and families may benefit from consultation by genetic specialists in a cardiac neurodevelopmental clinic. OBJECTIVE: This study assessed the burden of genetic disorders and utility of genetics evaluation in a cardiac neurodevelopmental clinic. METHODS: A retrospective chart review was conducted of patients evaluated in a cardiac neurodevelopmental clinic from 6 December, 2011 to 16 April, 2013. All patients were seen by a cardiovascular geneticist with genetic counselling support. RESULTS: A total of 214 patients were included in this study; 64 of these patients had a pre-existing genetic or syndromic diagnosis. Following genetics evaluation, an additional 19 were given a new clinical or laboratory-confirmed genetic diagnosis including environmental such as teratogenic exposures, malformation associations, chromosomal disorders, and single-gene disorders. Genetic testing was recommended for 112 patients; radiological imaging to screen for congenital anomalies for 17 patients; subspecialist medical referrals for 73 patients; and non-genetic clinical laboratory testing for 14 patients. Syndrome-specific guidelines were available and followed for 25 patients with known diagnosis. American Academy of Pediatrics Red Book asplenia guideline recommendations were given for five heterotaxy patients, and family-based cardiac screening was recommended for 23 families affected by left ventricular outflow tract obstruction. CONCLUSION: Genetics involvement in a cardiac neurodevelopmental clinic is helpful in identifying new unifying diagnoses and providing syndrome-specific care, which may impact the patient's overall health status and neurodevelopmental outcome.

Neurosurgery
**Boyce-Fappiano D**, **Elibe E**, **Lee IY**, **Rock J**, **Siddiqui MS**, and **Siddiqui F**. Combined stereotactic radiosurgery and percutaneous vertebral augmentation for pain control in pathological vertebral compression fractures *Int J Radiat Oncol Biol Phys* 2016; 96(2s):E87. PMID: 27675486. Full Text Abstract

Henry Ford Health System, Detroit, MI.

Neurosurgery
**Boyce-Fappiano D**, **Elibe E**, **Lee IY**, **Rock J**, **Siddiqui MS**, and **Siddiqui F**. Single-fraction stereotactic radiosurgery for renal cell carcinoma spine metastasis *Int J Radiat Oncol Biol Phys* 2016; 96(2s):E519. PMID: 27674908. Full Text Abstract

Henry Ford Health System, Detroit, MI.

Neurosurgery
Cloughesy TF, Aghi M, Bota D, Chen C, Elder JB, **Kalkanis SN**, Kaptain GJ, Kesari S, Landolfi J, **Mikkelsen T**, Portnow J, Robbins JM, Ostertag D, Chu A, Huang T, and Vogelbaum MA. Prior radiation in subjects who were treated with toca 511 and toca fc across 3 toca 511 phase 1 trials *Int J Radiat Oncol Biol Phys* 2016; 96(2s):E66-e67. PMID: 27675287. Full Text Abstract

UCLA, Los Angeles, CA.
UCSF, San Francisco, CA.
UCI, Irvine, CA.
University of California, San Diego, La Jolla, CA.
Ohio State University, Columbus, OH.
Henry Ford Hospital, Detroit, MI.
Hackensack University Medical Center, Hackensack, NJ.
UCSD, San Diego, CA; John Wayne Cancer Institute, Santa Monica, CA.
JFK Medical Center, Edison, NJ.
City of Hope, Duarte, CA.
Tocagen Inc., San Diego, CA.
Cleveland Clinic Foundation, Cleveland, OH.

Neurosurgery
**Elibe E**, **Boyce-Fappiano D**, **Walker EM**, **Lee IY**, **Rock J**, **Siddiqui S**, and **Siddiqui F**. Significance of hormone therapy and bisphosphonate use on vertebral compression fracture (vcf) incidence following spine stereotactic body radiation therapy (sbrt) for breast cancer metastases *Int J Radiat Oncol Biol Phys* 2016; 96(2s):E509. PMID: 27674881. Full Text Abstract

Henry Ford Health System, Detroit, MI.

Neurosurgery
**Hong X**, **Meng Y**, and **Kalkanis SN**. Serum proteins are extracted along with monolayer cells in plasticware and interfere with protein analysis *J Biol Methods* 2016; 3(4)PMID: 27631018. Full Text

Department of Neurosurgery, Henry Ford Health System, Detroit, Michigan 48202, USA.

Washing and lysing monolayer cells directly from cell culture plasticware is a commonly used method for protein extraction. We found that multiple protein bands were enriched in samples with low cell numbers from the 6-well plate cultures. These proteins contributed to the overestimation of cell proteins and led to the uneven protein loading in Western blotting analysis. In Coomassie blue stained SDS-PAGE gels, the main enriched protein band is about 69 kDa and it makes up 13.6% of total protein from 104 U251n cells. Analyzed by mass spectrometry, we identified two of the enriched proteins: bovine serum albumin and bovine serum transferrin. We further observed that serum proteins could be extracted from other cell culture plates, dishes and flasks even after washing the cells 3 times with PBS. A total of 2.3 mg of protein was collected from a single well of the 6-well plate. A trace amount of the protein band was still visible after washing the cells 5 times with PBS. Thus, serum proteins should be considered if extracting proteins from plasticware, especially for samples with low cell numbers.

Neurosurgery
Jolly DJ, Robbins JM, Ostertag D, Ibanez C, Kasahara N, Gruber H, **Kalkanis SN**, Vogelbaum M, Aghi MK, Cloughesy T, Chu A, Das A, and Skillings J. Ascending dose trials of a retroviral replicating vector (toca 511) in patients with recurrent high-grade glioma: Clinical update, molecular analyses, and proposed mechanism of action *Mol Ther* 2016; 24:S27-S27. PMID: Not assigned. Abstract

Neurosurgery
**Lim S**, Carabini LM, Kim RD, Khanna R, Dahdaleh NS, and Smith ZA. Evaluation of ASA classification as thirty-day morbidity predictor after single-level elective anterior cervical discectomy and fusion *Spine J* 2016;PMID: 27669670. Full Text

Department of Neurological Surgery, Henry Ford Hospital, 2799 W Grand Blvd, Detoirt, MI 48202.. Electronic address: slim2@hfhs.org.
Department of Neurological Surgery, Feinberg School of Medicine, Northwestern University, NMH/Arkes Family Pavilion Suite 2210, 676 N Saint Clair, Chicago, IL 60611.; Department of Anesthesiology, Feinberg School of Medicine, Northwestern University, NMH/Arkes Family Pavilion Suite 2210, 676 N Saint Clair, Chicago, IL 60611.. Electronic address: l-carabini@northwestern.edu.
Department of Surgery, University of Rochester, 601 Elmwood Ave, Rochester, NY 14620.. Electronic address: Bobby.Kim@my.rfums.org.
Department of Neurological Surgery, Feinberg School of Medicine, Northwestern University, NMH/Arkes Family Pavilion Suite 2210, 676 N Saint Clair, Chicago, IL 60611.. Electronic address: ryan-khanna@fsm.northwestern.edu.
Department of Neurological Surgery, Feinberg School of Medicine, Northwestern University, NMH/Arkes Family Pavilion Suite 2210, 676 N Saint Clair, Chicago, IL 60611.. Electronic address: nader.dahdaleh@northwestern.edu.
Department of Neurological Surgery, Feinberg School of Medicine, Northwestern University, NMH/Arkes Family Pavilion Suite 2210, 676 N Saint Clair, Chicago, IL 60611.. Electronic address: zsmith1@nm.org.

BACKGROUND CONTEXT: Higher ASA classification is a known predictor of postoperative complication in diverse surgical settings. However, its predictive value is not established in single-level elective anterior cervical discectomy and fusion (SLE-ACDF). PURPOSE: To evaluate the predictive value of American Society of Anesthesiology (ASA) classification system on 30-day morbidity following SLE-ACDF STUDY DESIGN/SETTING: Patients who underwent SLE-ACDF between 2011-2013 were selected from the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database. PATIENT SAMPLE: 6,148 patients selected from 2011-2013 ACS NSQIP database OUTCOME MEASURES: All outcomes are self-report measures as tracked by dedicated clinical reviewers via prospective review of inpatient charts, outpatient clinic visits, and direct contact with the surgical team. METHODS: Propensity score-matching and multiple logistic regression analyses were performed to evaluate ASA classification as 30-day morbidity predictor. This study has no financial conflict, and has no potential conflict of interest to disclose. RESULTS: 6148 patients were analyzed in this study. Patients in the ASA >2 cohort had higher incidence of comorbidities and postoperative complications (overall complication, pneumonia, unplanned intubation, ventilator dependent > 48 hours, CVA/stroke, catastrophic outcome, and airway complication). Propensity score matching yielded 1628 pairs of well-matched patients. Multivariable analyses with the propensity-score matched dataset revealed the following associations between ASA class > 2 and 30-day outcomes: any complication (OR 0.82, 95% CI 0.48-1.41), pneumonia (OR 1.22, 95% CI 0.33-4.56), unplanned intubation (OR 1.49, 95% CI 0.41-5.36), ventilator > 48 hours (OR 5.92, 95% CI 0.69-50.96), catastrophic outcome (OR 1.02, 95% CI 0.39-2.71) and airway complication (OR 2.21, 95% CI 0.67-7.29). CONCLUSIONS: Although we did not detect associations between ASA class > 2 and adverse 30-day outcomes following SLE-ACDF, imprecision of estimates precludes definitive inferences. While ASA classification allows simple assessment of patients' physiological status, their overall perioperative risk factors need to be considered collectively for adequate optimization and improved outcomes in SLE-ACDF.

Neurosurgery
**Pabaney AH**, **Rammo RA**, **Tahir RA**, and **Seyfried D**. Development of a de novo AVM following ischemic stroke: Case report and review of the current literature *World Neurosurg* 2016;PMID: 27671884. Full Text

Department of Neurosurgery, Henry Ford Hospital, Detroit, Michigan. Electronic address: ahpabaney@gmail.com.

BACKGROUND: Arteriovenous Malformations (AVMs) are hypothesized to be static, congenital lesions developing as early as 4 weeks of fetal life. New literature has shown that AVMs may represent dynamic and reactive vascular lesions arising from cerebral infarction, inflammation, or trauma. A literature search reveals 17 previously reported cases of new AVM formation after previous negative imaging studies. This reactive development or "second hit" theory suggests that at a molecular level, growth factors may play a vital role in aberrant angiogenesis and

maturation of an arterio-venous fistula into an AVM. CASE DESCRIPTION: A 52 year old female presented with a ruptured left frontal AVM demonstrated by CTA and DSA. The patient had suffered an acute ischemic stroke in the similar cerebral vascular territory 8 years prior due to left internal carotid artery (ICA) occlusion. Detailed neuroimaging at that time failed to reveal any vascular malformation, suggesting that the AVM might have developed in response to initial vascular insult. CONCLUSIONS: We believe that there might exist a subset of AVMs that display dynamic characteristics and could potentially appear, grow or resolve spontaneously without intervention, especially in the presence of local growth factors and molecular signaling cascades. When combined with a previous cerebral insult such as stroke, trauma, or inflammation, de novo AVM formation may represent a "second hit" with abnormal angiogenesis and vessel formation.

Obstetrics, Gynecology and Women's Health Services
**Alrahmani L**, **Adekola H**, and **Awonuga A**. Trauma in multi-fetal gestations *Reprod Sci* 2016; 23:111A-111A. PMID: Not assigned. Abstract

Obstetrics, Gynecology and Women's Health Services
**Lee JK**, **Mahan M**, **Khan N**, **Hanna R**, and **Elshaikh MA**. Survival outcomes in women with international federation of gynecology and obstetrics stage IIIC2 endometrial carcinoma *Int J Radiat Oncol Biol Phys* 2016; 96(2s):E308. PMID: 27674336. Full Text Abstract

Henry Ford Health System, Detroit, MI.
Henry Ford Hospital, Lansing, MI.

Obstetrics, Gynecology and Women's Health Services
**Munkarah A**, **Hamid S**, **Chhina J**, Mert I, **Jackson L**, **Hensley-Alford S**, **Chitale D**, **Giri S**, and **Rattan R**. Targeting of free fatty acid signaling in ovarian cancer may serve as a potential therapeutic approach *Clin Cancer Res* 2016; 22PMID: Not assigned. Abstract

Recent studies have revealed an association between adipocyte driven free fatty acids (FFA) and the aggressiveness of epithelial ovarian cancer (EOC). Adipocyte derived free fatty acids (FFA) seem to promote epithelial ovarian cancer (EOC) growth and progression by acting as mitochondrial fuel source to support the energy requirements of EOC cells. Apart from acting as a fuel source, FFA may also enhance tumor growth through other signaling pathways that can promote proliferation and regulate metabolism. Recently, a family of FFA activated G-protein coupled receptors (FFAR/GPCRs) was identified, including: FFAR1/GPR40, FFAR2/GPR42, FFAR3/GPR41, FFAR4/GPR120 and GPR84. Using RT-PCR, we have found that exposing EOC cells to adipocytes results in overexpression of FFAR1/GPR40 in multiple ovarian cancer cell lines (ID8, A2780, C200, OVCAR3 and SKOV3). In mRNA extracted from formalin-fixed paraffin embedded tumor specimens, approximately 80% of high-grade serous ovarian carcinomas exhibited increased FFAR1 expression. Additionally, analysis of TCGA database revealed that patients with tumors exhibiting increased mRNA expression of FFAR1/GPR40 had poor overall survival and progression free survival. We have also found that targeting FFAR1 using its specific antagonist GW1100 inhibited the proliferation of A2780, ID8, C200, OVCAR3 and SKOV3 cell lines and resulted in downstream inhibition of insulin secretion and the Akt signaling pathway. On the other hand, treatment of the same cells with the FFAR1 agonist ,CAY10587, had no effect on proliferation. Thus, we conclude that FFAR1 may play an important role in the regulation of FFA mediated EOC cell proliferation. Targeting of FFAR1/GPR40 may be an attractive strategy in EOC, particularly for EOC patients presenting with high adiposity.

Orthopaedics
**Chiu MD**, Vasileff WK, **Moutzouros V**, **Van Holsbeeck M**, **Parsons TW**, and **Mott MP**. Bilateral and simultaneous septic arthritis of the acromioclavicular joint in an immunocompromised patient: A case report and review of the literature *Current Orthopaedic Practice* 2016; 27(5):570-574. PMID: Not assigned. Full Text

W.K. Vasileff, Department of Orthopaedics, Ohio State University, 725 Prior Hall, Columbus, United States

Otolaryngology - Head and Neck Surgery
**Al Feghali KA**, Ghanem AI, **Chang S**, **Ghanem T**, **Burmeister C**, **Keller C**, and **Siddiqui F**. Smoking predicts for worse pathological features in oral cavity squamous cell carcinoma *Int J Radiat Oncol Biol Phys* 2016; 96(2s):E386. PMID: 27674550. Full Text Abstract

Henry Ford Health System, Detroit, MI; American University of Beirut Medical Center, Beirut, Lebanon.
Alexandria University, Alexandria, Egypt.
Henry Ford Health System, Detroit, MI.

Otolaryngology - Head and Neck Surgery
Choi SH, Terrell JE, Bradford CR, **Ghanem T**, Spector ME, Wolf GT, Lipkus IM, and Duffy SA. Does quitting smoking make a difference among newly diagnosed head and neck cancer patients? *Nicotine Tob Res* 2016;PMID: 27613928. Full Text

College of Nursing, Michigan State University, East Lansing, MI;
University of Michigan Health System, Ann Arbor, MI;
Henry Ford Hospital, Detroit, MI;
School of Nursing, Duke University, Durham, NC;
College of Nursing, Ohio State University, Columbus, OH; Center for Clinical Management Research, VA Ann Arbor Healthcare System, Ann Arbor, MI duffy.278@osu.edu.

INTRODUCTION: To determine if smoking after a cancer diagnosis makes a difference in mortality among newly diagnosed head and neck cancer patients. METHODS: Longitudinal data were collected from newly diagnosed head and neck cancer patients with a median follow-up time of 1627 days (N = 590). Mortality was censored at 8 years or September 1, 2011, whichever came first. Based on smoking status, all patients were categorized into four groups: continuing smokers, quitters, former smokers, or never-smokers. A broad range of covariates were included in the analyses. Kaplan-Meier curves, bivariate and multivariate Cox proportional hazards models were constructed. RESULTS: Eight-year overall mortality and cancer-specific mortality were 40.5% (239/590) and 25.4% (150/590), respectively. Smoking status after a cancer diagnosis predicted overall mortality and cancer-specific mortality. Compared to never-smokers, continuing smokers had the highest hazard ratio (HR) of dying from all causes (HR = 2.71, 95% confidence interval [CI] = 1.48-4.98). Those who smoked at diagnosis, but quit and did not relapse-quitters-had an improved hazard ratio of dying (HR = 2.38, 95% CI = 1.29-4.36) and former smokers at diagnosis with no relapse after diagnosis-former smokers-had the lowest hazard ratio of dying from all causes (HR = 1.68, 95% CI = 1.12-2.56). Similarly, quitters had a slightly higher hazard ratio of dying from cancer-specific reasons (HR = 2.38, 95% CI = 1.13-5.01) than never-smokers, which was similar to current smokers (HR = 2.07, 95% CI = 0.96-4.47), followed by former smokers (HR = 1.70, 95% CI = 1.00-2.89). CONCLUSIONS: Compared to never-smokers, continuing smokers have the highest HR of overall mortality followed by quitters and former smokers, which indicates that smoking cessation, even after a cancer diagnosis, may improve overall mortality among newly diagnosed head and neck cancer patients. Health care providers should consider incorporating smoking cessation interventions into standard cancer treatment to improve survival among this population. IMPLICATIONS: Using prospective observational longitudinal data from 590 head and neck cancer patients, this study showed that continuing smokers have the highest overall mortality relative to never-smokers, which indicates that smoking cessation, even after a cancer diagnosis, may have beneficial effects on long-term overall mortality. Health care providers should consider incorporating smoking cessation interventions into standard cancer treatment to improve survival among this population.

Otolaryngology - Head and Neck Surgery
**Ghanem AI**, **Al Feghali KA**, **Chang S**, **Ghanem T**, **Burmeister C**, and **Siddiqui F**. Clinicopathologic features and survival outcomes among young patients with squamous cell carcinoma of the oral cavity *Int J Radiat Oncol Biol Phys* 2016; 96(2s):E364. PMID: 27674490. Full Text Abstract

Henry Ford Health System, Detroit, MI; Alexandria University, Alexandria, Egypt.
Henry Ford Health system, Detroit, MI; American University of Beirut Medical Center, Beirut, Lebanon.
Henry Ford Health System, Detroit, MI.

Otolaryngology - Head and Neck Surgery
**Swegal W**, and **Chang S**. Tumor board checklists affect pretreatment clinic referral patterns *Int J Rad Onc Biol Phys* 2016; 94(4):902-903. PMID: Not assigned. Abstract

Purpose/Objective(s) Checklists have been utilized within the surgical community in recent years as a way to ensure that certain crucial steps or processes are completed. They are a process-related effort to ensure quality patient care. Patients with newly diagnosed head and neck cancer require multidisciplinary preoperative evaluation and counselling prior to their treatment, and postsurgical patients require proper review for referrals for adjuvant treatments. A checklist system was implemented at our tumor board during 2013 in order to improve quality of care

and adherence to National Comprehensive Cancer Network guidelines. Materials/Methods We conducted a retrospective analysis of newly diagnosed head and neck cancer patients presented at our institution's multidisciplinary tumor board between the years of 2010 and 2015. The year 2013 was considered the point when we started to use checklists during the tumor board discussion. We compared 100 newly diagnosed patients before the checklist was implemented to 100 patients afterward. Compliance with tumor board recommendations and pretreatment evaluation within 1 month were compared between groups. Pretreatment evaluation included appointments with a clinical psychologist, speech language pathologist, and nutritionist. Analysis was also performed on referral for audiogram and dental evaluation, as well as whether patients were reviewed for clinical trials. Results Preliminary analysis suggests that appropriate and completed referrals to medical oncology were similar between the 2 groups ( P ≥.99). This was similar to radiation oncology, where 93% patients in the prechecklist era and 100% patients from the postchecklist group were correctly referred or not referred ( P =0.3). Difference in referral patterns to pretreatment evaluation and counseling trended toward significant. Referral patterns for speech language pathology ( P =.19), clinical psychology ( P =.25), and nutrition ( P =.06) all trended toward a significant difference with overall more appropriate referrals occurring after the checklist was implemented. This was a similar trend with optimization clinic ( P =.23) and audiology ( P =.06). Appropriate referrals to dental ( P =.006) were significantly increased with the implementation of the checklist, and a great proportion of patients were reviewed for clinical trials ( P =.002). Conclusion The use of the checklist during the tumor board presentation helped to increase follow through and adherence to recommendations for pretreatment evaluation. We hope to further highlight the benefits of the tumor board checklist with review of all newly diagnosed head and neck patients prior to and after implementation.

Pathology

**Al Feghali KA**, Ghanem AI, **Chang S**, **Ghanem T**, **Burmeister C**, **Keller C**, and **Siddiqui F**. Smoking predicts for worse pathological features in oral cavity squamous cell carcinoma *Int J Radiat Oncol Biol Phys* 2016; 96(2s):E386. PMID: 27674550. Full Text Abstract

Henry Ford Health System, Detroit, MI; American University of Beirut Medical Center, Beirut, Lebanon.
Alexandria University, Alexandria, Egypt.
Henry Ford Health System, Detroit, MI.

Pathology

Choi SH, Terrell JE, Bradford CR, **Ghanem T**, Spector ME, Wolf GT, Lipkus IM, and Duffy SA. Does quitting smoking make a difference among newly diagnosed head and neck cancer patients? *Nicotine Tob Res* 2016;PMID: 27613928. Full Text

College of Nursing, Michigan State University, East Lansing, MI;
University of Michigan Health System, Ann Arbor, MI;
Henry Ford Hospital, Detroit, MI;
School of Nursing, Duke University, Durham, NC;
College of Nursing, Ohio State University, Columbus, OH; Center for Clinical Management Research, VA Ann Arbor Healthcare System, Ann Arbor, MI duffy.278@osu.edu.

INTRODUCTION: To determine if smoking after a cancer diagnosis makes a difference in mortality among newly diagnosed head and neck cancer patients. METHODS: Longitudinal data were collected from newly diagnosed head and neck cancer patients with a median follow-up time of 1627 days (N = 590). Mortality was censored at 8 years or September 1, 2011, whichever came first. Based on smoking status, all patients were categorized into four groups: continuing smokers, quitters, former smokers, or never-smokers. A broad range of covariates were included in the analyses. Kaplan-Meier curves, bivariate and multivariate Cox proportional hazards models were constructed. RESULTS: Eight-year overall mortality and cancer-specific mortality were 40.5% (239/590) and 25.4% (150/590), respectively. Smoking status after a cancer diagnosis predicted overall mortality and cancer-specific mortality. Compared to never-smokers, continuing smokers had the highest hazard ratio (HR) of dying from all causes (HR = 2.71, 95% confidence interval [CI] = 1.48-4.98). Those who smoked at diagnosis, but quit and did not relapse-quitters-had an improved hazard ratio of dying (HR = 2.38, 95% CI = 1.29-4.36) and former smokers at diagnosis with no relapse after diagnosis-former smokers-had the lowest hazard ratio of dying from all causes (HR = 1.68, 95% CI = 1.12-2.56). Similarly, quitters had a slightly higher hazard ratio of dying from cancer-specific reasons (HR = 2.38, 95% CI = 1.13-5.01) than never-smokers, which was similar to current smokers (HR = 2.07, 95% CI = 0.96-4.47), followed by former smokers (HR = 1.70, 95% CI = 1.00-2.89). CONCLUSIONS: Compared to never-smokers, continuing smokers have the highest HR of overall mortality followed by quitters and former smokers, which indicates that smoking cessation, even after a cancer diagnosis, may improve overall mortality among newly diagnosed head and neck cancer patients. Health care providers should consider incorporating smoking cessation interventions into standard cancer treatment to improve survival among this population. IMPLICATIONS: Using prospective

observational longitudinal data from 590 head and neck cancer patients, this study showed that continuing smokers have the highest overall mortality relative to never-smokers, which indicates that smoking cessation, even after a cancer diagnosis, may have beneficial effects on long-term overall mortality. Health care providers should consider incorporating smoking cessation interventions into standard cancer treatment to improve survival among this population.

Pathology

**Parikh Y**, **Sharma KJ**, **Parikh SJ**, and **Hall D**. Intramammary schwannoma: a palpable breast mass *Radiol Case Rep* 2016; 11(3):129-133. PMID: 27594933. Full Text

Departments of Radiology and Pathology, Henry Ford Allegiance Health, 204 N East Ave, Jackson, MI 49201, USA.

Schwannomas are benign tumors arising from the peripheral nerve sheath, commonly occurring in the head, neck, and extensor surfaces of the extremities. They can be associated with neurofibromatosis type II. Our case describes a 48-year-old woman with a 2-week history of a left-sided palpable breast mass. She was referred to radiology, where additional imaging revealed a 1.1-cm mass. A biopsy was performed; histology revealed an intramammary schwannoma. Mammography findings include a well-defined mass without calcification. Ultrasound images have shown hypoechoic, encapsulated, and well-defined lesions without calcification. Histologically, schwannomas reveal alternating Antoni A and Antoni B cellular areas. Schwannomas are also S100-positive on immunohistochemistry. This case is best categorized as a BI-RADS 4A lesions. This case report highlights the importance of both imaging and pathology in the diagnosis of breast neoplasms. Although breast schwannomas are not a common entity, they are an important consideration when evaluating a breast mass.

Pathology

**Samuel LP**, Balada-Llasat JM, Harrington A, and Cavagnolo R. Correction for samuel et al., multicenter assessment of gram stain error rates *J Clin Microbiol* 2016; 54(9):2405. PMID: 27578160. Full Text

Henry Ford Health System, Detroit, Michigan, USA.
The Ohio State University Wexner Medical Center, Columbus, Ohio, USA.
University of Illinois at Chicago, Chicago, Illinois, USA.
med fusion, Lewisville, Texas, USA.

Pathology

Smith SC, Trpkov K, Chen YB, Mehra R, Sirohi D, Ohe C, Cani AK, Hovelson DH, Omata K, McHugh JB, Jochum W, Colecchia M, Amin M, Divatia MK, Hes O, Menon S, Werneck da Cunha I, Tripodi S, Brimo F, Gill AJ, Osunkoya AO, Magi-Galluzzi C, Sibony M, **Williamson SR**, Nesi G, Picken MM, Maclean F, Agaimy A, Cheng L, Epstein JI, Reuter VE, Tickoo SK, Tomlins SA, and Amin MB. Tubulocystic carcinoma of the kidney with poorly differentiated foci: A frequent morphologic pattern of fumarate hydratase-deficient renal cell carcinoma *Am J Surg Pathol* 2016;PMID: 27635946. Full Text

*Departments of Pathology and Urology, VCU Health, Richmond, VA daggerCalgary Laboratory Services and University of Calgary, Calgary, AB paragraph sign paragraph signDepartment of Pathology, McGill University, Montreal, QC, Canada double daggerDepartment of Pathology, Memorial Sloan Kettering Cancer Center, New York, NY section signDepartment of Pathology, University of Michigan parallel parallel parallel parallelMichigan Center for Translational Pathology, Department of Urology, Comprehensive Cancer Center, University of Michigan, Ann Arbor **Department of Pathology, William Beaumont Health System, Royal Oak parallel parallel parallelDepartment of Pathology, Henry Ford Health System, Detroit, MI parallelDepartment of Pathology and Laboratory Medicine, Cedars-Sinai Medical Center, Los Angeles, CA paragraph signInstitute of Pathology, Kantonsspital St. Gallen, Switzerland #Department of Pathology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy daggerdaggerDepartment of Pathology, Charles University and University Hospital, Plzen, Czech Republic double daggerdouble daggerDepartment of Pathology and Uro-oncology Disease Management Group, Tata Memorial Hospital, Mumbai, India section sign section signDepartment of Anatomic Pathology, A.C. Camargo Cancer Center, Sao Paulo, Brazil parallel parallelDepartment of Pathology, Azienda Ospedaliera Universitaria Senese, Siena, Italy ##Cancer Diagnosis and Pathology Group, Kolling Institue of Medical Research, Royal North Shore Hospital ***Sydney Medical School, University of Sydney, Sydney ****Douglass Hanly Moir Pathology, Macquarie Park, NSW, Australia daggerdaggerdaggerDepartment of Pathology, Emory University, Atlanta, GA double daggerdouble daggerdouble daggerRobert J. Tomsich Pathology and Laboratory Medicine Institute Cleveland Clinic, Cleveland, OH section sign section sign section signDepartement d'Anatomie Pathologique, Hopital Cochin, Universite Paris Descartes, Paris, France paragraph sign paragraph sign paragraph signDivision of Pathological Anatomy, University of Florence,

Florence, Italy ###Department of Pathology, Loyola University, Maywood, IL daggerdaggerdaggerdaggerInstitute of Pathology, Friedrich-Alexander University, University Hospital, Erlangen, Germany double daggerdouble daggerdouble daggerdouble daggerDepartment of Pathology, Indiana University School of Medicine, Indianapolis, IN section sign section sign section sign section signDepartment of Pathology, Johns Hopkins Medical Institutions, Baltimore, MD.

An emerging group of high-grade renal cell carcinomas (RCCs), particularly carcinomas arising in the hereditary leiomyomatosis renal cell carcinoma syndrome (HLRCC), show fumarate hydratase (FH) gene mutation and loss of function. On the basis of similar cytomorphology and clinicopathologic features between these tumors and cases described as tubulocystic carcinomas with poorly differentiated foci (TC-PD) of infiltrative adenocarcinoma, we hypothesized a relationship between these entities. First, 29 RCCs with morphology of TC-PD were identified retrospectively and assessed for FH expression and aberrant succination (2SC) by immunohistochemistry (IHC), with targeted next-generation sequencing of 409 genes-including FH-performed on a subset. The 29 TC-PD RCCs included 21 males and 8 females, aged 16 to 86 years (median, 46), with tumors measuring 3 to 21 cm (median, 9) arising in the right (n=16) and left (n=13) kidneys. Family history or stigmata of HLRCC were identifiable only retrospectively in 3 (12%). These tumors were aggressive, with 79% showing perinephric extension, nodal involvement in 41%, and metastasis in 86%. Of these, 16 (55%) demonstrated loss of FH by IHC (14/14 with positive 2SC). In contrast, 5 (17%) showed a wild-type immunoprofile of FH+/2SC-. An intriguing group of 8 (28%) showed variable FH+/- positivity, but with strong/diffuse 2SC+. Next-generation sequencing revealed 8 cases with FH mutations, including 5 FH-/2SC+ and 3 FH+/-/2SC+ cases, but none in FH+/2SC- cases. Secondly, we retrospectively reviewed the morphology of 2 well-characterized cohorts of RCCs with FH-deficiency determined by IHC or sequencing (n=23 and n=9), unselected for TC-PD pattern, identifying the TC-PD morphology in 10 (31%). We conclude that RCCs with TC-PD morphology are enriched for FH deficiency, and we recommend additional workup, including referral to genetic counseling, for prospective cases. In addition, based on these and other observations, we propose the term "FH-deficient RCC" as a provisional term for tumors with a combination of suggestive morphology and immunophenotype but where genetic confirmation is unavailable upon diagnosis. This term will serve as a provisional nomenclature that will enable triage of individual cases for genetic counseling and testing, while designating these cases for prospective studies of their relationship to HLRCC.

Pathology
**Tuthill JM**. Analysis of the impact and value of a specimen tracking and routing system implementation for anatomic pathology *Virchows Archiv* 2016; 469:S192. PMID: Not assigned. Abstract

J.M. Tuthill, Henry Ford Health System, Pathology, Detroit, United States

Objective: Accurate and effective specimen tracking and routing in a surgical pathology laboratory is critical for improving efficiency, reducing error, and improving patient care. Performing specimen tracking and routing in the traditional manner could cost significant time and resources, with minimal to no, real-time workflow monitoring. Method: Sunquest CoPath, as the laboratory information stystem, integrated with specimen management routing and tracking. Additional hardware requirements include Windows based workstations, 2-D barcode scanners, slide label and cassette printers/etchers, and network. Results: An automated tracking and routing system was successfully implemented with the necessary hardware and software. Compared to our current laboratory information system, CoPath+SMART provided more accurate routing, detailed tracking, and valuable workflow monitoring functions. Conclusion: As the major histology lab for a tertiary regional medical center, the lab benefitted from an automated specimen tracking and routing system. Increased work efficiency, reduced error, and better lab management were achieved. This required changes in laboratory culture, workforce adjustment, and a well-tailored plan to increase benefit/cost ratio.

Pathology
**Tuthill JM**. Immunohistochemistry and special stains automated instrument interfaces *Virchows Archiv* 2016; 469:S303. PMID: Not assigned. Abstract

J.M. Tuthill, Henry Ford Health System, Pathology, Detroit, United States

Objective: To implement an interface between the anatomic pathology LIS and automated immunohistochemistry and special stain instruments. Method: We partnered with our vendors, Sunquest Information Systems and Dako, to implement a bi-directional HL7 interface between our APLIS, (Sunquest CoPath) and our automated immunohistochemistry (IHC) and special staining platforms, eliminating dual order entry and associated errors while improving workflow efficiency and capacity. Results: System implementation resulted in direct time savings of 575.7 Hrs/YR for IHC staining automation and 118.2 Hrs/YR for special stains increasing capacity and efficiency in

histology. Transposition, slide relabeling and run time errors were eliminated improving patient safety and diagnostic accuracy. Conclusion: The impact this project was the simplification of the workflow and run setup process, as orders were seamlessly transferred electronically between the AP-LIS and the IHC and special stain autostainer instruments. The implementation of unique ID technology and the HL7 interface has greatly reduced patient mis-identification. By eliminating slide relabeling from the process, we have further automated the workflow, which has resulted in the savings of hundreds of hours of labor. The histology lab is now able to better allocate resources, while at the same time, increasing efficiency and capacity.

Plastic Surgery

**Reddy V**, and Coffey MJ. Plastic surgery and suicide: A clinical guide for plastic surgeons *Plast Reconstr Surg Glob Open* 2016; 4(8):e828. PMID: 27622096. Full Text

Henry Ford Macomb Hospital, Henry Ford Health System, Clinton Township, Mich.; Neurostimulation and Clinical Informatics, Menninger Clinic, Houston, Tex.; and Department of Psychiatry and Behavioral Sciences, Baylor College of Medicine, Houston, Tex.

Several studies have identified an increased risk of suicide among patient populations which a plastic surgeon may have a high risk of encountering: women undergoing breast augmentation, cosmetic surgery patients, and breast cancer patients. No formal guidelines exist to assist a plastic surgeon when faced with such a patient, and not every plastic surgery team has mental health clinicians that are readily accessible for consultation or referral. The goal of this clinical guide is to offer plastic surgeons a set of practical approaches to manage potentially suicidal patients. In addition, the authors review a screening tool, which can assist surgeons when encountering high-risk patients.

Psychology

**Bryce K**, **Pehote M**, and **Lanfear D**. Cognitive functioning and post-LVAD outcomes: Influence of comorbidities and specific cognitive domains *J Card Fail* 2016; 22:S124. PMID: Not assigned. Abstract

K. Bryce, Henry Ford Hospital, Detroit, United States

Introduction: Left ventricular assist devices (LVAD) are accepted therapy for end stage heart failure, but optimal patient selection remains challenging. Our group and others recently showed that baseline cognitive impairment is associated with worse outcomes post LVAD. We investigated whether this was impacted overall comorbidity burden, and which dimensions of cognitive function were most critical. Methods: A retrospective review was conducted on 100 consecutive patients who received continuous flow LVADs over a three year period (2011 and 2014) who were administered The Montreal Cognitive Assessment (MoCA) at the time of their pre-surgical psychological evaluation. Those who did not survive to discharge were excluded. Demographic information, MoCA scores and patient outcomes were collected. The primary endpoint of interest was time to hospital readmission tested using Cox regression models adjusted for potential confounders (age, race, gender, indication, and INTERMACS category). Comorbidity burden was assessed using the Charlson index. Standard MoCA subscores for Executive function, Attention, Naming, Abstraction, Language, and Orientation were tested as categorical variables (dichotomized at the median). Results: Average age was 55.6 (±12.29), 22% were female (n = 22), 42% were non-white race (n = 42), and 69% were destination therapy (n = 69). Charlson index was higher in patients with worse baseline MoCA (mean 4.5 vs 3.6, P = .021), but this did not impact the association of MoCA score with time to readmission (Charlson p = NS, MoCA category P = .005 HR = 2.0). When each subscore was tested in regression models only Attention was associated with risk of readmission (HR 2.5, P = .029). Conclusions: Among patients receiving LVADs, baseline cognitive dysfunction is associated with a greater burden of comorbidities, but this did not account for the increased hospital readmission rates among cognitively impaired patients. The cognitive domain that appears most important to post-LVAD outcomes is Attention/Concentration; the mechanism involved is unclear and deserves further investigation.

Public Health Sciences

**Al Feghali KA**, Ghanem AI, **Chang S**, **Ghanem T**, **Burmeister C**, **Keller C**, and **Siddiqui F**. Smoking predicts for worse pathological features in oral cavity squamous cell carcinoma *Int J Radiat Oncol Biol Phys* 2016; 96(2s):E386. PMID: 27674550. Full Text Abstract

Henry Ford Health System, Detroit, MI; American University of Beirut Medical Center, Beirut, Lebanon.
Alexandria University, Alexandria, Egypt.
Henry Ford Health System, Detroit, MI.

Public Health Sciences

Fujimura KE, **Sitarik AR**, **Havstad S**, Lin DL, Levan S, Fadrosh D, Panzer AR, LaMere B, Rackaityte E, Lukacs NW, **Wegienka G**, Boushey HA, Ownby DR, **Zoratti EM**, **Levin AM**, **Johnson CC**, and Lynch SV. Neonatal gut microbiota associates with childhood multisensitized atopy and T cell differentiation *Nat Med* 2016;PMID: 27618652. Full Text

Division of Gastroenterology, Department of Medicine, University of California, San Francisco, San Francisco, California, USA.
Department of Public Health Sciences, Henry Ford Health System, Detroit, Michigan, USA.
Department of Pathology, University of Michigan Medical School, Ann Arbor, Michigan, USA.
Pulmonary, Critical Care, Allergy and Sleep Medicine, Department of Medicine, University of California, San Francisco, San Francisco, California, USA.
Section of Allergy-Immunology, Augusta University, Augusta, Georgia, USA. .
Department of Internal Medicine, Division of Allergy and Immunology, Henry Ford Health System, Detroit, Michigan, USA.

Gut microbiota bacterial depletions and altered metabolic activity at 3 months are implicated in childhood atopy and asthma. We hypothesized that compositionally distinct human neonatal gut microbiota (NGM) exist, and are differentially related to relative risk (RR) of childhood atopy and asthma. Using stool samples (n = 298; aged 1-11 months) from a US birth cohort and 16S rRNA sequencing, neonates (median age, 35 d) were divisible into three microbiota composition states (NGM1-3). Each incurred a substantially different RR for multisensitized atopy at age 2 years and doctor-diagnosed asthma at age 4 years. The highest risk group, labeled NGM3, showed lower relative abundance of certain bacteria (for example, Bifidobacterium, Akkermansia and Faecalibacterium), higher relative abundance of particular fungi (Candida and Rhodotorula) and a distinct fecal metabolome enriched for pro-inflammatory metabolites. Ex vivo culture of human adult peripheral T cells with sterile fecal water from NGM3 subjects increased the proportion of CD4+ cells producing interleukin (IL)-4 and reduced the relative abundance of CD4+CD25+FOXP3+ cells. 12,13-DiHOME, enriched in NGM3 versus lower-risk NGM states, recapitulated the effect of NGM3 fecal water on relative CD4+CD25+FOXP3+ cell abundance. These findings suggest that neonatal gut microbiome dysbiosis might promote CD4+ T cell dysfunction associated with childhood atopy.

Public Health Sciences

**Ghanem AI**, **Al Feghali KA**, **Chang S**, **Ghanem T**, **Burmeister C**, and **Siddiqui F**. Clinicopathologic features and survival outcomes among young patients with squamous cell carcinoma of the oral cavity *Int J Radiat Oncol Biol Phys* 2016; 96(2s):E364. PMID: 27674490. Full Text Abstract

Henry Ford Health System, Detroit, MI; Alexandria University, Alexandria, Egypt.
Henry Ford Health system, Detroit, MI; American University of Beirut Medical Center, Beirut, Lebanon.
Henry Ford Health System, Detroit, MI.

Public Health Sciences

**Kaljee LM**, Kilgore P, **Prentiss T**, **Lamerato L**, **Moreno D**, **Arshad S**, and **Zervos M**. 'You need to be an advocate for yourself': Factors associated with decision-making regarding influenza and pneumococcal vaccine use among U.S. older adults from within a large metropolitan health system *Hum Vaccin Immunother* 2016:0. PMID: 27625007. Article Request Form

a Global Health Initiative, Henry Ford Health System , 2799 West Grand Blvd., CFP # 202 Detroit , MI USA 48202.
b Eugene Applebaum School of Pharmacy and Health Sciences, Wayne State University , Detroit , MI USA.
c Henry Ford Health System, Public Health Sciences and Research , Detroit , MI USA.
d Division of Infectious Disease, Henry Ford Health System , 2799 West Grand Blvd., CFP #302 Detroit , MI USA 48202.

In the United States, influenza and pneumonia account significantly to emergency room use and hospitalization of adults >65 years. The Centers for Disease Control and Prevention recommends use of the annual influenza vaccine and two pneumococcal vaccines for older adults to decrease risks of morbidity and mortality. However, actual vaccine up-take is estimated at 61.3% for pneumococcal vaccines and 65% for influenza vaccine in the 2013-2014 season. Vaccine up-take is affected by multiple socio-cultural and economic factors including general healthcare access and utilization, social networks and norms, communication with health providers and health information sources, as well as perceptions related to vaccines and targeted diseases. In this study, eight focus group discussions (total N = 48) were conducted with adults 65+ years living in urban and suburban communities in the Detroit Metropolitan Area. The research objective was to increase understanding of barriers and facilitators to vaccine up-take in this age cohort

within the context of general healthcare availability and accessibility, social networks, information sources, and personal perceptions of diseases and vaccines. The data suggest the need to integrate broader health care service experiences, concepts of knowledge of one's own well-being and vulnerabilities, and self-advocacy as factors associated with older adults' vaccine-use decisions. These data also support recognition of multiple levels of vaccine acceptance which can be disease specific. Implications include potential for increasing vaccine up-take through general improvement in health care delivery and services, as well as specific vaccine-focused patient and provider education programs.

Public Health Sciences
**Lee JK**, **Mahan M**, **Khan N**, **Hanna R**, and **Elshaikh MA**. Survival outcomes in women with international federation of gynecology and obstetrics stage IIIC2 endometrial carcinoma *Int J Radiat Oncol Biol Phys* 2016; 96(2s):E308. PMID: 27674336. Full Text Abstract

Henry Ford Health System, Detroit, MI.
Henry Ford Hospital, Lansing, MI.

Public Health Sciences
**Michaels AT**, **Radjef R**, **She R**, **Liu B**, **Peterson E**, Pinto Y, **Williams K**, **Sabbah H**, and **Lanfear D**. Improving risk prediction in heart failure: Maggic + natriuretic peptides *J Card Fail* 2016; 22:S99. PMID: Not assigned. Abstract

A.T. Michaels, Henry Ford Hospital, Detroit, United States

Background: Risk stratification of patients with heart failure (HF) remains challenging but is a critical need. The MAGGIC score is a clinical risk model derived from meta-analysis of nearly 40k patients. Natriuretic peptides (NP) have consistently shown powerful risk prediction in HF patients, but the incremental value in addition to MAGGIC score is not known. Methods: In this single center study 4264 patients were analyzed from two cohorts; a prospective ambulatory registry of HF patients (n = 1314) who had baseline NTproBNP levels measured, and a retrospective cohort collected utilizing administrative data from hospital discharges for HF (January 1st, 2014 through July 30th, 2015; n = 2503) with clinical BNP levels measured at or near discharge. The hospital discharge cohort were all assigned NYHA class IV. The primary end-point was all cause mortality. Performance of the MAGGIC score and NP levels was assessed within each cohort utilizing Cox regression and receiver operating curves (ROC) analysis (MAGGIC alone vs. MAGGIC+NP) with the net reclassification improvement (NRI) also calculated. Results: The overall cohort had an average age of 71.2 years, was 47.8% females, and 41% self-identified African Americans. Median follow up was 1.52 years during which there were 1139 deaths (27%). The MAGGIC score was a strong predictor of outcome in both cohorts (P < .001). In ROC analysis of the ambulatory registry, NP significantly improved area under the curve (AUC) compared to MAGGIC alone from 0.74 to 0.79 (P = .002) and had a NRI of 0.354 (Figure). In contrast, within the hospital discharge cohort NP levels did not significantly add to MAGGIC score (AUC 0.681 vs. 0.676, NRI = 0.033, P = .284) (Figure). Conclusion: In our study, NP levels in the ambulatory setting significantly improved risk stratification provided by the MAGGIC score, but discharge NP levels did not improve MAGGIC prediction of posthospital survival. Overall risk stratification and particularly NP utility is much better in the ambulatory setting. (Figure Presented).

Public Health Sciences
**Michaels AT**, **Radjef R**, **She R**, **Peterson E**, **Liu B**, and **Lanfear DE**. Predicting mortality at discharge following hospitalization for acute heart failure *J Card Fail* 2016; 22:S21-S22. PMID: Not assigned. Abstract

A.T. Michaels, Henry Ford Hospital, Detroit, United States

Background: Risk stratification for heart failure (HF) patients remains a critical need, particularly among those hospitalized where many clinical decisions are being made at discharge. Recently a robust risk model, the MAGGIC score, was derived from data on nearly 40k patients. This provides 1 year mortality estimates and is available as an online clinical tool. Whether it is useful to risk-stratify patients being discharged from the hospital is unknown. Methods: This single center study analyzed a total of 4264 patients from 2 cohorts; one utilizing administrative data from hospital discharges for HF (January 1st, 2014 through July 30th, 2015, n = 2503) and a prospective registry of ambulatory HF patients (n = 1761), both based in southeast Michigan. For the hospital discharge subjects, when tabulating MAGGIC all patients were assigned NYHA class IV. The primary endpoint was all-cause mortality. Vital status was assessed utilizing system administrative data and the social security death master file. Performance of the MAGGIC score was evaluated within cohorts and compared across the two groups using Cox models stratified by cohort and then with an interaction term (MAGGIC∗Cohort). Calibration was assessed by comparing observed vs.

MAGGICpredicted 1 year mortality. Results: Overall the study patients had an average age of 71.2 years, 47.8% were female and 41% were self-identified African Americans, and there were 1139 deaths (27%) over a median follow up of 1.52 years. The hospital discharge cohort was overall much higher risk than the ambulatory cohort (figure). The MAGGIC score was a strong predictor of outcomes in both groups (both P < .001). With a HR (per MAGGIC point) of 1.13 in the ambulatory registry and 1.10 in the hospital discharge patients. In ROC analysis MAGGIC showed an area under the curve (AUC) of 0.74, but an AUC in the hospital discharge cohort of 0.67. When modeled using an interaction term, MAGGIC did appear to be more predictive in the ambulatory group with an interaction coefficient of 0.03 (P = .004). Although calibration appeared suboptimal in both cohorts (Figure), with MAGGIC underestimating the true risk, this appeared similar in both cohorts. Discussion: The MAGGIC score is able to provide important prognostic information on patients being discharged from the hospital for HF, though the performance was somewhat inferior than in a comparable ambulatory cohort. MAGGIC underestimated risk in both ambulatory and hospital cohorts, suggesting calibration may need to be reassessed in more real-world patient data sets. (Figure Presented).

Public Health Sciences

**Miller JB**, **Lewandowski C**, Wira CR, **Taylor A**, **Burmeister C**, and Welch R. Volume of plasma expansion and functional outcomes in stroke *Neurocrit Care* 2016;PMID: 27629275. Full Text

Department of Emergency Medicine, Henry Ford Hospital, 2799 W Grand Blvd, Detroit, MI, 48202, USA. jmiller6@hfhs.org.
Department of Internal Medicine, Henry Ford Hospital, Detroit, MI, USA. jmiller6@hfhs.org.
Wayne State University, Detroit, MI, USA. jmiller6@hfhs.org.
Department of Emergency Medicine, Henry Ford Hospital, 2799 W Grand Blvd, Detroit, MI, 48202, USA.
Wayne State University, Detroit, MI, USA.
Department of Emergency Medicine, Yale University School of Medicine, New Haven, CT, USA.
Department of Public Health Sciences, Henry Ford Hospital, Detroit, MI, USA.
Department of Emergency Medicine, Wayne State University, Detroit, MI, USA.

BACKGROUND: Plasma expansion in acute ischemic stroke has potential to improve cerebral perfusion, but the long-term effects on functional outcome are mixed in prior trials. The goal of this study was to evaluate how the magnitude of plasma expansion affects neurological recovery in acute stroke. METHODS: This was a secondary analysis of data from the Albumin in Acute Stroke Part 2 trial investigating the relationship between the magnitude of overall intravenous volume infusion (crystalloid and colloid) to clinical outcome. The data were inclusive of 841 patients with a mean age of 64 years and a median National Institutes of Health Stroke Scale (NIHSS) of 11. In a multivariable-adjusted logistic regression model, this analysis tested the volume of plasma expansion over the first 48 h of hospitalization as a predictor of favorable outcome, defined as either a modified Rankin Scale score of 0 or 1 or a NIHSS score of 0 or 1 at 90 days. This model included all study patients, irrespective of albumin or isotonic saline treatment. RESULTS: Patients that received higher volumes of plasma expansion more frequently had large vessel ischemic stroke and higher NIHSS scores. The multivariable-adjusted model revealed that there was decreased odds of a favorable outcome for every 250 ml additional volume plasma expansion over the first 48 h (OR 0.91, 95 % CI, 0.88-0.94). CONCLUSIONS: The present study demonstrates an association between greater volume of plasma expansion and worse neurological recovery.

Public Health Sciences

Ownby DR, and **Johnson CC**. Dogs, cats and asthma: Will we ever really know the true risks and benefits? *J Allergy Clin Immunol* 2016;PMID: 27670242. Full Text

Professor of Pediatrics, Medical College of Georgia at Augusta University, Augusta, GA. Electronic address: downby@augusta.edu.
Chair, Public Health Sciences, Henry Ford Health System, Detroit, MI. Electronic address: cjohnso1@hfhs.org.

Public Health Sciences

**Radjef R**, **Michaels A**, **Peterson E**, **She R**, **Liu B**, **Williams K**, **Sabbah H**, and **Lanfear D**. Performance of maggic score in African Americans compared to whites *J Card Fail* 2016; 22:S101. PMID: Not assigned. Abstract

R. Radjef, Henry Ford Hospital, Detroit, United States

Background: Risk stratification is critical in Heart Failure (HF) care. The MAGGIC score is a validated tool derived from a large multi-study cohort of nearly 40,000 but very few of the patients self-identified as Black or of African

Ancestry (less than 400). There is little data assessing MAGGIC score utility in African Americans (AA). Methods: This single center study analyzed a total of 4264 patients from 2 cohorts; one utilizing administrative data from hospital discharges for HF (January 1st, 2014 through July 30th, 2015, n = 2503) and a prospective registry of ambulatory HF patients (n = 1761), both based in southeast Michigan. Baseline characteristics were collected to tabulate MAGGIC score and test its risk stratification in selfidentified African Americans (AA) and whites. The primary endpoint was time to all-cause mortality. Death was detected using system records and the social security death master file. Cox models with MAGGIC score as the only variable stratified by race, and a combined model including MAGGIC, race, and MAGGIC∗race were tested. P < .05 was considered significant. Results: Overall, 1748 patients (41%) were AA, and a total of 1151 (27%) patients died during follow up. MAGGIC score was strongly and similarly predictive of survival in both race groups. Among AA, each MAGGIC point carried HR of 1.12 (95%CI 1.10, 1.14; P < .001) while in whites the HR was 1.13 (95%CI 1.12, 1.14; P < .001). Formal test of interaction of MAGGIC by race was not significant (P = .153). However, there was a difference in survival by race, with African Americans showing a survival advantage (HR = 0.72, P = .001) which appears to be isolated to the highest risk subgroup (Figure). Conclusion: These data support the utility of the MAGGIC score for risk stratification in African Americans who suffer from HF. However, there may still be residual differences in outcomes between AA and whites despite overall risk adjustment, particularly in highest risk subgroup. (Figure Presented).

Public Health Sciences

Rand KA, Song C, Dean E, Serie DJ, Curtin K, Sheng X, Hu D, Huff CA, Bernal-Mizrachi L, Tomasson MH, Ailwadhi S, Singhal S, Pawlish KS, Peters ES, CH BL, Stram A, Van Den Berg DJ, Edlund CK, Conti DV, Zimmerman TM, Hwang AE, Huntsman S, Graff JJ, Nooka A, Kong Y, Pregja SL, Berndt SI, Blot WJ, Carpten JD, Casey G, Chu LW, Diver WR, Stevens VL, Lieber MR, Goodman PJ, Hennis AJ, Hsing AW, Mehta J, Kittles RA, Kolb S, Klein EA, Leske CM, Murphy AB, Nemesure B, **Neslund-Dudas C**, Strom SS, Vij R, **Rybicki BA**, Stanford JL, Signorello L, Witte JS, Ambrosone CB, Bhatti P, John EM, Bernstein L, Zheng W, Olshan AF, Hu JJ, Ziegler RG, Nyante SJ, Bandera EV, Birmann BM, Ingles SA, Press MF, Atanackovic D, Glenn M, Cannon-Albright L, Jones B, Tricot G, Martin TG, Kumar SK, Wolf JL, Deming SL, Rothman N, Brooks-Wilson A, Rajkumar SV, Kolonel LN, Chanock SJ, Slager SL, Severson RK, **Janakirman N**, Terebelo HJ, Brown EE, De Roos AJ, Mohrbacher A, Colditz GA, Giles GG, Spinelli JJ, Chiu BC, Munshi NC, Anderson KC, Levy J, Zonder JA, Orlowski RZ, Lonial S, Camp NJ, Vachon CM, Ziv E, Stram DO, Hazelett DJ, and Cozen W. A meta-analysis of multiple myeloma risk regions in African and European ancestry populations identifies putatively functional loci *Cancer Epidemiol Biomarkers Prev* 2016;PMID: 27587788.
Article Request Form

Department of Preventive Medicine, University of Southern California.
Preventive Medicine, Keck School of Medicine of USC and Norris Comprehensive Cancer Center, University of Southern California.
Sutter Health.
Health Sciences Research, Mayo Clinic.
Human Genetics, University of Utah.
Keck School of Medicine, USC.
Division of General Internal Medicine, University of California at San Francisco.
Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University School of Medicine.
Hematology and Medical Oncology, Winship Cancer Institute of Emory University.
Department of Medicine, Washington University.
Mayo Clinic.
Robert H. Lurie Cancer Center, Northwestern University.
Cancer Epidemiology Services, New Jersey Department of Health & Senior Services.
Dept. of Epidemiology, Louisiana School of Public Health.
Karmanos Cancer Institute, Wayne State University School of Medicine.
Genomic Health, Inc.
Keck School of Medicine at USC and Norris Comprehensive Cancer Center, University of Southern California.
Department of Preventive Medicine, Norris Comprehensive Cancer Center, Keck School of Medicine, University of Southern California.
Medical Oncology, University of Chicago.
University of Southern California Keck School of Medicine.
Rutgers-Robert Wood Johnson Medical School, Rutgers State University of New Jersey.
Hematology and Medical Oncology, Emory University School of Medicine.
Keck School of Medicine of USC and Norris Comprehensive Cancer Center, University of Southern California.
Cancer Epidemiology and Genetics, National Cancer Institute.
Division of Epidemiology, Department of Medicine, Vanderbilt University School of Medicine.
Keck School of Medicine, Norris Comprehensive Cancer Center, University of Southern California, Los Angeles, California, USA.

Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health.
Epidemiology Research Program, American Cancer Society.
Keck School of Medicine of USC, University of Southern California.
Southwest Oncology Group Statistical Center.
Stony Brook University.
Department of Research, Cancer Prevention Institute of California.
Northwestern University School of Medicine.
Surgery, University of Arizona.
Division of Public Health Sciences, Fred Hutchinson Cancer Research Center.
Glickman Urological and Kidney Institute, Cleveland Clinic.
State University of New York at Stony Brook.
Feinberg School of Medicine, Department of Urology, Northwestern University.
Stony Brook University Medical Center.
Department of Public Health Sciences, Henry Ford Health System.
epidemiology, U.T MD Anderson Cancer Center.
Department of Medicine, Washington University in Saint Louis School of Medicine.
Department of Epidemiology, Harvard School of Public Health.
Epidemiology and Biostatistics, UCSF.
Cancer Prevention and Control, Roswell Park Cancer Institute.
Fred Hutchinson Cancer Research Center.
Department of Epidemiology, Cancer Prevention Institute of California.
Population Sciences/Cancer Etiology, City of Hope.
Department of Epidemiology, University of North Carolina at Chapel Hill.
Public Health Sciences, University of Miami Leonard Miller School of Medicine.
Division of Cancer Epidemiology and Genetics, Hormonal and Reproductive Epidemiology Branch, National Cancer Institute.
Department of Radiology, University of North Carolina at Chapel Hill.
Population Science, Rutgers Cancer Institute of New Jersey.
Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School.
Department of Preventive Medicine, USC.
Pathology, University of Southern California.
Hematology and Hematologic Malignancies, Huntsman Cancer Institute.
Hematology-Oncology, University of Utah.
Division of Genetic Epidemiology, Department of Medicine, University of Utah School of Medicine.
Medicine, University of Utah.
The Univeristy of Iowa.
Oncology, UCSF Medical Center.
Hematology, Mayo Clinic.
University of California at San Francisco.
Vanderbilt Epidemiology Center, Vanderbilt.
National Cancer Institute.
Michael Smith Genome Sciences Centre, BC Cancer Agency.
Hematologic research, Mayo Clinic Rochester.
University of Hawaii.
Division of Cancer Epidemiology and Genetics, National Cancer Institute; National Institute of Health.
Department of Health Sciences Research, Mayo Clinic.
Department of Family Meidicne and Public Health Sciences, Wayne State University.
Henry Ford Hospital.
Providence Hospital.
Pathology, UAB.
Department of Environmental and Occupational Health, Drexel University School of Public Health.
Oncology, University of Southern California.
Division of Public Health Sciences, Department of Surgery, Washington University School of Medicine and Alvin J. Siteman Cancer Center.
Cancer Epidemiology Centre, Cancer Council Victoria.
Cancer Control Research, BC Cancer Agency.
University of Chicago.
Jerome Lipper Multiple Myeloma Center,Department of Medical Oncology, Dana-Farber Cancer Insitute.
Jerome Lipper Multiple Myeloma Center,Department of Medical Oncology, Dana-Farber Cancer Institute.
MMRF, Multiple Myeloma Research Consortuim.
Department of Oncology, Karmanos Cancer Center, Wayne State University.

Lymphoma/Myeloma, The University of Texas MD Anderson Cancer Center.
Hematology and Medical Oncology, Winship Cancer Institute, Emory University.
Department of Health Sciences Research, Division of Epidemiology, Mayo Clinic.
Division of General Internal Medicine, University of California, San Francisco.
University of Southern California.
Cedars-Sinai Medical Center.
Preventive Medicine, Keck School of Medicine of USC and Norris Comprehensive Cancer Center, University of Southern California wcozen@usc.edu.

BACKGROUND: Genome-wide association studies (GWAS) in European populations have identified genetic risk variants associated with multiple myeloma (MM). METHODS: We performed association testing of common variation in eight regions in 1,264 MM patients and 1,479 controls of European ancestry (EA) and 1,305 MM patients and 7,078 controls of African ancestry (AA) and conducted a meta-analysis to localize the signals, with epigenetic annotation used to predict functionality. RESULTS: We found that variants in 7p15.3, 17p11.2, 22q13.1 were statistically significantly ($p<0.05$) associated with MM risk in AAs and EAs and the variant in 3p22.1 was associated in EAs only. In a combined AA-EA meta-analysis, variation in five regions (2p23.3, 3p22.1, 7p15.3, 17p11.2, 22q13.1) was statistically signficantly associated with MM risk. In 3p22.1, the correlated variants clustered within the gene body of ULK4. Correlated variants in 7p15.3 clustered around an enhancer at the 3' end of the CDCA7L transcription termination site. A missense variant at 17p11.2 (rs34562254, Pro251Leu, OR=1.32, p=2.93x10-7) in TNFRSF13B, encodes a lymphocyte-specific protein in the tumor necrosis factor receptor family that interacts with the NF-kappaB pathway. SNPs correlated with the index signal in 22q13.1 cluster around the promoter and enhancer regions of CBX7. CONCLUSIONS: We found that reported MM susceptibility regions contain risk variants important across populations supporting the use of multiple racial/ethnic groups with different underlying genetic architecture to enhance the localization and identification of putatively functional alleles. IMPACT: A subset of reported risk loci for multiple myeloma have consistent affects across populations and are likely to be functional.

Public Health Sciences

Schwartz AG, Lusk CM, Wenzlaff AS, Watza D, Pandolfi S, Mantha L, Cote ML, Soubani AO, Walworth G, Wozniak A, **Neslund-Dudas C**, **Ardisana AA**, **Flynn MJ**, **Song T**, **Spizarny DL**, **Kvale PA**, **Chapman RA**, and Gadgeel SM. Risk of lung cancer associated with COPD phenotype based on quantitative image analysis *Cancer Epidemiol Biomarkers Prev* 2016; 25(9):1341-1347. PMID: 27383774. Article Request Form

Karmanos Cancer Institute, Detroit, Michigan. Department of Oncology, Wayne State University School of Medicine, Detroit, Michigan. schwarta@karmanos.org.
Karmanos Cancer Institute, Detroit, Michigan. Department of Oncology, Wayne State University School of Medicine, Detroit, Michigan.
Department of Oncology, Wayne State University School of Medicine, Detroit, Michigan.
Karmanos Cancer Institute, Detroit, Michigan.
Karmanos Cancer Institute, Detroit, Michigan. Department of Internal Medicine, Wayne State University School of Medicine, Detroit, Michigan.
Department of Radiology, Karmanos Cancer Institute, Detroit, Michigan.
Department of Public Health Sciences, Henry Ford Health System, Detroit, Michigan. Josephine Ford Cancer Institute, Henry Ford Health System, Detroit, Michigan.
Josephine Ford Cancer Institute, Henry Ford Health System, Detroit, Michigan. Department of Radiology, Henry Ford Health System, Detroit, Michigan.
Josephine Ford Cancer Institute, Henry Ford Health System, Detroit, Michigan. Department of Pulmonary and Critical Care Medicine, Henry Ford Health System, Detroit, Michigan.
Josephine Ford Cancer Institute, Henry Ford Health System, Detroit, Michigan. Department of Hematology/Oncology, Henry Ford Health System, Detroit, Michigan.

BACKGROUND: Chronic obstructive pulmonary disease (COPD) is a risk factor for lung cancer. This study evaluates alternative measures of COPD based on spirometry and quantitative image analysis to better define a phenotype that predicts lung cancer risk. METHODS: A total of 341 lung cancer cases and 752 volunteer controls, ages 21 to 89 years, participated in a structured interview, standardized CT scan, and spirometry. Logistic regression, adjusted for age, race, gender, pack-years, and inspiratory and expiratory total lung volume, was used to estimate the odds of lung cancer associated with FEV1/FVC, percent voxels less than -950 Hounsfield units on the inspiratory scan (HUI) and percent voxels less than -856 HU on expiratory scan (HUE). RESULTS: The odds of lung cancer were increased 1.4- to 3.1-fold among those with COPD compared with those without, regardless of assessment method; however, in multivariable modeling, only percent voxels <-856 HUE as a continuous measure of air trapping [OR = 1.04; 95% confidence interval (CI), 1.03-1.06] and FEV1/FVC < 0.70 (OR = 1.71; 95% CI, 1.21-2.41) were independent predictors of lung cancer risk. Nearly 10% of lung cancer cases were negative on all objective measures of COPD.

CONCLUSION: Measures of air trapping using quantitative imaging, in addition to FEV1/FVC, can identify individuals at high risk of lung cancer and should be considered as supplementary measures at the time of screening for lung cancer. IMPACT: Quantitative measures of air trapping based on imaging provide additional information for the identification of high-risk groups who might benefit the most from lung cancer screening. Cancer Epidemiol Biomarkers Prev; 25(9); 1341-7.

Public Health Sciences

Spradling PR, Xing J, **Rupp LB**, Moorman AC, **Gordon SC**, Teshale ET, **Lu M**, Boscarino JA, Schmidt MA, Trinacty CM, and Holmberg SD. Distribution of disease phase, treatment prescription and severe liver disease among 1598 patients with chronic hepatitis B in the Chronic Hepatitis Cohort Study, 2006-2013 *Aliment Pharmacol Ther* 2016;PMID: 27640985. Full Text

Division of Viral Hepatitis, National Centers for HIV, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention, Atlanta, GA, USA. pspradling@cdc.gov.
Division of Viral Hepatitis, National Centers for HIV, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention, Atlanta, GA, USA.
Henry Ford Health System, Detroit, MI, USA.
Center for Health Research, Geisinger Health System, Danville, PA, USA.
The Center for Health Research, Kaiser Permanente-Northwest, Portland, OR, USA.
The Center for Health Research, Kaiser Permanente-Hawaii, Honolulu, Hawaii.

BACKGROUND: Limited information exists regarding the distribution of disease phases, treatment prescription and severe liver disease among patients with chronic hepatitis B (CHB) in US general healthcare settings. AIM: To determine the distribution of disease phases, treatment prescription and severe liver disease among patients with CHB in general US healthcare settings. METHODS: We analysed demographic and clinical data collected during 2006-2013 from patients with confirmed CHB in the Chronic Hepatitis Cohort Study, an observational cohort study involving patients from healthcare organisations in Michigan, Pennsylvania, Oregon and Hawaii. CHB phases were classified according to American Association for the Study of Liver Disease guidelines. RESULTS: Of 1598 CHB patients with >/=12 months of follow-up (median 6.3 years), 457 (29%) were immune active during follow-up [11% hepatitis B e antigen (HBeAg)-positive, 16% HBeAg-negative, and 2% HBeAg status unknown], 10 (0.6%) were immune tolerant, 112 (7%) were inactive through the duration of follow-up and 886 (55%) were phase indeterminate. Patients with cirrhosis were identified within each group (among 21% of immune active, 3% of inactive and 9% of indeterminate phase patients) except among those with immune-tolerant CHB. Prescription of treatment was 59% among immune active patients and 84% among patients with cirrhosis and hepatitis B virus (HBV) DNA >2000 IU/mL. CONCLUSIONS: Approximately, one-third of the cohort had active disease during follow-up; 60% of eligible patients were prescribed treatment. Our findings underscore the importance of ascertainment of fibrosis status in addition to regular assessment of ALT and HBV DNA levels.

Public Health Sciences

**Vance S**, **Al Feghali KA**, **Taylor A**, **Kaur M**, **Neslund-Dudas C**, **Chetty IJ**, **Simoff M**, **Ajlouni M**, and **Movsas B**. Do race and income influence quality of life (QOL) or survival outcomes after lung stereotactic body radiation therapy (SBRT)? a prospective study *Int J Radiat Oncol Biol Phys* 2016; 96(2s):E534. PMID: 27674948. Full Text Abstract

Henry Ford Health System, Detroit, MI.

Public Health Sciences

Zhang X, Crawford EL, Blomquist TM, Khuder SA, Yeo J, **Levin AM**, and Willey JC. Haplotype and diplotype analyses of variation in ERCC5 transcription cis-regulation in normal bronchial epithelial cells *Physiol Genomics* 2016; 48(7):537-543. PMID: 27235448. Full Text

Division of Pulmonary/Critical Care and Sleep Medicine, Department of Medicine, University of Toledo Health Sciences Campus, Toledo, Ohio;
Department of Pathology, University of Toledo Health Sciences Campus, Toledo, Ohio;
Departments of Medicine and Public Health and Homeland Security, University of Toledo Health Science Campus, Toledo, Ohio; and.
Department of Public Health Sciences, Henry Ford Health System, Detroit, Michigan.
Division of Pulmonary/Critical Care and Sleep Medicine, Department of Medicine, University of Toledo Health Sciences Campus, Toledo, Ohio; Department of Pathology, University of Toledo Health Sciences Campus, Toledo, Ohio; James.Willey2@utoledo.edu.

Excision repair cross-complementation group 5 (ERCC5) gene plays an important role in nucleotide excision repair, and dysregulation of ERCC5 is associated with increased lung cancer risk. Haplotype and diplotype analyses were conducted in normal bronchial epithelial cells (NBEC) to better understand mechanisms responsible for interindividual variation in transcript abundance regulation of ERCC5 We determined genotypes at putative ERCC5 cis-regulatory SNPs (cis-rSNP) rs751402 and rs2296147, and marker SNPs rs1047768 and rs17655. ERCC5 allele-specific transcript abundance was assessed by a recently developed targeted sequencing method. Syntenic relationships among alleles at rs751402, rs2296147, and rs1047768 were assessed by allele-specific PCR followed by Sanger sequencing. We then assessed association of ERCC5 allele-specific expression at rs1047768 with haplotype and diplotype structure at cis-rSNPs rs751402 and rs2296147. Genotype analysis revealed significantly ($P < 0.005$) higher interindividual variation in allelic ratios in cDNA samples relative to matched gDNA samples at both rs1047768 and rs17655. By diplotype analysis, mean expression was higher at the rs1047768 alleles syntenic with rs2296147 T allele compared with rs2296147 C allele. Furthermore, mean expression was lower at rs17655 C allele, which is syntenic with G allele at a linked SNP rs873601 ($D' = 0.95$). These data support the conclusions that in NBEC, T allele at SNP rs2296147 upregulates ERCC5, variation at rs751402 does not alter ERCC5 regulation, and that C allele at SNP rs17655 downregulates ERCC5 Variation in ERCC5 transcript abundance associated with allelic variation at these SNPs could result in variation in NER function in NBEC and lung cancer risk.

Public Health Sciences

Zhu CS, Huang WY, Pinsky PF, Berg CD, Sherman M, Yu KJ, Carrick DM, Black A, Hoover R, Lenz P, Williams C, Hawkins L, Chaloux M, Yurgalevitch S, Mathew S, Miller A, Olivo V, Khan A, Pretzel SM, Multerer D, Beckmann P, **Broski KG**, and Freedman ND. The prostate, lung, colorectal and ovarian cancer (PLCO) screening trial pathology tissue resource *Cancer Epidemiol Biomarkers Prev* 2016;PMID: 27635065. Article Request Form

Division of Cancer Prevention, National Cancer Institute zhucla@mail.nih.gov.
Division of Cancer Epidemiology and Genetics, National Cancer Institute.
Division of Cancer Prevention, National Cancer Institute.
Division of Cancer Control and Population Sciences, National Cancer Institute.
Clinical Research Directorate/Clinical Monitoring Research Program, Leidos Biomedical Research, Inc.
Information Management Services, Inc.
Westat.
University of Colorado Cancer Center.
Marshfield Clinic.
University of Minnesota.
Henry Ford Health System.

BACKGROUND: Pathology tissue specimens with associated epidemiological and clinical data are valuable for cancer research. The Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial undertook a large-scale effort to create a public resource of pathology tissues from PLCO participants who developed a cancer during the trial. METHODS: Formalin-Fixed Paraffin-Embedded (FFPE) tissue blocks were obtained from pathology laboratories on a loan basis for central processing of tissue microarrays, with additional free-standing tissue cores collected for nucleic acid extraction. RESULTS: Pathology tissue specimens have been obtained for prostate cancer (n=1,052), lung cancer (n=434), colorectal cancer (n=673) and adenoma (n=658), ovarian cancer and borderline tumors (n=212), breast cancer (n=870) and bladder cancer (n=201). The process of creating this resource was complex, involving multi-disciplinary teams with expertise in pathology, epidemiology, information technology, project management and specialized laboratories. CONCLUSIONS: Creating the PLCO tissue resource required a multi-step process including obtaining medical records and contacting pathology departments where pathology materials were stored after obtaining necessary patient consent and authorization. The potential to link tissue biomarkers to prospectively collected epidemiological information, screening and clinical data, and matched blood or buccal samples offers valuable opportunities to study etiologic heterogeneity, mechanisms of carcinogenesis and biomarkers for early detection and prognosis. IMPACT: The methods and protocols developed for this effort, and the detailed description of this resource provided here will be useful for those seeking to use PLCO pathology tissue specimens for their research and may also inform future tissue collection efforts in other settings.

Pulmonary

Schwartz AG, Lusk CM, Wenzlaff AS, Watza D, Pandolfi S, Mantha L, Cote ML, Soubani AO, Walworth G, Wozniak A, **Neslund-Dudas C**, **Ardisana AA**, **Flynn MJ**, **Song T**, **Spizarny DL**, **Kvale PA**, **Chapman RA**, and Gadgeel SM. Risk of lung cancer associated with COPD phenotype based on quantitative image analysis *Cancer Epidemiol Biomarkers Prev* 2016; 25(9):1341-1347. PMID: 27383774. Article Request Form

Karmanos Cancer Institute, Detroit, Michigan. Department of Oncology, Wayne State University School of Medicine, Detroit, Michigan. schwarta@karmanos.org.
Karmanos Cancer Institute, Detroit, Michigan. Department of Oncology, Wayne State University School of Medicine, Detroit, Michigan.
Department of Oncology, Wayne State University School of Medicine, Detroit, Michigan.
Karmanos Cancer Institute, Detroit, Michigan.
Karmanos Cancer Institute, Detroit, Michigan. Department of Internal Medicine, Wayne State University School of Medicine, Detroit, Michigan.
Department of Radiology, Karmanos Cancer Institute, Detroit, Michigan.
Department of Public Health Sciences, Henry Ford Health System, Detroit, Michigan. Josephine Ford Cancer Institute, Henry Ford Health System, Detroit, Michigan.
Josephine Ford Cancer Institute, Henry Ford Health System, Detroit, Michigan. Department of Radiology, Henry Ford Health System, Detroit, Michigan.
Josephine Ford Cancer Institute, Henry Ford Health System, Detroit, Michigan. Department of Pulmonary and Critical Care Medicine, Henry Ford Health System, Detroit, Michigan.
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Pulmonary
**Vance S**, **Al Feghali KA**, **Taylor A**, **Kaur M**, **Neslund-Dudas C**, **Chetty IJ**, **Simoff M**, **Ajlouni M**, and **Movsas B**. Do race and income influence quality of life (QOL) or survival outcomes after lung stereotactic body radiation therapy (SBRT)? a prospective study *Int J Radiat Oncol Biol Phys* 2016; 96(2s):E534. PMID: 27674948. Full Text Abstract

Henry Ford Health System, Detroit, MI.

Radiation Oncology
**Al Feghali KA**, Ghanem AI, **Chang S**, **Ghanem T**, **Burmeister C**, **Keller C**, and **Siddiqui F**. Smoking predicts for worse pathological features in oral cavity squamous cell carcinoma *Int J Radiat Oncol Biol Phys* 2016; 96(2s):E386. PMID: 27674550. Full Text Abstract

Henry Ford Health System, Detroit, MI; American University of Beirut Medical Center, Beirut, Lebanon.
Alexandria University, Alexandria, Egypt.
Henry Ford Health System, Detroit, MI.

Radiation Oncology
**Al Feghali KA**, **Kolozsvary A**, **Lapanowski K**, **Isrow D**, **Brown SL**, and **Kim JH**. A novel mechanism of radiosensitization by metformin *Int J Radiat Oncol Biol Phys* 2016; 96(2s):E574. PMID: 27675054. Full Text Abstract

Henry Ford Health System, Detroit, MI.

Radiation Oncology
Awan MJ, Zakem SJ, Ward MC, Machtay M, Riaz N, Caudell JJ, Dunlap NE, **Isrow D**, Dault J, Higgins KA, Beitler JJ, **Siddiqui F**, Trotti A, Lee N, Koyfman S, Heron DE, and Yao M. Reirradiation outcomes after upfront larynx preservation or total laryngectomy: A multi-institutional analysis *Int J Radiat Oncol Biol Phys* 2016; 96(2s):E376. PMID: 27674522. Full Text Abstract

Case Western Reserve University, Cleveland, OH; University Hospitals, Case Medical Center, Cleveland, OH.
Cleveland Clinic Foundation, Cleveland, OH.
Cleveland Clinic, Cleveland, OH.
Radiation Oncology, University Hospitals Seidman Cancer Center, Case Comprehensive Cancer Center, Cleveland, OH.
Memorial Sloan Kettering Cancer Center, New York, NY.
H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL.
University of Louisville, Louisville, KY.
Henry Ford Health System, Detroit, MI.
Florida State University College of Medicine, Tallahassee, FL.
Department of Radiation Oncology, Winship Cancer Institute at Emory University, Atlanta, GA.
Department of Otolaryngology Head and Neck Surgery, Emory University, Atlanta, GA.
Moffitt Cancer Center and Research Institute, Tampa, FL.
University of Pittsburgh Cancer Institute, Pittsburgh, PA.
University Hospitals, Case Medical Center, Cleveland, OH.

Radiation Oncology
**Bagher-Ebadian H**, **Siddiqui F**, **Liu C**, **Movsas B**, and **Chetty IJ**. Prediction of response to radiation therapy treatment of head and neck cancers using an artificial neural network developed from cone beam computed tomography image textural information *Int J Radiat Oncol Biol Phys* 2016; 96(2s):S98. PMID: 27676067. Full Text Abstract

Henry Ford Health System, Detroit, MI.

Radiation Oncology
**Boyce-Fappiano D**, **Elibe E**, **Lee IY**, **Rock J**, **Siddiqui MS**, and **Siddiqui F**. Combined stereotactic radiosurgery and percutaneous vertebral augmentation for pain control in pathological vertebral compression fractures *Int J Radiat Oncol Biol Phys* 2016; 96(2s):E87. PMID: 27675486. Full Text Abstract

Henry Ford Health System, Detroit, MI.

Radiation Oncology
**Boyce-Fappiano D**, **Elibe E**, **Lee IY**, **Rock J**, **Siddiqui MS**, and **Siddiqui F**. Single-fraction stereotactic radiosurgery for renal cell carcinoma spine metastasis *Int J Radiat Oncol Biol Phys* 2016; 96(2s):E519. PMID: 27674908. Full Text Abstract

Henry Ford Health System, Detroit, MI.

Radiation Oncology
**Brown SL**, **Elmghirbi R**, **Nagaraja T**, **Keenan KA**, **Lapanowski K**, **Panda S**, **Inder P**, **Cabral G**, Liu L, **Kim JH**, **Movsas B**, **Chetty IJ**, **Ewing JR**, and Parry R. Toward a noninvasive measurement of cancer stem cells and tumor aggressiveness *Int J Radiat Oncol Biol Phys* 2016; 96(2s):E592. PMID: 27675105. Full Text Abstract

Henry Ford Health System, Detroit, MI.
Henry Ford Health System, Detroit, MI; Oakland University, Rochester, MI.
University of Windsor, Windsor, ON, Canada.
Varian Medical Systems, Palo Alto, CA, United States.

Radiation Oncology

Caudell JJ, Ward MC, Koyfman S, Riaz N, Dunlap NE, **Isrow D**, Zakem SJ, Awan MJ, Vargo J, Heron DE, Higgins KA, Beitler JJ, Yao M, Machtay M, Trotti A, **Siddiqui F**, and Lee N. Multi-institution analysis of intensity modulated radiation therapy-based reirradiation for head and neck cancer: Improved risk-benefit profile in the modern era *Int J Radiat Oncol Biol Phys* 2016; 96(2s):S115-s116. PMID: 27675560. Full Text Abstract

H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL.
Cleveland Clinic, Cleveland, OH.
Memorial Sloan-Kettering Cancer Center, New York, NY.
University of Louisville, Louisville, KY.
Henry Ford Health System, Detroit, MI.
Cleveland Clinic Foundation, Cleveland, OH.
University Hospitals, Case Medical Center, Cleveland, OH.
University of Pittsburgh Cancer Institute, Pittsburgh, PA.
Department of Radiation Oncology, Winship Cancer Institute at Emory University, Atlanta, GA.
Department of Otolaryngology Head and Neck Surgery, Emory University, Atlanta, GA.
Case Western Reserve University School of Medicine, Cleveland, OH.
Moffitt Cancer Center and Research Institute, Tampa, FL.
Memorial Sloan Kettering Cancer Center, New York, NY.

Radiation Oncology

**Chetvertkov MA**, **Siddiqui F**, Kim J, **Chetty I**, **Kumarasiri A**, **Liu C**, and **Gordon JJ**. Use of regularized principal component analysis to model anatomical changes during head and neck radiation therapy for treatment adaptation and response assessment *Med Phys* 2016; 43(10):5307-5319. PMID: Not yet assigned. Full Text

M.A. Chetvertkov, Department of Radiation Oncology, Wayne State University, School of Medicine, Detroit, United States

Purpose: To develop standard (SPCA) and regularized (RPCA) principal component analysis models of anatomical changes from daily cone beam CTs (CBCTs) of head and neck (H&N) patients and assess their potential use in adaptive radiation therapy, and for extracting quantitative information for treatment response assessment. Methods: Planning CT images of ten H&N patients were artificially deformed to create digital phantom images, which modeled systematic anatomical changes during radiation therapy. Artificial deformations closely mirrored patients actual deformations and were interpolated to generate 35 synthetic CBCTs, representing evolving anatomy over 35 fractions. Deformation vector fields (DVFs) were acquired between pCT and synthetic CBCTs (i.e., digital phantoms) and between pCT and clinical CBCTs. Patient-specific SPCA and RPCA models were built from these synthetic and clinical DVF sets. EigenDVFs (EDVFs) having the largest eigenvalues were hypothesized to capture the major anatomical deformations during treatment. Results: Principal component analysis (PCA) models achieve variable results, depending on the size and location of anatomical change. Random changes prevent or degrade PCAs ability to detect underlying systematic change. RPCA is able to detect smaller systematic changes against the background of random fraction-to-fraction changes and is therefore more successful than SPCA at capturing systematic changes early in treatment. SPCA models were less successful at modeling systematic changes in clinical patient images, which contain a wider range of random motion than synthetic CBCTs, while the regularized approach was able to extract major modes of motion. Conclusions: Leading EDVFs from the both PCA approaches have the potential to capture systematic anatomical change during H&N radiotherapy when systematic changes are large enough with respect to random fraction-to-fraction changes. In all cases the RPCA approach appears to be more reliable at capturing systematic changes, enabling dosimetric consequences to be projected once trends are established early in a treatment course, or based on population models.

Radiation Oncology

Dehkordi AN, Kamali-Asl A, **Ewing JR**, and **Bagher-Ebadian H**. An adaptive model for direct estimation of extravascular-extracellular space in dynamic contrast-enhanced magnetic resonance imaging studies *Int J Radiat Oncol Biol Phys* 2016; 96(2s):E644. PMID: 27675247. Full Text Abstract

Shahid Beheshti University, Tehran, Iran (Islamic Republic of Korea); Henry Ford Hospital, Detroit, MI.
Shahid Beheshti University, Tehran, Iran (Islamic Republic of Korea).
Henry Ford Hospital, Detroit, MI; Oakland University, Rochester, MI.
Oakland University, Rochester, MI; Henry Ford Health System, Detroit, MI.

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Den RB, Yousefi K, Trock B, Davicioni E, Tosoian J, Thompson D, Choeurng V, Haddad Z, Tran PT, Trabulsi E, Gomella LG, Lallas CD, **Abdollah F**, Feng FY, Dicker AP, Freedland SJ, Karnes JR, Schaeffer EM, and Ross AE. Efficacy of postoperative radiation in a prostatectomy cohort adjusted for clinical and genomic risk *Int J Radiat Oncol Biol Phys* 2016; 96(2s):S103-s104. PMID: 27675531. Full Text Abstract

Sidney Kimmel Medical College at Thomas Jefferson University, Sidney Kimmel Cancer Center, Philadelphia, PA.
GenomeDx Biosciences, Vancouver, BC, Canada.
James Buchanan Brady Urological Institute, Johns Hopkins Hospital, Baltimore, MD.
Emmes Canada, Burnaby, BC, Canada.
GenomeDx Biosciences Inc., Vancouver, BC, Canada.
Johns Hopkins University School of Medicine, Baltimore, MD.
Sidney Kimmel Medical College of Thomas Jefferson University, Philadelphia, PA.
Vattikuti Urology Institute, Henry Ford Hospital, Detroit, MI.
University of Michigan, Ann Arbor, MI.
Cedars-Sinai Medical Center, Los Angeles, CA; Veteran Affairs Medical Center, Durham, NC.
Mayo Clinic Rochester, Rochester, MN.
Northwestern University, Chicago, IL.
Johns Hopkins University, Baltimore, MD.

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**Elibe E**, **Boyce-Fappiano D**, **Walker EM**, **Lee IY**, **Rock J**, **Siddiqui S**, and **Siddiqui F**. Significance of hormone therapy and bisphosphonate use on vertebral compression fracture (vcf) incidence following spine stereotactic body radiation therapy (sbrt) for breast cancer metastases *Int J Radiat Oncol Biol Phys* 2016; 96(2s):E509. PMID: 27674881. Full Text Abstract

Henry Ford Health System, Detroit, MI.

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**Elshaikh MA**. In reply to Binder et al "adult comorbidity evaluation 27 score in endometrial cancer patient" *Am J Obstet Gynecol* 2016;PMID: 27640945. Full Text

Senior Staff Physician - Department of Radiation Oncology, Henry Ford Hospital; Clinical Professor, Wayne State School of Medicine. Electronic address: melshai1@hfhs.org.

Radiation Oncology
Feng M, Matuszak MM, Boike TP, Grills IS, Kestin LL, **Movsas B**, Paximadis PA, Griffith KA, Gustafson GS, Moran JM, Nurushev TS, Radawski JD, Pierce LJ, Hayman JA, and Schipper M. Predictors of heart dose from lung radiation therapy in a large consortium of community and academic practices *Int J Radiat Oncol Biol Phys* 2016; 96(2s):E482. PMID: 27674809. Full Text Abstract

University of Michigan, Ann Arbor, MI.
Department of Radiation Oncology, University of Michigan, Ann Arbor, MI.
McLaren Northern Michigan, Petoskey, MI.
Beaumont Health System, Royal Oak, MI.
Michigan Healthcare Professionals, Farmington Hills, MI.
Henry Ford Health System, Detroit, MI.
Karmanos Cancer Center, Detroit, MI.
21st Century Oncology, Pontiac, MI.
West Michigan Cancer Center, Rsockford, MI.

Radiation Oncology
Feng M, Moran JM, Benedetti L, Boike TP, Dryden D, **Fraser C**, Griffith KA, Gustafson GS, Haywood J, Jagsi R, Matuszak MM, Nurushev TS, Radawski JD, Speers C, **Walker EM**, Hayman JA, and Pierce LJ. Time trends and predictors of heart dose from breast radiation therapy in a large consortium of community and academic practices *Int J Radiat Oncol Biol Phys* 2016; 96(2s):E15-e16. PMID: 27673907. Full Text

University of Michigan, Ann Arbor, MI.

Beaumont Health System, Royal Oak, MI, United States.
McLaren Northern Michigan, Petoskey, MI.
McLaren Northern Michigan, Petoskey, MA.
Henry Ford Hospital, Detroit, MI.
Beaumont Health System, Royal Oak, MI.
Mercy Hospital, Muskegon, MI.
The University of Michigan Health System, Ann Arbor, MI.
Department of Radiation Oncology, University of Michigan, Ann Arbor, MI.
21st Century Oncology, Pontiac, MI.
West Michigan Cancer Center, Rockford, MI.
Henry Ford Health System, Detroit, MI.

Radiation Oncology
**Freytag SO**, **Movsas B**, and **Stricker H**. Clinical trials of oncolytic adenovirus-mediated gene therapy *Mol Ther* 2016; 24:S205-S205. PMID: Not assigned. Abstract

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**Ghanem AI**, **Al Feghali KA**, **Chang S**, **Ghanem T**, **Burmeister C**, and **Siddiqui F**. Clinicopathologic features and survival outcomes among young patients with squamous cell carcinoma of the oral cavity *Int J Radiat Oncol Biol Phys* 2016; 96(2s):E364. PMID: 27674490. Full Text Abstract

Henry Ford Health System, Detroit, MI; Alexandria University, Alexandria, Egypt.
Henry Ford Health system, Detroit, MI; American University of Beirut Medical Center, Beirut, Lebanon.
Henry Ford Health System, Detroit, MI.

Radiation Oncology
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The University of Michigan Health System, Ann Arbor, MI.
University of Michigan, Ann Arbor, MI.
Department of Radiation Oncology, University of Michigan, Ann Arbor, MI.
McLaren Northern Michigan, Petoskey, MI.
Beaumont Health System, Royal Oak, MI.
Traverse Bay Radiation Oncology, Traverse City, MI.
21st Century Oncology, Pontiac, MI.
West Michigan Cancer Center, Rockford, MI, United States.
Henry Ford Health System, Detroit, MI.

Radiation Oncology
Karam I, Yao M, Heron DE, Poon I, Koyfman S, Yom SS, **Siddiqui F**, Lartigau E, Cengiz M, Yamazaki H, Hara W, Phan J, Vargo J, Lee VH, Foote RL, Harter KW, Lee N, Sahgal A, and Lo SS. Consensus statement from the international stereotactic body radiotherapy consortium for head and neck carcinoma-technical factors *Int J Radiat Oncol Biol Phys* 2016; 96(2s):E382-e383. PMID: 27674541. Full Text Abstract

Sunnybrook Odette Cancer Centre, Toronto, ON, Canada; University of Toronto, Toronto, ON, Canada.
University Hospitals, Case Medical Center, Cleveland, OH.
University of Pittsburgh Cancer Institute, Pittsburgh, PA.
Cleveland Clinic, Cleveland, OH.
University of California San Francisco, San Francisco, CA.
Henry Ford Hospital, Detroit, MI; Henry Ford Health System, Detroit, MI.
Centre Oscar Lambret, Lille, France.
Hacettepe University Medical School, Ankara, Turkey.
Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, Japan.
Stanford Radiation Oncology, Stanford, CA.
The University of Texas MD Anderson Cancer Center, Division of Radiation Oncology, Houston, TX.
Department of Clinical Oncology, Queen Mary Hospital, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong, Hong Kong.
Department of Radiation Oncology; Mayo Clinic, Rochester, MN.
Georgetown University Medical Center, Washington, DC.
Memorial Sloan Kettering Cancer Center, New York, NY.
Radiation Oncology, University Hospitals Seidman Cancer Center, Case Comprehensive Cancer Center, Cleveland, OH.

Radiation Oncology
Karam I, Yao M, Heron DE, Poon I, Koyfman S, Yom SS, **Siddiqui F**, Lartigau E, Cengiz M, Yamazaki H, Hara W, Phan J, Vargo J, Lee VH, Foote RL, Harter KW, Lee N, Sahgal A, and Lo SS. Consensus statement from the international stereotactic body radiotherapy consortium for head and neck carcinoma-patient selection and pre- and post-stereotactic body radiation therapy evaluation *Int J Radiat Oncol Biol Phys* 2016; 96(2s):E364-e365. PMID: 27674489. Full Text Abstract

Sunnybrook Odette Cancer Centre, Toronto, ON, Canada; University of Toronto, Toronto, ON, Canada.
University Hospitals, Case Medical Center, Cleveland, OH.
University of Pittsburgh Cancer Institute, Pittsburgh, PA.
Cleveland Clinic, Cleveland, OH.
University of California San Francisco, San Francisco, CA.
Henry Ford Hospital, Detroit, MI; Henry Ford Health System, Detroit, MI.
Centre Oscar Lambret, Lille, France.
Hacettepe University Medical School, Ankara, Turkey.
Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, Japan.
Stanford Radiation Oncology, Stanford, CA.
The University of Texas MD Anderson Cancer Center, Division of Radiation Oncology, Houston, TX.
Department of Clinical Oncology, Queen Mary Hospital, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong, Hong Kong.
Department of Radiation Oncology, Mayo Clinic, Rochester, MN.
Georgetown University Hospital & Vincent T. Lombardi Comprehensive Cancer Center, Washington, DC.
Memorial Sloan Kettering Cancer Center, New York, NY.
Radiation Oncology, University Hospitals Seidman Cancer Center, Case Comprehensive Cancer Center, Cleveland, OH.

Radiation Oncology
**Kim J**, **Wu Q**, **Zhao B**, **Wen N**, **Ajlouni M**, **Movsas B**, and **Chetty IJ**. To gate or not to gate - dosimetric evaluation comparing Gated vs. ITV-based methodologies in stereotactic ablative body radiotherapy (SABR) treatment of lung cancer *Radiat Oncol* 2016; 11(1):125. PMID: 27659780. Full Text

Department of Radiation Oncology, Henry Ford Health System, 2799 W. Grand Blvd, Detroit, MI, 48202, USA. jkim8@hfhs.org.
Department of Radiation Oncology, Henry Ford Health System, 2799 W. Grand Blvd, Detroit, MI, 48202, USA.

BACKGROUND: To compare retrospectively generated gated plans to conventional internal target volume (ITV)-based plans and to evaluate whether gated radiotherapy provides clinically relevant dosimetric improvements to organs-at-risk (OARs). METHODS: Evaluation was performed of 150 stereotactic ablative radiotherapy treatment plans delivered to 128 early-stage (T1-T3 (<5 cm)) NSCLC patients. To generate gated plans, original ITV-based plans were re-optimized and re-calculated on the end-exhale phase and using gated planning target volumes (PTV). Gated and ITV-based plans were produced for 3 x 18 Gy and 4 x 12 Gy fractionation regimens. Dose differences between gated and ITV-based plans were analyzed as a function of both three-dimensional motion and tumor volume. OARs were analyzed using RTOG and AAPM dose constraints. RESULTS: Differences between gated and ITV-based plans for all OAR indices were largest for the 3 x 18 Gy regimen. For this regimen, MLD differences calculated by subtracting the gated values from the ITV-based values (ITV vs. Gated) were 0.10 +/- 0.56 Gy for peripheral island (N = 57), 0.16 +/- 0.64 Gy for peripheral lung-wall seated (N = 57), and 0.10 +/- 0.64 Gy for central tumors (N = 36). Variations in V20 were similarly low, with the greatest differences occurring in peripheral tumors (0.20 +/- 1.17 %). Additionally, average differences (in 2Gy-equivalence) between ITV and gated lung indices fell well below clinical tolerance values for all fractionation regimens, with no clinically meaningful differences observed from the 4 x 12 Gy regimen and rarely for the 3 x 18 Gy regimen (<2 % of cases). Dosimetric differences between gated and ITV-based methods did generally increase with increasing tumor motion and decreasing tumor volume. Dose to ribs and bronchial tree were slightly higher in gated plans compared to ITV-based plans and slightly lower for esophagus, heart, spinal cord, and trachea. CONCLUSIONS: Analysis of 150 SABR-based lung cancer treatment plans did not show a substantial benefit for the gating regimen when compared to ITV-based treatment plans. Small benefits were observed only for the largest tumor motion (exceeding 2 cm) and the high dose treatment regimen (3 x 18 Gy), though these benefits did not appear to be clinically relevant.

Radiation Oncology
Mahmoud OM, Gabel M, Gibbon D, Leiser A, Isani S, Cracchiolo B, Khan AJ, and **Elshaikh MA**. Can chemotherapy boost the survival benefit of adjuvant radiation therapy in early-stage cervical cancer with intermediate risk factors: A population-based study *Int J Radiat Oncol Biol Phys* 2016; 96(2s):E287. PMID: 27674277. Full Text

Rutgers Cancer Institute of New Jersey, New Brunswick, NJ.
CINJ/RWJ, Trenton, NJ.
CINJ, New Brunswick, NJ.
NJMS, Newark, NJ.
Henry Ford Health System, Detroit, MI.

Radiation Oncology
Mahmoud OM, Gabel M, Jhawar S, Gibbon D, Cracchiolo B, Leiser A, Isani S, Khan AJ, and **Elshaikh MA**. How important is chemotherapy timing and treatment duration in the adjuvant management of cervical cancer? *Int J Radiat Oncol Biol Phys* 2016; 96(2s):E290. PMID: 27674287. Full Text Abstract

Rutgers Cancer Institute of New Jersey, New Brunswick, NJ.
CINJ/RWJ, Trenton, NJ.
Rutgers-Robert Wood Johnson Medical School/Cancer Institute of New Jersey, New Brunswick, NJ.
CINJ, New Brunswick, NJ.
NJMS, Newark, NJ.
Henry Ford Health System, Detroit, MI.

Radiation Oncology
Mahmoud OM, Green WR, Gabel M, Gibbon D, Leiser A, Isani S, Cracchiolo B, Khan AJ, and **Elshaikh MA**. Replicating landoni's study in the era of chemotherapy: Postoperative or radical concurrent chemoradiation therapy in early-stage cervical cancer? *Int J Radiat Oncol Biol Phys* 2016; 96(2s):E300. PMID: 27674314. Full Text Abstract

Rutgers Cancer Institute of New Jersey, New Brunswick, NJ.
Rutgers - Cancer Institute of New Jersey, New Brunswick, NJ.
CINJ/RWJ, Trenton, NJ.
CINJ, New Brunswick, NJ.
NJMS, Newark, NJ.
Henry Ford Health System, Detroit, MI.

Radiation Oncology
Mayadev JS, **Elshaikh MA**, Christie A, Nagel C, **Khan N**, Kennedy V, Lea J, **Ghanem A**, Miller DS, Xie XJ, Folkert M, and Albuquerque KV. Prognostic significance of nodal location in stage IIIC endometrial carcinoma: Implications for optimal adjuvant therapy *Int J Radiat Oncol Biol Phys* 2016; 96(2s):E303. PMID: 27674322. Full Text Abstract

University of California Davis Comprehensive Cancer Center, Sacramento, CA.
Henry Ford Health System, Detroit, MI.
University of Texas Southwestern Medical Center, Dallas, TX.
UH Case Medical Center, Cleveland, OH.
Henry Ford Hospital, Detroit, MI.
UC Davis Gynecology Oncology, Sacramento, CA.
UT Southwestern Medical Center, Dallas, TX.
Henry Ford, Detroit, MI.
The University of Texas Southwestern Medical Center, Dallas, TX, United States.

Radiation Oncology
**Modh A**, **McHargue CA**, **Lim H**, and **Siddiqui F**. Single-fraction radiation therapy provides highly effective palliation for cutaneous t-cell lymphoma *Int J Radiat Oncol Biol Phys* 2016; 96(2s):E492. PMID: 27674835. Full Text Abstract

Henry Ford Health System, Detroit, MI.

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Karmanos Cancer Center, Detroit, MI.
University of Michigan, Ann Arbor, MI.
Department of Radiation Oncology, University of Michigan, Ann Arbor, MI.
McLaren Northern Michigan, Petoskey, MI.
Beaumont Health System, Royal Oak, MI.
21st Century Oncology, Pontiac, MI.
Henry Ford Health System, Detroit, MI.
West Michigan Cancer Center, Rockford, MI.

Radiation Oncology
Siebers JV, and **Gordon JJ**. Regarding: "The dosimetric impact of image guided radiation therapy by intratumoral fiducial markers" *Pract Radiat Oncol* 2016;PMID: 27665054. Article Request Form

Department of Radiation Oncology, University of Virginia Health System, Charlottesville, Virginia.
Department of Radiation Oncology, Henry Ford Health System, Detroit, Michigan.

Radiation Oncology
Small W, Jr., Hayes JP, Suh WW, Abdel-Wahab M, Abrams RA, Azad N, Das P, **Dragovic J**, Goodman KA, Jabbour SK, Jones WE, 3rd, Konski AA, Koong AC, Kumar R, Lee P, Pawlik TM, and Herman JM. Acr appropriateness criteria(r) borderline and unresectable pancreas cancer *Oncology (Williston Park)* 2016; 30(7):619-624, 627, 632. PMID: 27422109. Full Text

The American College of Radiology Appropriateness Criteria(R) are evidence-based guidelines for specific clinical conditions that are reviewed every 3 years by a multidisciplinary expert panel. The guideline development and review include an extensive analysis of current medical literature from peer-reviewed journals and the application of a well-established consensus methodology (modified Delphi) to rate the appropriateness of imaging and treatment procedures by the panel. In those instances where evidence is lacking or not definitive, expert opinion may be used to recommend imaging or treatment. The panel reviewed the pertinent literature and voted on five variants to establish appropriate recommended treatment of borderline and unresectable pancreatic cancer. The guidelines reviewed the use of radiation, chemotherapy, and surgery. Radiation technique, dose, and targets were evaluated, as

was the recommended chemotherapy, administered either alone or concurrently with radiation. This report will aid clinicians in determining guidelines for the optimal treatment of borderline and unresectable pancreatic cancer.

Radiation Oncology
**Vance S**, **Al Feghali KA**, **Taylor A**, **Kaur M**, **Neslund-Dudas C**, **Chetty IJ**, **Simoff M**, **Ajlouni M**, and **Movsas B**. Do race and income influence quality of life (QOL) or survival outcomes after lung stereotactic body radiation therapy (SBRT)? a prospective study *Int J Radiat Oncol Biol Phys* 2016; 96(2s):E534. PMID: 27674948. Full Text Abstract

Henry Ford Health System, Detroit, MI.

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Vargo J, Ward MC, Caudell JJ, Riaz N, Dunlap NE, **Isrow D**, Zakem SJ, Dault J, Awan MJ, Higgins KA, Beitler JJ, Yao M, Machtay M, **Siddiqui F**, Trotti A, Lee N, Koyfman S, and Heron DE. Optimal treatment selection of stereotactic body radiation therapy and intensity modulated radiation therapy for reirradiation of head and neck cancer: A multi-institution comparison *Int J Radiat Oncol Biol Phys* 2016; 96(2s):S114-s115. PMID: 27675558. Full Text Abstract

University of Pittsburgh Cancer Institute, Pittsburgh, PA.
Cleveland Clinic, Cleveland, OH.
H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL.
Memorial Sloan Kettering Cancer Center, New York, NY.
University of Louisville, Louisville, KY.
Henry Ford Health System, Detroit, MI.
Cleveland Clinic Foundation, Cleveland, OH.
Florida State University College of Medicine, Tallahassee, FL.
Case Western Reserve University, Cleveland, OH.
Department of Radiation Oncology, Winship Cancer Institute at Emory University, Atlanta, GA.
Department of Otolaryngology Head and Neck Surgery, Emory University, Atlanta, GA.
University Hospitals, Case Medical Center, Cleveland, OH.
Radiation Oncology, University Hospitals Seidman Cancer Center, Case Comprehensive Cancer Center, Cleveland, OH.
Moffitt Cancer Center and Research Institute, Tampa, FL.

Radiation Oncology
Ward MC, Riaz N, Caudell JJ, Dunlap NE, **Isrow D**, Zakem SJ, Dault J, Awan MJ, Vargo J, Heron DE, Higgins KA, Beitler JJ, Yao M, Machtay M, **Siddiqui F**, Trotti A, Lee N, and Koyfman S. Multi-institution analysis of intensity modulated radiation therapy-based reirradiation for head and neck cancer: Prognostic factors and recursive partitioning analysis for overall survival *Int J Radiat Oncol Biol Phys* 2016; 96(2s):S115. PMID: 27675561. Full Text Abstract

Cleveland Clinic, Cleveland, OH.
Memorial Sloan-Kettering Cancer Center, New York, NY.
H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL.
University of Louisville, Louisville, KY.
Henry Ford Health System, Detroit, MI.
Cleveland Clinic Foundation, Cleveland, OH.
Florida State University College of Medicine, Tallahassee, FL.
University Hospitals, Case Medical Center, Cleveland, OH.
University of Pittsburgh Cancer Institute, Pittsburgh, PA.
Department of Radiation Oncology, Winship Cancer Institute at Emory University, Atlanta, GA.
Department of Otolaryngology Head and Neck Surgery, Emory University, Atlanta, GA.
Radiation Oncology, University Hospitals Seidman Cancer Center, Case Comprehensive Cancer Center, Cleveland, OH.
Moffitt Cancer Center and Research Institute, Tampa, FL.
Memorial Sloan Kettering Cancer Center, New York, NY.

Radiation Oncology

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Nell Hodgson Woodruff School of Nursing, Winship Cancer Institute at Emory University, Atlanta, GA.
NRG Oncology Statistics and Data Management Center, Philadelphia, PA.
Duke University, Durham, NC.
University of Chicago, Department of Public Health Sciences, Chicago, IL.
Washington University School of Medicine, St Louis, MO.
Baylor Scott & White Healthcare Temple Clinic, Temple, TX.
York Cancer Center, York, PA, United States.
Western University, London, ON, Canada.
McMaster University, Hamilton, ON, Canada.
Kaiser Permanente Northern California, Santa Clara, CA.
Dana-Farber Cancer Institute and Brigham and Women's Hospital, Boston, MA.
Emory University, Atlanta, GA.
Department of Radiation Oncology, Mayo Clinic, Rochester, MN.
Wilmot Cancer Institute, University of Rochester, Rochester, NY.
Cedars-Sinai Medical Center, Los Angeles, CA.
Henry Ford Health System, Detroit, MI.

Radiation Oncology

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Henry Ford Health System, Detroit, MI.

Radiation Oncology

**Wu Q**, **Snyder KC**, **Liu C**, **Huang Y**, **Zhao B**, **Chetty IJ**, and **Wen N**. Optimization of treatment geometry to reduce normal brain dose in radiosurgery of multiple brain metastases with single-isocenter volumetric modulated arc therapy *Sci Rep* 2016; 6:34511. PMID: 27688047. Full Text

Department of Radiation Oncology, Henry Ford Health System, MI, USA.

Treatment of patients with multiple brain metastases using a single-isocenter volumetric modulated arc therapy (VMAT) has been shown to decrease treatment time with the tradeoff of larger low dose to the normal brain tissue. We have developed an efficient Projection Summing Optimization Algorithm to optimize the treatment geometry in order to reduce dose to normal brain tissue for radiosurgery of multiple metastases with single-isocenter VMAT. The algorithm: (a) measures coordinates of outer boundary points of each lesion to be treated using the Eclipse Scripting Application Programming Interface, (b) determines the rotations of couch, collimator, and gantry using three matrices about the cardinal axes, (c) projects the outer boundary points of the lesion on to Beam Eye View projection plane, (d) optimizes couch and collimator angles by selecting the least total unblocked area for each specific treatment arc, and (e) generates a treatment plan with the optimized angles. The results showed significant reduction in the mean dose and low dose volume to normal brain, while maintaining the similar treatment plan qualities on the thirteen patients treated previously. The algorithm has the flexibility with regard to the beam arrangements and can be integrated in the treatment planning system for clinical application directly.

Radiation Oncology

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Henry Ford Health System, Detroit, MI.

Radiation Oncology

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Department of Oncology, Wayne State University, Detroit, MI, USA.
Department of Radiation Oncology, Henry Ford Hospital, Detroit, MI, USA.
Department of Radiation Oncology, Henry Ford Hospital, Detroit, MI, USA nwen1@hfhs.org.

PURPOSE: To determine the localization uncertainties associated with 2-dimensional/3-dimensional image registration in comparison to 3-dimensional/3-dimensional image registration in 6 dimensions on a Varian Edge Linac under various imaging conditions. METHODS: The systematic errors in 6 dimensions were assessed by comparing automatic 2-dimensional/3-dimensional (kV/MV vs computed tomography) with 3-dimensional/3-dimensional (cone beam computed tomography vs computed tomography) image registrations under various conditions encountered in clinical applications. The 2-dimensional/3-dimensional image registration uncertainties for 88 patients with different treatment sites including intracranial and extracranial were evaluated by statistically analyzing 2-dimensional/3-dimensional pretreatment verification shifts of 192 fractions in stereotactic radiosurgery and stereotactic body radiotherapy. RESULTS: The systematic errors of 2-dimensional/3-dimensional image registration using kV-kV, MV-kV, and MV-MV image pairs were within 0.3 mm and 0.3 degrees for the translational and rotational directions within a 95% confidence interval. No significant difference (P > .05) in target localization was observed with various computed tomography slice thicknesses (0.8, 1, 2, and 3 mm). Two-dimensional/3-dimensional registration had the best accuracy when pattern intensity and content filter were used. For intracranial sites, means +/- standard deviations of translational errors were -0.20 +/- 0.70 mm, 0.04 +/- 0.50 mm, and 0.10 +/- 0.40 mm for the longitudinal, lateral, and vertical directions, respectively. For extracranial sites, means +/- standard deviations of translational errors were -0.04 +/- 1.00 mm, 0.2 +/- 1.0 mm, and 0.1 +/- 1.0 mm for the longitudinal, lateral, and vertical directions, respectively. Two-dimensional/3-dimensional image registration for intracranial and extracranial sites had comparable systematic errors that were approximately 0.2 mm in the translational direction and 0.08 degrees in the rotational direction. CONCLUSION: The standard 2-dimensional/3-dimensional image registration tool available on the Varian Edge radiosurgery device, a state-of-the-art system, is helpful for robust and accurate target positioning for image-guided stereotactic radiosurgery.

Radiology

Mendiratta-Lala M, **Park H**, **Kolicaj N**, **Mendiratta V**, and **Bassi D**. Small intrahepatic peripheral cholangiocarcinomas as mimics of hepatocellular carcinoma in multiphasic CT *Abdom Radiol (NY)* 2016;PMID: 27590067. Article Request Form

School of Medicine, University of Michigan, 1500 East Medical Center Drive, UH B2 A209R, Ann Arbor, MI, 48109, USA. mmendira@med.umich.edu.
Henry Ford Hospital, 2799 West Grand Blvd, Detroit, MI, 48202, USA.

PURPOSE: Liver transplant guidelines for diagnosing hepatocellular carcinoma (HCC) do not mandate pathologic confirmation; instead, 'classic' imaging features alone are deemed satisfactory. Intrahepatic peripheral mass forming cholangiocarcinoma (IHPMCC) is a relative contraindication for transplantation due to high rate of recurrence and poor prognosis. This study examines the imaging findings of IHPMCC, to aid in the identification and differentiation from potentially confounding cases of HCC. METHODS: After IRB approval, 43 tissue-proven cases of IHPMCC on multiphase CT were retrospectively reviewed by 2 fellowship-trained radiologists. Tumor size, presence of cirrhosis, tumor capsule, vascular invasion, tumor markers, and enhancement pattern were assessed. A grading system was assigned as determined by enhancement pattern to background liver on arterial, portal venous, and equilibrium phases, ranging from typical HCC to typical IHPMCC enhancement pattern. RESULTS: Analysis based on our grading system shows 5 (11.6%) tumors demonstrating grade 1-2 enhancement, 9 (21%) grade 3-4 enhancement, and 29 (67.4%) grade 5 enhancement. Kruskal-Wallis test comparing CA19-9 between the five groups, Wilcoxin rank-sum test comparing tumor markers with presence or absence of tumor capsule, vascular invasion and cirrhosis, and nonparametric Pearson's correlation coefficient comparing tumor markers to tumor size were not statistically significant (p > 0.05). CONCLUSION: Typical enhancement pattern of IHPMCC consisting of arterial phase hypoenhancement with progressive, centripetal-delayed enhancement is present in the majority of cases (68%). Five cases (11.7%) showed enhancement features potentially mimicking HCC, all of which are under 3.5 cm in size. Thus, small hyperenhancing lesions in a cirrhotic liver should be carefully scrutinized in light of differing therapy options from HCC, particularly in transplant situations.

Radiology

**Parikh Y**, **Sharma KJ**, **Parikh SJ**, and **Hall D**. Intramammary schwannoma: a palpable breast mass *Radiol Case Rep* 2016; 11(3):129-133. PMID: 27594933. Full Text

Departments of Radiology and Pathology, Henry Ford Allegiance Health, 204 N East Ave, Jackson, MI 49201, USA.

Schwannomas are benign tumors arising from the peripheral nerve sheath, commonly occurring in the head, neck, and extensor surfaces of the extremities. They can be associated with neurofibromatosis type II. Our case describes a 48-year-old woman with a 2-week history of a left-sided palpable breast mass. She was referred to radiology, where additional imaging revealed a 1.1-cm mass. A biopsy was performed; histology revealed an intramammary schwannoma. Mammography findings include a well-defined mass without calcification. Ultrasound images have shown hypoechoic, encapsulated, and well-defined lesions without calcification. Histologically, schwannomas reveal alternating Antoni A and Antoni B cellular areas. Schwannomas are also S100-positive on immunohistochemistry. This case is best categorized as a BI-RADS 4A lesions. This case report highlights the importance of both imaging and pathology in the diagnosis of breast neoplasms. Although breast schwannomas are not a common entity, they are an important consideration when evaluating a breast mass.

Radiology

Schwartz AG, Lusk CM, Wenzlaff AS, Watza D, Pandolfi S, Mantha L, Cote ML, Soubani AO, Walworth G, Wozniak A, **Neslund-Dudas C**, **Ardisana AA**, **Flynn MJ**, **Song T**, **Spizarny DL**, **Kvale PA**, **Chapman RA**, and Gadgeel SM. Risk of lung cancer associated with COPD phenotype based on quantitative image analysis *Cancer Epidemiol Biomarkers Prev* 2016; 25(9):1341-1347. PMID: 27383774. Article Request Form

Karmanos Cancer Institute, Detroit, Michigan. Department of Oncology, Wayne State University School of Medicine, Detroit, Michigan. schwarta@karmanos.org.
Karmanos Cancer Institute, Detroit, Michigan. Department of Oncology, Wayne State University School of Medicine, Detroit, Michigan.
Department of Oncology, Wayne State University School of Medicine, Detroit, Michigan.
Karmanos Cancer Institute, Detroit, Michigan.
Karmanos Cancer Institute, Detroit, Michigan. Department of Internal Medicine, Wayne State University School of Medicine, Detroit, Michigan.
Department of Radiology, Karmanos Cancer Institute, Detroit, Michigan.
Department of Public Health Sciences, Henry Ford Health System, Detroit, Michigan. Josephine Ford Cancer Institute, Henry Ford Health System, Detroit, Michigan.
Josephine Ford Cancer Institute, Henry Ford Health System, Detroit, Michigan. Department of Radiology, Henry Ford Health System, Detroit, Michigan.
Josephine Ford Cancer Institute, Henry Ford Health System, Detroit, Michigan. Department of Pulmonary and Critical Care Medicine, Henry Ford Health System, Detroit, Michigan.
Josephine Ford Cancer Institute, Henry Ford Health System, Detroit, Michigan. Department of Hematology/Oncology, Henry Ford Health System, Detroit, Michigan.

BACKGROUND: Chronic obstructive pulmonary disease (COPD) is a risk factor for lung cancer. This study evaluates alternative measures of COPD based on spirometry and quantitative image analysis to better define a phenotype that predicts lung cancer risk. METHODS: A total of 341 lung cancer cases and 752 volunteer controls, ages 21 to 89 years, participated in a structured interview, standardized CT scan, and spirometry. Logistic regression, adjusted for age, race, gender, pack-years, and inspiratory and expiratory total lung volume, was used to estimate the odds of lung cancer associated with FEV1/FVC, percent voxels less than -950 Hounsfield units on the inspiratory scan (HUI) and percent voxels less than -856 HU on expiratory scan (HUE). RESULTS: The odds of lung cancer were increased 1.4- to 3.1-fold among those with COPD compared with those without, regardless of assessment method; however, in multivariable modeling, only percent voxels <-856 HUE as a continuous measure of air trapping [OR = 1.04; 95% confidence interval (CI), 1.03-1.06] and FEV1/FVC < 0.70 (OR = 1.71; 95% CI, 1.21-2.41) were independent predictors of lung cancer risk. Nearly 10% of lung cancer cases were negative on all objective measures of COPD. CONCLUSION: Measures of air trapping using quantitative imaging, in addition to FEV1/FVC, can identify individuals at high risk of lung cancer and should be considered as supplementary measures at the time of screening for lung cancer. IMPACT: Quantitative measures of air trapping based on imaging provide additional information for the identification of high-risk groups who might benefit the most from lung cancer screening. Cancer Epidemiol Biomarkers Prev; 25(9); 1341-7.

Radiology

**Wasade VS**, Balki I, **Bowyer SM**, **Gaddam S**, **Mohammadi-Nejad AR**, **Nazem-Zadeh MR**, **Soltanian-Zadeh H**, **Zillgitt A**, and **Spanaki-Varelas M**. Controllable yawning expressed as focal seizures of frontal lobe epilepsy *Epilepsy Behav Case Rep* 2016; 6:61-63. PMID: 27668178. Full Text

Department of Neurology, Henry Ford Health System, Detroit, MI 48202, USA.
University of Toronto, Ontario M5S 1A1, Canada.
Department of Radiology (Image Analysis Laboratory), Henry Ford Health System, Detroit, MI 48202, USA; Control and Intelligent Processing Center of Excellence (CIPCE), School of Electrical and Computer Engineering, University of Tehran, Tehran 14395-515, Iran.
Department of Radiology (Image Analysis Laboratory), Henry Ford Health System, Detroit, MI 48202, USA.

Excessive yawning was described in some neurological conditions as part of periictal or ictal manifestations of epilepsy, most commonly temporal lobe. We present the first case of controllable yawning as a primary seizure semiology with dominant frontal lobe involvement in a 20-year-old man. Video electroencephalography recorded 8 yawning episodes accompanied with right arm movement correlating with rhythmic diffuse theta range activity with left hemispheric predominance. Magnetoencephalography coherence source imaging was consistent with persistent neuronal networks with areas of high coherence reliably present over the left lateral orbitofrontal region. Epileptogenic areas may have widespread networks involving the dominant frontal lobe in unique symptomatogenic areas.

Research Administration

**Brown SL**, **Elmghirbi R**, **Nagaraja T**, **Keenan KA**, **Lapanowski K**, **Panda S**, **Inder P**, **Cabral G**, Liu L, **Kim JH**, **Movsas B**, **Chetty IJ**, **Ewing JR**, and Parry R. Toward a noninvasive measurement of cancer stem cells and tumor aggressiveness *Int J Radiat Oncol Biol Phys* 2016; 96(2s):E592. PMID: 27675105. Full Text Abstract

Henry Ford Health System, Detroit, MI.
Henry Ford Health System, Detroit, MI; Oakland University, Rochester, MI.
University of Windsor, Windsor, ON, Canada.
Varian Medical Systems, Palo Alto, CA, United States.

Research Administration

**Michaels AT**, **Radjef R**, **She R**, **Liu B**, **Peterson E**, Pinto Y, **Williams K**, **Sabbah H**, and **Lanfear D**. Improving risk prediction in heart failure: Maggic + natriuretic peptides *J Card Fail* 2016; 22:S99. PMID: Not assigned. Abstract

A.T. Michaels, Henry Ford Hospital, Detroit, United States

Background: Risk stratification of patients with heart failure (HF) remains challenging but is a critical need. The MAGGIC score is a clinical risk model derived from meta-analysis of nearly 40k patients. Natriuretic peptides (NP) have consistently shown powerful risk prediction in HF patients, but the incremental value in addition to MAGGIC score is not known. Methods: In this single center study 4264 patients were analyzed from two cohorts; a prospective ambulatory registry of HF patients (n = 1314) who had baseline NTproBNP levels measured, and a retrospective cohort collected utilizing administrative data from hospital discharges for HF (January 1st, 2014 through July 30th, 2015; n = 2503) with clinical BNP levels measured at or near discharge. The hospital discharge cohort were all assigned NYHA class IV. The primary end-point was all cause mortality. Performance of the MAGGIC score and NP levels was assessed within each cohort utilizing Cox regression and receiver operating curves (ROC) analysis (MAGGIC alone vs. MAGGIC+NP) with the net reclassification improvement (NRI) also calculated. Results: The overall cohort had an average age of 71.2 years, was 47.8% females, and 41% self-identified African Americans. Median follow up was 1.52 years during which there were 1139 deaths (27%). The MAGGIC score was a strong predictor of outcome in both cohorts (P < .001). In ROC analysis of the ambulatory registry, NP significantly improved area under the curve (AUC) compared to MAGGIC alone from 0.74 to 0.79 (P = .002) and had a NRI of 0.354 (Figure). In contrast, within the hospital discharge cohort NP levels did not significantly add to MAGGIC score (AUC 0.681 vs. 0.676, NRI = 0.033, P = .284) (Figure). Conclusion: In our study, NP levels in the ambulatory setting significantly improved risk stratification provided by the MAGGIC score, but discharge NP levels did not improve MAGGIC prediction of posthospital survival. Overall risk stratification and particularly NP utility is much better in the ambulatory setting. (Figure Presented).

Research Administration

**Radjef R**, **Michaels A**, **Peterson E**, **She R**, **Liu B**, **Williams K**, **Sabbah H**, and **Lanfear D**. Performance of maggic score in African Americans compared to whites *J Card Fail* 2016; 22:S101. PMID: Not assigned. Abstract

R. Radjef, Henry Ford Hospital, Detroit, United States

Background: Risk stratification is critical in Heart Failure (HF) care. The MAGGIC score is a validated tool derived from a large multi-study cohort of nearly 40,000 but very few of the patients self-identified as Black or of African Ancestry (less than 400). There is little data assessing MAGGIC score utility in African Americans (AA). Methods: This single center study analyzed a total of 4264 patients from 2 cohorts; one utilizing administrative data from hospital discharges for HF (January 1st, 2014 through July 30th, 2015, n = 2503) and a prospective registry of ambulatory HF patients (n = 1761), both based in southeast Michigan. Baseline characteristics were collected to tabulate MAGGIC score and test its risk stratification in selfidentified African Americans (AA) and whites. The primary endpoint was time to all-cause mortality. Death was detected using system records and the social security death master file. Cox models with MAGGIC score as the only variable stratified by race, and a combined model including MAGGIC, race, and MAGGIC∗race were tested. P < .05 was considered significant. Results: Overall, 1748 patients (41%) were AA, and a total of 1151 (27%) patients died during follow up. MAGGIC score was strongly and similarly predictive of survival in both race groups. Among AA, each MAGGIC point carried HR of 1.12 (95%CI 1.10, 1.14; P < .001) while in whites the HR was 1.13 (95%CI 1.12, 1.14; P < .001). Formal test of interaction of MAGGIC by race was not significant (P = .153). However, there was a difference in survival by race, with African Americans showing a survival advantage (HR = 0.72, P = .001) which appears to be isolated to the highest risk subgroup (Figure). Conclusion: These data support the utility of the MAGGIC score for risk stratification in African Americans who suffer from HF. However, there may still be residual differences in outcomes between AA and whites despite overall risk adjustment, particularly in highest risk subgroup. (Figure Presented).

Research Administration

**Wolf B**. Successful outcomes of older adolescents and adults with profound biotinidase deficiency identified by newborn screening *Genet Med* 2016;PMID: 27657684. Article Request Form

Department of Research Administration, Henry Ford Hospital, Detroit, Michigan, USA.
Center for Molecular Medicine and Genetics, Wayne State University School of Medicine, Detroit, Michigan, USA.

PURPOSE: We began screening newborns for biotinidase deficiency disorder in 1984, and now all states in the United States and many countries perform this screening. The purpose of this study was to determine the outcomes of older adolescent and adult individuals with the disorder identified by newborn screening. SUBJECTS AND METHODS: We located and surveyed, by questionnaire and telephone interviews, 44 individuals with profound biotinidase deficiency identified by newborn screening with a mean age of 23.1 years. RESULTS: All individuals had successfully completed high school, and many were attending or had completed college or graduate school. Compliance in using biotin has been excellent. Several individuals developed a variety of symptoms when they discontinued biotin for days or weeks. These features readily resolved when biotin was resumed. In addition, five treated women had nine uneventful pregnancies and deliveries. CONCLUSIONS: Newborn screening for profound biotinidase deficiency and early treatment with biotin result in excellent outcomes for older adolescents and adults with the disorder. In addition, mothers with profound biotinidase deficiency who were treated with biotin had pregnancies with good outcomes. These outcome results indicate that newborn screening for biotinidase deficiency is one of the most successful newborn screening programs.Genet Med advance online publication 22 September 2016Genetics in Medicine (2016); doi:10.1038/gim.2016.135.

Sleep Medicine

Verster JC, Fernstrand AM, Van De Loo AJAE, **Roth T**, and Garssen J. The impact of dietary intake of tryptophan, niacin, and vitamin B6 on sleep *Journal of Sleep Research* 2016; 25:127. PMID: Not assigned. Abstract

J.C. Verster, Utrecht University, Division of Pharmacology, Utrecht, Netherlands

Objective: To examine the impact of dietary intake of tryptophan, niacin, and vitamin B6 intake on sleep. Methods: A survey was conducted among N = 509 Dutch university students (28.1% men, mean ± SD age was 20.8 ± 2.4 years old). Dietary intake of tryptophan, niacin and vitamin B6 was assessed with a short semi-quantitative food group questionnaire. Insomnia, sleep quality (0-10 score) and total sleep time (TST) were assessed using the SLEEP-50 questionnaire. Dietary intake of tryptophan, niacin and vitamin B6 was associated with insomnia scores, sleep quality and TST using nonparametric correlations. Results: Insomnia scores correlated significantly with dietary intake of tryptophan (r = -0.180, P = 0.0001), niacin (r = -0.157, P = 0.001) and Vitamin B6 (r = -0.134, P = 0.001). Niacin and

Vitamin B6 intake also correlated significant with sleep quality (r = 0.094, P = 0.045 and r = 0.123, P = 0.009, respectively). No significant correlations were found with TST. In men, insomnia scores correlated significantly with dietary intake of tryptophan (r = -0.287, P = 0.002), niacin (r = -0.243, P = 0.008) and Vitamin B6 (r = -0.204, P = 0.029). Sleep quality scores also correlated significantly with dietary intake of tryptophan (r = 0.205, P = 0.026), niacin (r = -0.240, P = 0.008), and Vitamin B6 (r = 0.218, P = 0.018). In women, vitamin B6 dietary intake was significantly associated with insomnia (r = -0.152, P = 0.006), but none of the other correlations were significant. Conclusion: Dietary intake of tryptophan, niacin and vitamin B6 are significantly, albeit modest, associated with insomnia and sleep quality.

Sleep Medicine

Verster JC, Peters LV, Van De Loo AJAE, Bouwmeester NH, Tiplady B, Alford C, and **Roth T**. Next-morning effects of hypnotic drugs on attention, psychomotor performance, and memory functioning: Implications for traffic safety *J Sleep Res* 2016; 25:126-127. PMID: Not assigned. Abstract

J.C. Verster, Division of Pharmacology, Utrecht University, Utrecht, Netherlands

Objective: A recent meta-analysis showed that on-road highway driving is significantly impaired the morning following bedtime administration of the recommended dose of benzodiazepine drugs and zopiclone. The objective of this study was to conduct metaanalyses to determine which specific cognitive domains that are relevant to driving are impaired the day following bedtime administration of hypnotic drugs. Methods: A literature search (Pubmed, Embase, PsycInfo, Scopus, Web of Science, and Cochrane) yielded N = 33.969 potentially relevant publications. Studies were included if they assessed nextmorning effects on cognition, attention, psychomotor performance, or memory functioning, and if hypnotic drugs were administered in recommended dosages at bedtime. Studies had to be double-blind, placebo-controlled, and conducted in healthy subjects (18-65 years old). Separate meta-analyses were conducted for the cognitive domains sustained- and divided attention, psychomotor speed and accuracy, motor control, and short-term, long-term, and workingmemory. Included treatments were limited to benzodiazepine hypnotics and z-drugs. N = 28 studies reported sufficient data to be included in the meta analyses. Results: Significant impairment was found for the domains divided attention (P = 0.0001), short-term memory (P = 0.0001), long-term memory (P = 0.0001), psychomotor accuracy (P = 0.013), and a trend towards significance for sustained attention (P = 0.06). No significant effects were found for working memory (P = 0.794), psychomotor speed (P = 0.686), and motor control (P = 0.345). Conclusion: The analyses revealed next-morning performance impairment in various cognitive domains, including memory, attention and psychomotor performance. These skills and abilities are highly relevant to daily activities such as driving. Future analyses should be conducted to confirm these findings in elderly and patients.

Surgery

**Bryce K**, **Pehote M**, and **Lanfear D**. Cognitive functioning and post-LVAD outcomes: Influence of comorbidities and specific cognitive domains *J Card Fail* 2016; 22:S124. PMID: Not assigned. Abstract

K. Bryce, Henry Ford Hospital, Detroit, United States

Introduction: Left ventricular assist devices (LVAD) are accepted therapy for end stage heart failure, but optimal patient selection remains challenging. Our group and others recently showed that baseline cognitive impairment is associated with worse outcomes post LVAD. We investigated whether this was impacted overall comorbidity burden, and which dimensions of cognitive function were most critical. Methods: A retrospective review was conducted on 100 consecutive patients who received continuous flow LVADs over a three year period (2011 and 2014) who were administered The Montreal Cognitive Assessment (MoCA) at the time of their pre-surgical psychological evaluation. Those who did not survive to discharge were excluded. Demographic information, MoCA scores and patient outcomes were collected. The primary endpoint of interest was time to hospital readmission tested using Cox regression models adjusted for potential confounders (age, race, gender, indication, and INTERMACS category). Comorbidity burden was assessed using the Charlson index. Standard MoCA subscores for Executive function, Attention, Naming, Abstraction, Language, and Orientation were tested as categorical variables (dichotomized at the median). Results: Average age was 55.6 (±12.29), 22% were female (n = 22), 42% were non-white race (n = 42), and 69% were destination therapy (n = 69). Charlson index was higher in patients with worse baseline MoCA (mean 4.5 vs 3.6, P = .021), but this did not impact the association of MoCA score with time to readmission (Charlson p = NS, MoCA category P = .005 HR = 2.0). When each subscore was tested in regression models only Attention was associated with risk of readmission (HR 2.5, P = .029). Conclusions: Among patients receiving LVADs, baseline cognitive dysfunction is associated with a greater burden of comorbidities, but this did not account for the increased hospital readmission rates among cognitively impaired patients. The cognitive domain that appears most important to post-LVAD outcomes is Attention/Concentration; the mechanism involved is unclear and deserves further investigation.

Surgery
Davis FM, Horne D, Grey SF, Mansour A, **Nypaver T**, Grossman P, Gurm H, and Henke P. Surgical site infection: Incidence, prediction, and risk factors following open lower extremity bypass surgery *J Vasc Surg* 2016; 64(3):870-870. PMID: Not assigned. Abstract

Surgery
**Goodwin M**, **Ito K**, **Gupta AH**, and **Rivers EP**. Protocolized care for early shock resuscitation *Curr Opin Crit Care* 2016; 22(5):416-423. PMID: 27583584. Full Text

aDepartment of SurgerybDepartment of Emergency Medicine, Henry Ford Hospital, Wayne State University, Detroit, Michigan, USA.

PURPOSE OF REVIEW: Protocolized care for early shock resuscitation (PCESR) has been intensely examined over the last decade. The purpose is to review the pathophysiologic basis, historical origin, clinical applications, components and outcome implications of PCESR. RECENT FINDINGS: PCESR is a multifaceted systems-based approach that includes early detection of high-risk patients and interventions to rapidly reverse hemodynamic perturbations that result in global or regional tissue hypoxia. It has been applied to perioperative surgery, trauma, cardiology (heart failure and acute myocardial infarction), pulmonary embolus, cardiac arrest, undifferentiated shock, postoperative cardiac surgery and pediatric septic shock. When this approach is used for adult septic shock, in particular, it is associated with a mortality reduction from 46.5 to less than 30% over the last 2 decades. Challenges to these findings are seen when repeated trials contain enrollment, diagnostic and therapeutic methodological differences. SUMMARY: PCESR is more than a hemodynamic optimization procedure. It also provides an educational framework for the less experienced and objective recognition of clinical improvement or deterioration. It further minimizes practices' variation and provides objective measures that can be audited, evaluated and amendable to continuous quality improvement. As a result, morbidity and mortality are improved.

Surgery
**Hans S**, and **Catanescu I**. Results of early versus delayed carotid endarterectomy after a recent mild to moderate stroke *J Vasc Surg* 2016; 64(3):879-880. PMID: Not assigned. Abstract

Objective Patients with recent stroke represent a heterogeneous group in which the risks of carotid endarterectomy (CEA) vary according to the clinical presentation and the findings on imaging studies. Herein we compared the results of early vs delayed CEA after a recent stroke in patients with similar neurologic presentation. Methods Retrospective analysis of patients undergoing CEA after sustaining a stroke in the distribution of the branches of the middle cerebral artery with ≥70% ipsilateral internal carotid artery stenosis (January 1998 to April 2016) was performed in two mid-sized teaching hospitals. Data have been kept on a continuous basis in the vascular registries. All patients were evaluated by a stroke neurologist with documentation of the deficit by the National Institutes of Health (NIH) Stroke Scale. Patients with transient ischemic attack or a severe stroke (NIH Stroke Scale score >15) were excluded. An indwelling shunt was used if patients developed a neurologic deficit with carotid cross-clamping under cervical block anesthesia or if ischemic electroencephalographic changes developed under general anesthesia. Results Of 82 consecutive patients undergoing CEA for mild to moderate stroke, 55 patients had CEA within 2 weeks of stroke (group A) and 27 patients had CEA from 2 to 8 weeks of stroke (group B). All patients underwent initial carotid duplex ultrasound and a non-contrast-enhanced computed tomography scan of the head. There was a preponderance of men in group B. Risk factors in the form of coronary artery disease, hypertension, diabetes mellitus, hyperlipidemia, nicotine abuse, and chronic obstructive pulmonary disease were similar in both groups (Table). Magnetic resonance imaging of the brain (49), computed tomography angiography of the carotids in the neck (69), magnetic resonance angiography of the neck (14), and carotid and cerebral angiography (14) were performed. The NIH Stroke Scale score was similar in both groups (Table). Perioperative stroke developed in three patients, with mortality in all (stroke/mortality rate of 3.6%). Four patients (4.7%) developed postoperative seizures. There was no myocardial infarction, permanent cranial nerve palsy, or re-exploration for neck hematoma. Demographics, clinical presentation, and complications are shown in Table. Conclusions Early CEA in patients with mild to moderate stroke does not result in increased perioperative stroke/death or seizure compared with delayed CEA and therefore should be preferred to enhance secondary stroke prevention.

Surgery
**Kavousi Y**, **Crutchfield JM**, **Swanson C**, **Karamanos E**, and **Lin JC**. Use of telemedicine for management of patients with varicose vein disease *J Vasc Surg* 2016; 64(3):863-864. PMID: Not assigned. Abstract

[Kavousi, Yasaman; Crutchfield, Janelle M.; Swanson, Christine; Karamanos, Efstathios; Lin, Judith C.] Henry Ford Hlth Syst, Div Vasc Surg, Detroit, MI USA.

Surgery

**Petersen L**, Carlson K, Kopkash K, Witt T, and Madrigrano A. Preoperative antibiotics do not reduce postoperative infections following needle-localized lumpectomy *Breast J* 2016;PMID: 27615388. Full Text

Department of Surgery, Henry Ford Health System, Detroit, Michigan. petersen.lindsay@gmail.com.
Department of Surgery, Cedars-Sinai, Los Angeles, California.
Department of Surgery, Rush University Medical Center, Chicago, Illinois.

Many surgeons routinely use a single preoperative prophylactic dose of an antibiotic prior to needle-localized lumpectomy, despite the lack of evidence that this practice reduces the rate of infection. The aim of this study is to determine if antibiotic administration reduces wound infection for needle-localized lumpectomy. A retrospective chart review of patients that underwent needle-localized lumpectomy from 2010 to 2012 was conducted. Data regarding patient demographics, comorbid conditions, medical history, operative details, and pathology were collected. Surgical infections requiring opening of the wound or treatment with antibiotics were documented if occurred during the first 3 months following surgery. Fisher's exact tests were used for statistical analyses. Two hundred and twenty patients were identified. Thirty-six percent (80/220) of patients received preoperative prophylactic antibiotics. The antibiotic and the nonantibiotic group were similar in age, body mass index, tobacco use, history of radiation, history of neo-adjuvant chemotherapy, duration of surgery, duration needle in place, and pathology. Two percent (4/220) of patients had wound infections. Two percent (3/140) of patients in the nonantibiotic group had infections, versus 1% (1/80) in the antibiotic group. In an analysis of patients that developed infections (n = 4) and patients that did not (n = 216), there was no statistically significant difference in patient demographic, duration of surgery, duration of time needle in place, or pathology. It is safe to omit the use of antibiotics prior to needle-localized lumpectomy and avoid the cost of the medication, patient adverse reactions, and increase in resistant organisms.

Urology

Bardia A, **Sood A**, Mahmood F, Orhurhu V, Mueller A, Montealegre-Gallegos M, Shnider MR, Ultee KH, Schermerhorn ML, and Matyal R. Combined epidural-general anesthesia vs general anesthesia alone for elective abdominal aortic aneurysm repair *JAMA Surg* 2016;PMID: 27603002. Full Text

Department of Anesthesiology, Yale School of Medicine, New Haven, Connecticut.
Center for Outcomes Research, Analytics, and Evaluation, Vattikuti Urology Institute, Henry Ford Hospital, Detroit, Michigan3Center for Surgery and Public Health, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts.
Department of Anesthesiology, Critical Care and Pain Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts.
Department of Anesthesiology, Critical Care and Pain Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts5Department of Surgery, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts.
Department of Vascular Surgery, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts.

Importance: Epidural analgesia (EA) is used as an adjunct procedure for postoperative pain control during elective abdominal aortic aneurysm (AAA) surgery. In addition to analgesia, modulatory effects of EA on spinal sympathetic outflow result in improved organ perfusion with reduced complications. Reductions in postoperative complications lead to shorter convalescence and possibly improved 30-day survival. However, the effect of EA on long-term survival when used as an adjunct to general anesthesia (GA) during elective AAA surgery is unknown. Objective: To evaluate the association between combined EA-GA vs GA alone and long-term survival and postoperative complications in patients undergoing elective, open AAA repair. Design, Setting, and Participants: A retrospective analysis of prospectively collected data was performed. Patients undergoing elective AAA repair between January 1, 2003, and December 31, 2011, were identified within the Vascular Society Group of New England (VSGNE) database. Kaplan-Meier curves were used to estimate survival. Cox proportional hazards regression models and multivariable logistic regression models assessed the independent association of EA-GA use with postoperative mortality and morbidity, respectively. Data analysis was conducted from March 15, 2015, to September 2, 2015. Interventions: Combined EA-GA. Main Outcomes and Measures: The primary outcome measure was all-cause mortality. Secondary end points included postoperative bowel ischemia, respiratory complications, myocardial infarction, dialysis requirement, wound complications, and need for surgical reintervention within 30 days of surgery. Results: A total of 1540 patients underwent elective AAA repair during the study period. Of these, 410 patients (26.6%) were women and the median

(interquartile range) age was 71 (64-76) years; 980 individuals (63.6%) received EA-GA. Patients in the 2 groups were comparable in terms of age, comorbidities, and suprarenal clamp location. At 5 years, the Kaplan-Meier-estimated overall survival rates were 74% (95% CI, 72%-76%) and 65% (95% CI, 62%-68%) in the EA-GA and GA-alone groups, respectively (P < .01). In adjusted analyses, EA-GA use was associated with significantly lower hazards of mortality compared with GA alone (hazard ratio, 0.73; 95% CI, 0.57-0.92; P = .01). Patients receiving EA-GA also had lower odds of 30-day surgical reintervention (odds ratio [OR], 0.65; 95% CI, 0.44-0.94; P = .02) as well as postoperative bowel ischemia (OR, 0.54; 95% CI, 0.31-0.94; P = .03), pulmonary complications (OR, 0.62; 95% CI, 0.41-0.95; P = .03), and dialysis requirements (OR, 0.44; 95% CI, 0.23-0.88; P = .02). No significant differences were noted for the odds of wound (OR, 0.88; 95% CI, 0.38-1.44; P = .51) and cardiac (OR, 1.08; 95% CI, 0.59-1.78; P = .82) complications. Conclusions and Relevance: Combined EA-GA was associated with improved survival and significantly lower HRs and ORs for mortality and morbidity in patients undergoing elective AAA repair. The survival benefit may be attributable to reduced immediate postoperative adverse events. Based on these findings, EA-GA should be strongly considered in suitable patients.

Urology

**Dalela D**, **Karabon P**, **Sammon J**, **Sood A**, **Loppenberg B**, Trinh QD, **Menon M**, and **Abdollah F**. Generalizability of the prostate cancer intervention versus observation trial (PIVOT) results to contemporary North American men with prostate cancer *Eur Urol* 2016;PMID: 27638094. Full Text

VUI Center for Outcomes Research, Analytics and Evaluation, Vattikuti Urology Institute, Henry Ford Health System, Detroit, MI, USA.
VUI Center for Outcomes Research, Analytics and Evaluation, Vattikuti Urology Institute, Henry Ford Health System, Detroit, MI, USA; Public Health Sciences, Henry Ford Health System, Detroit, MI, USA.
VUI Center for Outcomes Research, Analytics and Evaluation, Vattikuti Urology Institute, Henry Ford Health System, Detroit, MI, USA; Division of Urological Surgery, Center for Surgery and Public Health, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA.
Division of Urological Surgery, Center for Surgery and Public Health, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA.
VUI Center for Outcomes Research, Analytics and Evaluation, Vattikuti Urology Institute, Henry Ford Health System, Detroit, MI, USA. Electronic address: firas.abdollah@gmail.com.

The Prostate Cancer Intervention Versus Observation Trial (PIVOT) concluded that radical prostatectomy (RP) offered no survival benefit compared with observation in men with clinically localized prostate cancer (PCa). We identified patients within the National Cancer Database (NCDB) for the period 2004-2012 who met the inclusion criteria of PIVOT (ie, histologically confirmed PCa, clinical stage T1-2NxM0, prostate-specific antigen <50 ng/ml, age <75 yr, estimated life expectancy >10 yr, and undergoing RP or observation as initial treatment within 12 mo of diagnosis) to confirm the generalizability of the PIVOT results to the US population. Life expectancy was calculated using the US Social Security Administration life tables and was adjusted for comorbidities at diagnosis. Compared with PIVOT, men in the NCDB were younger (mean age 60.3 vs 67.0 yr) and healthier (Charlson-Deyo comorbidity index of 0: 93% vs 56%; both p < 0.001). Furthermore, 42% of men randomized to receive RP in PIVOT harbored D'Amico low-risk PCa, whereas 32% of men undergoing RP in the NCDB had low-risk disease. Our findings were confirmed in a sensitivity analysis including men regardless of life expectancy but satisfying all other inclusion criteria of PIVOT. Given that the NCDB represents nearly 70% of all incident cancers diagnosed in the United States, our data provide further evidence that PIVOT results may not be generalizable to contemporary clinical practice. PATIENT SUMMARY: We observed that men diagnosed with clinically localized prostate cancer within the National Cancer Database (2004-2012) were younger, healthier, and more likely to have radical prostatectomy for higher risk disease than men in the Prostate Cancer Intervention Versus Observation Trial (PIVOT), raising questions about the applicability of PIVOT conclusions to the contemporary US population.

Urology

Den RB, Santiago-Jimenez M, Alter J, Schliekelman M, Wagner JR, Renzulli Ii JF, Lee DI, Brito CG, Monahan K, Gburek B, Kella N, Vallabhan G, **Abdollah F**, Trabulsi EJ, Lallas CD, Gomella LG, Woodlief TL, Haddad Z, Lam LL, Deheshi S, Wang Q, Choeurng V, du Plessis M, Jordan J, Parks B, Shin H, Buerki C, Yousefi K, Davicioni E, Patel VR, and Shah NL. Decipher correlation patterns post prostatectomy: initial experience from 2,342 prospective patients *Prostate Cancer Prostatic Dis* 2016;PMID: 27574020. Article Request Form

Department of Radiation Oncology, Sidney Kimmel Medical College of Thomas Jefferson University, Philadelphia, PA, USA.
GenomeDx Biosciences Inc., Vancouver, BC, Canada.
Urologic Oncology and Minimally Invasive Surgery, Hartford Healthcare Medical Group, Hartford, CT, USA.

Section of Minimally Invasive Urology, The Warren Alpert Medical School of Brown University, Providence, RI, USA.
Division of Urology, Penn Presbyterian Medical Center, Philadelphia, PA, USA.
Arizona Urology Specialists, Scottsdale, AZ, USA.
Penn Urology, Philadelphia, PA, USA.
The Urology and Prostate Institute, San Antonio, TX, USA.
Lubbock Urology, Lubbock, TX, USA.
Vattikuti Urology Institute, Henry Ford Hospital, Detroit, MI, USA.
Department of Urology, Sidney Kimmel Medical College of Thomas Jefferson University, Philadelphia, PA, USA.
Global Robotics Institute, Celebration, FL, USA.
Piedmont Health Care, Atlanta, GA, USA.

BACKGROUND: Currently, there are multiple commercially available RNA-based biomarkers that are Medicare approved and suggested for use by the National Comprehensive Cancer Network guidelines. There is uncertainty as to which patients benefit from genomic testing and for whom these tests should be ordered. Here, we examined the correlation patterns of Decipher assay to understand the relationship between the Decipher and patient tumor characteristics. METHODS: De-identified Decipher test results (including Decipher risk scores and clinicopathologic data) from 2 342 consecutive radical prostatectomy (RP) patients tested between January and September 2015 were analyzed. For clinical testing, tumor specimen from the highest Gleason grade was sampled using a 1.5 mm tissue punch. Decipher scores were calculated based on a previously locked model. Correlations between Decipher score and clinicopathologic variables were computed using Spearman's rank correlation. Mixed-effect linear models were used to study the association of practice type and Decipher score. The significance level was 0.05 for all tests. RESULTS: Decipher score had a positive correlation with pathologic Gleason score (PGS; r=0.37, 95% confidence interval (CI) 0.34-0.41), pathologic T-stage (r=0.31, 95% CI 0.28-0.35), CAPRA-S (r=0.32, 95% CI 0.28-0.37) and patient age (r=0.09, 95% CI 0.05-0.13). Decipher reclassified 52%, 76% and 40% of patients in CAPRA-S low-, intermediate- and high-risk groups, respectively. We detected a 28% incidence of high-risk disease through the Decipher score in pT2 patients and 7% low risk in pT3b/pT4, PGS 8-10 patients. There was no significant difference in the Decipher score between patients from community centers and those from academic centers (P=0.82). CONCLUSIONS: Although Decipher correlated with baseline tumor characteristics for over 2 000 patients, there was significant reclassification of tumor aggressiveness as compared to clinical parameters alone. Utilization of the Decipher genomic classifier can have major implications in assessment of postoperative risk that may impact physician-patient decision making and ultimately patient management.Prostate Cancer and Prostatic Diseases advance online publication, 30 August 2016; doi:10.1038/pcan.2016.38.

Urology

Feng FY, Karnes JR, Ashab HA, Trock B, Ross AE, Tsai H, Tosoian J, Erho NG, Alshalafa M, Choeurng V, Yousefi K, **Abdollah F**, Klein EA, Nguyen PL, Dicker AP, Den RB, Davicioni E, Jenkins RB, Lotan T, and Schaeffer EM. Development and validation of genomic signature that predicts androgen deprivation therapy treatment failure *Int J Radiat Oncol Biol Phys* 2016; 96(2s):E221. PMID: 27674101. Full Text Abstract

University of Michigan, Ann Arbor, MI.
Department of Urology, Mayo Clinic, Rochester, MN.
GenomeDx Biosciences, Vancouver, BC, Canada.
James Buchanan Brady Urological Institute, Johns Hopkins Hospital, Baltimore, MD.
Johns Hopkins University, Baltimore, MD.
JHMI, Baltimore, MD.
GenomeDx Biosciences Inc., Vancouver, BC, Canada.
Vattikuti Urology Institute, Henry Ford Hospital, Detroit, MI.
Cleveland Clinic, Cleveland, OH.
Dana-Farber Cancer Institute and Brigham and Women's Hospital, Boston, MA.
Department of Radiation Oncology, Thomas Jefferson University, Philadelphia, PA.
Sidney Kimmel Medical College at Thomas Jefferson University, Sidney Kimmel Cancer Center, Philadelphia, PA.
Mayo Clinic, Rochester, MN.
Johns Hopkins School of Medicine, Baltimore, MD.

Urology

Harms PW, Hocker TL, Zhao L, Chan MP, Andea AA, Wang M, Harms KL, Wang ML, **Carskadon S**, **Palanisamy N**, and Fullen DR. Loss of p16 expression and copy number changes of CDKN2A in a spectrum of spitzoid melanocytic lesions *Hum Pathol* 2016;PMID: 27569296. Full Text

Department of Pathology, University of Michigan Health System, Ann Arbor, MI, 48109, USA; Department of Dermatology, University of Michigan Health System, Ann Arbor, MI, 48109, USA. Electronic address: paulharm@med.umich.edu.
Department of Pathology, University of Michigan Health System, Ann Arbor, MI, 48109, USA.
Department of Biostatistics, University of Michigan Health System, Ann Arbor, MI, 48109, USA.
Department of Pathology, University of Michigan Health System, Ann Arbor, MI, 48109, USA; Department of Dermatology, University of Michigan Health System, Ann Arbor, MI, 48109, USA.
Department of Dermatology, University of Michigan Health System, Ann Arbor, MI, 48109, USA.
Vattikutti Urology Institute, Department of Urology, Henry Ford Health System, Detroit, MI, 48202, USA.

Spitzoid melanocytic lesions, including Spitz nevi (benign), spitzoid melanoma (malignant), and borderline atypical Spitz tumors (ASTs), frequently present challenges for accurate diagnosis and prognosis. Evaluation for loss of the tumor suppressor p16, encoded by CDKN2A gene on chromosome 9p21.3, has been proposed to be useful for evaluation of spitzoid melanocytic lesions. However, reports on the utility of p16 immunohistochemistry for spitzoid lesions have been conflicting, and few studies have directly compared p16 immunohistochemistry with fluorescence in situ hybridization (FISH) for CDKN2A genomic status. We analyzed a spectrum of benign (n=24), borderline (n=27), and malignant (n=19) spitzoid lesions for p16 protein expression by immunohistochemistry and CDKN2A copy number by FISH. Immunohistochemistry was evaluated by two scoring methods: h-score and two-tiered score (positive or negative for p16 loss). By immunohistochemistry, loss of p16 expression was not observed in Spitz nevi (0/24), but was seen in ASTs (7/27, 26%) and spitzoid melanomas (3/19, 16%). By h-score, p16 expression was significantly higher in Spitz nevi relative to ASTs or spitzoid melanomas. Similarly, copy number aberrations of CDKN2A by FISH were absent in Spitz nevi, but were found in 2/21 (9.5%) ASTs and 4/12 (33%) spitzoid melanomas. Our findings from this large cohort suggest p16 aberrations are highly specific for borderline and malignant spitzoid neoplasms relative to Spitz nevi. Similar to ASTs, p16 loss in spitzoid melanomas may occur in the presence or absence of genomic CDKN2A loss.

Urology

**Jindal T**, **Seisen T**, **Sood A**, **Menon M**, and **Abdollah F**. The importance of adjuvant therapy in patients with node-positive prostate cancer: A nationwide validation study *Urol Oncol* 2016;PMID: 27575918. Full Text

Vattikuti Urology Institute & Vattikuti Urology Institute (VUI) Center for Outcomes Research Analytics and Evaluation, Henry Ford Hospital, Detroit, MI.

Urology

Leyh-Bannurah SR, Gazdovich S, Budaus L, Zaffuto E, Dell'Oglio P, Briganti A, Abdollah F, Montorsi F, Schiffmann J, **Menon M**, Shariat SF, Fisch M, Chun F, Graefen M, and Karakiewicz PI. Population-based external validation of the updated 2012 partin tables in contemporary north american prostate cancer patients *Prostate* 2016;PMID: 27683103. Full Text

Cancer Prognostics and Health Outcomes Unit, University of Montreal Health Center, Montreal, Canada. s.bannurah@googlemail.com.
Martini-Clinic, Prostate Cancer Center Hamburg-Eppendorf, Hamburg, Germany. s.bannurah@googlemail.com.
Cancer Prognostics and Health Outcomes Unit, University of Montreal Health Center, Montreal, Canada.
Department of Urology, University of Montreal Health Center, Montreal, Canada.
Martini-Clinic, Prostate Cancer Center Hamburg-Eppendorf, Hamburg, Germany.
Department of Urology and Division of Experimental Oncology, URI, Urological Research Institute, IRCCS San Raffaele Scientific Institute, Milan, Italy.
Department of Urology, Academic Hospital Braunschweig, Braunschweig, Germany.
Vattikuti Urology Institute and VUI Center for Outcomes Research Analytics and Evaluation (VCORE), Henry Ford Hospital, Henry Ford Health System, Detroit, Michigan.
Department of Urology Medical University of Vienna, Vienna, Austria.
Department of Urology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany.

OBJECTIVE: To externally validate the updated 2012 Partin Tables in contemporary North American patients treated with radical prostatectomy (RP) for localized prostate cancer (PCa) at community institutions. MATERIALS AND METHODS: We examined records of 25,254 patients treated with RP and pelvic lymph node dissection (PLND) between 2010 and 2013, within the surveillance, epidemiology, and end results database. The ROC derived AUC assessed discriminant properties of the updated 2012 Partin Tables of organ confined disease (OC), extracapsular extension (ECE), seminal vesical invasion (SVI), and lymph node invasion (LNI). Calibration plots focused on calibration between predicted and observed rates. RESULTS: Proportions of OC, ECE, SVI, and LNI at RP were

69.8%, 18.4%, 7.4%, and 4.4%, respectively. Accuracy for prediction of OC, ECE, SVI, and LNI was 70.4%, 59.9%, 72.9%, and 77.1%, respectively. In subgroup analyses in patients with nodal yield >10, accuracy for LNI prediction was 76.0%. Subgroup analyses in elderly patients and in African American patients revealed decreased accuracy for prediction of all four endpoints. Last but not least, SVI and LNI calibration plots showed excellent agreement, versus good agreement for OC (maximum underestimation of 10%) and poor agreement for ECE (maximum overestimation of 12%). CONCLUSION: Taken together, the updated 2012 Partin Tables can be unequivocally endorsed for prediction of OC, SVI, and LNI in community-based patients with localized PCa. Conversely, ECE predictions failed to reach the minimum accuracy requirements of 70%. Prostate (c) 2016 Wiley Periodicals, Inc.

Urology

Majumder M, House R, **Palanisamy N**, Qie S, Day TA, Neskey D, Diehl JA, and Palanisamy V. RNA-binding protein FXR1 regulates p21 and TERC RNA to bypass p53-mediated cellular senescence in OSCC *PLoS Genet* 2016; 12(9):e1006306. PMID: 27606879. Full Text

Department of Oral Health Sciences and Center for Oral Health Research, College of Dental Medicine, Medical University of South Carolina, Charleston, South Carolina, United States of America.
Department of Urology, Henry Ford Health System, Vattikuti Urology Institute, Detroit, Michigan, United States of America.
Biochemistry and Molecular Biology, Medical University of South Carolina, Charleston, South Carolina, United States of America.
Department of Otolaryngology-Head and Neck Surgery, College of Medicine, Medical University of South Carolina, Charleston, South Carolina, United States of America.

RNA-binding proteins (RBP) regulate numerous aspects of co- and post-transcriptional gene expression in cancer cells. Here, we demonstrate that RBP, fragile X-related protein 1 (FXR1), plays an essential role in cellular senescence by utilizing mRNA turnover pathway. We report that overexpressed FXR1 in head and neck squamous cell carcinoma targets (G-quadruplex (G4) RNA structure within) both mRNA encoding p21 (Cyclin-Dependent Kinase Inhibitor 1A (CDKN1A, Cip1) and the non-coding RNA Telomerase RNA Component (TERC), and regulates their turnover to avoid senescence. Silencing of FXR1 in cancer cells triggers the activation of Cyclin-Dependent Kinase Inhibitors, p53, increases DNA damage, and ultimately, cellular senescence. Overexpressed FXR1 binds and destabilizes p21 mRNA, subsequently reduces p21 protein expression in oral cancer cells. In addition, FXR1 also binds and stabilizes TERC RNA and suppresses the cellular senescence possibly through telomerase activity. Finally, we report that FXR1-regulated senescence is irreversible and FXR1-depleted cells fail to form colonies to re-enter cellular proliferation. Collectively, FXR1 displays a novel mechanism of controlling the expression of p21 through p53-dependent manner to bypass cellular senescence in oral cancer cells.