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Henry Ford Health System Publication List – April 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 May, and then imported into EndNote for formatting.There are 150 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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Anesthesiology

Kaveeshvar H, Kashouty R, and **Loomba V**. Spontaneous carotid dissection in a patient after incidental amphetamine salt overdose presenting as cluster like headache *Neurology* 2016; 86(16)PMID: Not assigned. Abstract

H. Kaveeshvar, Henry Ford Hospital, Detroit, United States

Objective: To highlight cluster like headache can be due to very serious underlying pathology which should not be overlooked Background: Cluster headache has been documented to be the first presenting symptom of an internal carotid dissection. Furthermore, an abrupt increase in blood pressure has been linked to a spontaneous carotid dissection. There are no previous cases reports linking overdose of prescribed amphetamines salts to carotid dissection. Methods: Case Report Results: We present a case report of a 29-year-old man who overdosed on his prescribed attention deficit hyperactivity disorder medication and subsequently developed an internal carotid dissection, which initially manifested as a cluster headache Conclusions: Amphetamines have been linked to ischemic and hemorrhagic strokes in several studies, mainly in young patients. This case provides awareness of this potential complication of amphetamine salt prescription as well as serves to remind physicians of the potential of cluster headache as the presenting symptom of a carotid dissection.

Cardiology / Cardiovascular Research

Ahmed H, Zhao D, Guallar E, Blaha MJ, **Brawner CA**, **Keteyian SJ**, **Al-Mallah MH**, and Michos ED. Gender and fitness status influence age-related decline in peak heart rate achievement: Insight from the fit cohort *Circulation* 2016; 133PMID: Not assigned. Abstract

H. Ahmed, Johns Hopkins Univ, Sch of Medicine, Baltimore, United States

Background: The declines in peak heart rate (HR) and fitness level with age are related; however, whether this association differs based on gender is not well appreciated. In a large cross-sectional cohort of women and men referred for a clinically indicated exercise treadmill test (ETT), we set out to determine whether the decrease in peak HR by age varied by gender (and fitness) in the Henry Ford Exercise Testing (FIT) project Methods: We analyzed data on 38,196 apparently-healthy patients aged 18-96 [mean age 51 ± 12 yrs, 25% black, 48% women] who completed an ETT. Those with history of coronary heart disease, congestive heart failure, diabetes on medications, atrial fibrillation or flutter, or taking AV nodal blocking medications were excluded. Being "fit" was defined as achieving ≥ the median MET level for each sex/age-decile group. Peak HR vs age was plotted, and regression lines were used to determine the intercept and slope for each group Results: Men had higher peak HR than women but with a greater decline over time; the respective intercepts and slopes for peak HR estimates were 202.9 and 0.90 for men and 197.3 and 0.80 for women, (p-interaction = 0.023). Fit people also started out with higher peak HR but approached unfit people at higher age groups; respective intercept and slope by fitness status were 203.0 and 0.87 for fit and 194.7 and 0.83 for unfit (p-interaction <0.001). Separate regression lines were generated for categories of fit men/unfit men, fit
women/unfit women (Figure). Fit and unfit men had similar declines in peak HR with increasing age (slope=0.92); whereas fit women (slope=0.81) had a slightly greater decline in peak HR with increasing age than unfit women (slope=0.73). However, peak absolute HR for fit people still remains higher than for unfit people even into elderly

ages Conclusion: In this cross-sectional cohort of patients referred for a clinical ETT, we found that the age-related decline in peak HR is influenced by both gender and fitness status.

Cardiology / Cardiovascular Research

Ardell JL, Andresen MC, Armour JA, Billman GE, Chen PS, Foreman RD, Herring N, O'Leary DS, **Sabbah HN**, Schultz HD, Sunagawa K, and Zucker IH. Translational Neurocardiology: preclinical models and cardioneural integrative aspects *J Physiol* 2016;PMID: 27098459. Full Text

University of California - Los Angeles (UCLA) Cardiac Arrhythmia Center, David Geffen School of Medicine, Los Angeles, CA, USA.
UCLA Neurocardiology Research Center of Excellence, David Geffen School of Medicine, Los Angeles, CA, USA.
Department of Physiology and Pharmacology Oregon Health & Science University Portland, OR.
Department of Physiology and Cell Biology, The Ohio State University, Columbus, OH.
The Krannert Institute of Cardiology and Division of Cardiology, Department of Medicine, Indiana University School of Medicine, Indianapolis, IN.
Department of Physiology, University of Oklahoma Health Sciences Center, Oklahoma City, OK.
Department of Physiology, Anatomy and Genetics, Univ. of Oxford, England.
Department of Physiology, Wayne State University, Detroit, MI.
Department of Medicine, Henry Ford Hospital, Detroit, MI.
Cellular and Integrative Physiology, University of Nebraska Medical Center, Omaha, NE.
Department of Cardiovascular Medicine, Kyushu University, Fukuoka, Japan.

Neuronal elements distributed throughout the cardiac nervous system, from the level of the insular cortex to the intrinsic cardiac nervous system, are in constant communication with one another to assure that cardiac output matches the dynamic process of regional blood flow demand. Neural elements in their various 'levels' become differentially recruited in the transduction of sensory inputs arising from the heart, major vessels, other visceral organs and somatic structures to optimize neuronal coordination of regional cardiac function. Figure 1 presents the contextual framework for these interactions. This white paper will review the relevant aspects of the structural and functional organization for autonomic control of the heart in normal conditions, how these systems remodel/adapt during cardiac disease, and finally how such knowledge can be leveraged in the evolving realm of autonomic regulation therapy for cardiac therapeutics.

Cardiology / Cardiovascular Research

Baumann RL, **Wang DD**, **Brooks K**, **Panchal R**, **Raymond T**, **Andrew T**, **Parikh S**, **Zweig B**, **Schairer J**, **Eng M**, **Nemeh H**, **Ananthasubramaniam K**, **Greenbaum A**, and **O'Neill W**. Echocardiographic assessment of changes in RV function in patients with mitral regurgitation undergoing mitraclip placement *J Am Coll Cardiol* 2016; 67(13):347. PMID: Not assigned. Abstract

R.L. Baumann, Henry Ford Hospital, Detroit, United States

Background: Few studies have evaluated the effect of percutaneous MitraClip® placement on right ventricular (RV) function following clip implantation. This study aims to assess the impact of successful MitraClip® implantation on post-procedure RV function in both functional and degenerative mitral regurgitation (MR). Methods: Between June 2013 and April 2015, 38 consecutive patients with severe MR underwent percutaneous edge-to-edge repair with a MitraClip®. Pre- and post-procedure transthoracic echocardiograms were analyzed to assess change in RV function based on the American Society of Echocardiography guidelines including the following variables: tricuspid annular plane systolic excursion (TAPSE), Tei index, fractional area change (FAC), RV dimensions (basal (D1), mid (D2) and long (D3)), right atrial (RA) area and pulmonary artery systolic pressure. Results: 28 patients had acceptable image quality for RV evaluation. Mean age was 76 ± 13.2 years, and 43% (12/28) of patients were women. The etiology of the MR was functional in 46% (13/28) of the cases and degenerative in 54% (15/28). Clip failure occurred in 2 patients. Overall, RV Tei index decreased from 0.36 ± 0.08 to 0.31 ± 0.08 (p = 0.028) and FAC increased from 39.6 ±10.3 to 46.9 ± 10.5 % (p = 0.014). Additionally, there was a trend toward improvement in post-procedure TAPSE (p = 0.699) and decrease in post-procedure pulmonary artery systolic pressure (p = 0.067), RA area (p= 0.113) and D1 dimensions (p=0.467) that did not meet statistical significance. Conclusions: Among patients undergoing MitraClip® placement for both degenerative and functional MR, there was clinically significant improvement in RV function as measured by Tei index and FAC across both genders after successful clip implantation. Trends towards improvement in TAPSE, PASP, RA area and D1 were also observed. Our single center study suggests there is improvement in RV function after successful MitraClip® implantation.

Cardiology / Cardiovascular Research

Bryce K, **Lanfear DE**, **Williams CT**, Lindenfeld J, Allen LA, and McIlvennan C. Risk of death or rehospitalization after LVAD and baseline cognitive status *J Heart Lung Transplant* 2016; 35(4):S126-S127. PMID: Not assigned. Abstract

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

Purpose: Optimal patient selection remains challenging for left ventricular assist devices (LVAD). Cognitive impairment is associated with worse outcomes in other patient populations, but there is little data in the setting of LVAD. Methods: A retrospective review at two centers was performed from 2011-2015. 147 patients received a continuous flow LVAD and were given the Montreal Cognitive Assessment (MoCA) pre-LVAD. The primary endpoint was time to death or rehospitalization. We also examined length of stay (LOS). We dichotomized MoCA at the median and tested for association using regression models adjusted for potential confounders (age, race, gender, indication, etiology, INTERMACS category). Results: Median cohort age was 57 (± 13), 19% were female, 31% were African American, and 66% destination therapy (DT). Mean MoCA score was 23.4(±3.7). MoCA differed only by indication (22.8 vs. 24.4, for DT vs. BTT, p= 0.015). In univariate analysis, low MoCA was associated with higher rates of death or readmission (p= 0.04, Figure). This was driven mostly by readmission rates (p= 0.048) with no significant difference in survival (p= 0.23). In adjusted models there was 50% increased risk of death or re hospitalization in the low MoCA group (HR 1.5, p= 0.035). There was a strong trend toward longer LOS in this group (4 days, p= 0.07). Conclusion: Baseline cognitive impairment is associated with worse outcomes after LVAD. Further study is needed to validate this association and evaluate possible mechanisms. (Figure presented).

Cardiology / Cardiovascular Research

Bryce K, **Tita C**, **Williams C**, **Morgan J**, **Nemeh H**, **Selektor Y**, **Borgi J**, **Velez M**, and **Lanfear D**. Cognitive functioning is associated with clinical outcomes after LVAD implantation *J Am Coll Cardiol* 2016; 67(13):1273. PMID: Not assigned. Abstract

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

Background: Left ventricular assist devices (LVAD) are accepted therapy for end stage heart failure, but optimal patient selection remains challenging. Cognitive impairment is associated with worse outcomes in other settings, but there is little data on LVAD outcomes. Methods: We performed a retrospective review of 100 consecutive patients who received continuous flow LVADs over a three year period ('11 to '14) and who completed the Montreal Cognitive Assessment (MoCA) at evaluation. Those not surviving to discharge were excluded. The primary endpoints were time to readmission and survival time. We dichotomized MoCA at the median and tested for association with event rates using Cox regression models adjusted for age, race, gender, indication, and INTERMACS category. Results: The average age was 55.6 (± 12.29), 22 patients were female, 42 were non-white race and 69 were destination therapy. Median MoCA was 24 (IQR 22 - 26). MoCA did not differ by race, gender, or INTERMACS, but did differ by indication (22.8 vs. 24.2 for DT vs. BTT, p=0.049). Low MoCA was associated with re-hospitalization in univariate analysis (p = 0.013, Figure). In adjusted models there was double the risk of hospitalization with low MoCA (HR 2.1 p=0.0054) and a trend towards worse survival (HR 2.8, p = 0.059). Conclusions: Lower cognitive function is associated with higher hospital readmission rates post-LVAD and trends towards worse survival. Further study is needed to validate this association and evaluate possible mechanisms. (Figure presented).

Cardiology / Cardiovascular Research

Carlyle L, **Wang DD**, **Taylor A**, **Swanson B**, **Wyman J**, **Pantelic M**, **Song T**, **Eng M**, **Paone G**, **Greenbaum A**, and **O'Neill W**. No two systoles the same: Personalizing transcatheter heart valve selection for transcatheter aortic valve replacement *J Am Coll Cardiol* 2016; 67(13):327. PMID: Not assigned. Abstract

L. Carlyle, Henry Ford Health System, Detroit, United States

Background: Traditional computed tomographic (CT) definition of systole is at 35% of the cardiac R-R interval. Hence, default sizing of the aortic annulus for transcatheter aortic valve replacement (TAVR) is based upon an automatically generated reconstruction at this fixed point of the R-R interval. However, given inherent variance in physiology related to each patient's cardiac anatomy and its transduction by the ECG-gating process, this assumption may be incorrect. No study has analyzed whether each patient's maximal systolic annular area truly occurs at exactly 35% interval of the cardiac cycle. Methods: 42 consecutive patients underwent TAVR implantation from 7/2015-10/2015 with the Edwards Sapien 3 valve. Pre-procedural CT scan was acquired and aortic annulus area was measured across the entire cardiac cycle (phases 5 to 95% at 10% intervals). Maximal area obtained from pre-procedural CT measurements dictated recommendations for TAVR sizing. Results: All patients underwent successful

TAVR; all CT scans were suitable for analysis. By Chi-squared analysis, recommended valve size differed in 18 of 42 patients ($p<0.0001$) when sizing by smallest measured systolic annular area to that by largest systolic annular area. If sizing strictly by 35% cardiac phase, 5 patients (11.9%, $p<0.0001$) would have received an undersized valve. If purely sized by diastole, 20 patients (47.6%, $p<0.0001$) would have received an undersized valve as compared to maximal systole. In 9% of patients, maximal systolic annular area occurred at the 5% cardiac phase, 16% at 15% phase, 33% at 25% phase, 31% at 35% phase, and 11% at 45% phase. Thus, 69% of patients had maximal annular area on a phase different from 35%. Post procedure, no aortic dissections or major adverse cardiac events occurred. When present, perivalvular leak post TAVR was no more than mild in 97.6% patients. Conclusions: The aortic annulus dynamically changes throughout the cardiac cycle on an individual basis. As such, no automated definition of maximum cardiac systole can be applied to all patients. A more personalized physiological approach to measurement of the aortic annulus may prevent avoidable TAVR valve undersizing and perivalvular leaks.

Cardiology / Cardiovascular Research

Casida J, Pagani FD, Yarandi H, **Williams C**, Lefebvre M, Fox S, and Lichtenberg P. Cognitive function and self-care in patients with left ventricular assist devices (LVADs) *J Heart Transplant* 2016; 35(4):S344. PMID: Not assigned. Abstract

J. Casida, School of Nursing, University of Michigan, Ann Arbor, United States

Purpose: Cognitive function is fundamental to a patient's capability to continually evaluate and perform self-care activities aimed at maintaining health and quality of life (QOL). However, information on cognitive function and self-care in LVAD patients is limited. We sought to examine the patterns and changes in cognitive function and self-care capabilities of patients before and after LVAD implant, and explore the relationships among 4 domains of cognitive function (learning, memory, psychomotor speed, and executive function) and self-care capabilities. Methods: We conducted an observational study on 39 subjects supported with a continuous flow LVAD with axial design from 2 VAD Centers in Michigan. Data were collected before (baseline) and at 1, 3 and 6 months after LVAD implant. Subjects' self-care-capabilities and cognitive function were measured with the Assessment of Self-Care Agency Scale (ASAS) and Cognitive Screening Test (CST), respectively. The 24-item ASAS has a possible sum score of 24 to 120 with higher score indicating better self-care capabilities. A zero CST index, derived from 4 domains of cognitive function, indicates an absence of cognitive impairment. Data were analyzed using descriptive, repeated measures ANOVA, and correlations statistical methods. Results: Subjects had a median age of 57 years (IQR, 52 to 64) and were predominantly Caucasian (53%) males (59%) with some college education (28%), but on disability (80%), and living with family (77%). At baseline, mean ASAS and CST scores were 95.0±9.3 and 0.68±1.0, respectively. Mean scores after LVAD were: 1 month (ASAS= 97.7±14.4, CST= 0.62±0.63); 3 months (ASAS= 99.1±11.1, CST= 0.41±0.86); and 6 months (ASAS= 99.3±12.8, CST= 0.48±0.80). The changes in ASAS scores were significant ($p< 0.05$), but the changes in CST scores were not. Also, the negative correlations among ASAS, 4 domains of cognitive function, and CST index ($r= -.05$ to $-.23$) were not significant. Conclusion: Our data demonstrated that subjects were capable of continually evaluating and performing their self-care needs despite possible cognitive impairment. Further research is warranted to confirm our data and to understand the mechanism of the relationship between cognition and self-care. This knowledge is crucial for testing interventions tailored for optimizing LVAD patients' self-care capabilities vital to maintaining health and QOL.

Cardiology / Cardiovascular Research

Danek BA, Karatasakis A, Karmpaliotis D, **Alaswad K**, Yeh RW, Jaffer FA, Patel M, Bahadorani J, Lombardi WL, Wyman MR, Grantham JA, Doing A, Moses JW, Kirtane A, Parikh M, Ali ZA, Kalra S, Kandzari DE, Lembo N, Garcia S, Rangan BV, Thompson CA, Banerjee S, and Brilakis ES. Use of antegrade dissection re-entry in coronary chronic total occlusion percutaneous coronary intervention in a contemporary multicenter registry *Int J Cardiol* 2016; 214:428-437. PMID: 27088405. Full Text

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BACKGROUND: We assessed efficacy and safety of chronic total occlusion (CTO) percutaneous coronary intervention (PCI) using antegrade dissection re-entry (ADR). METHODS: We examined outcomes of ADR among 1313 CTO PCIs performed at 11 US centers between 2012-2015. RESULTS: 84.1% of patients were men. Prevalence of prior coronary artery bypass graft surgery was 34.3%. Overall technical and procedural success were 90.1% and 88.7%, respectively. In-hospital major adverse cardiovascular events (MACE) occurred in 31 patients (2.4%). ADR was used in 458 cases (34.9%), and was the first strategy in 169 cases (12.9%). ADR cases were angiographically more complex than non-ADR cases (mean J-CTO score: 2.8+/-1.2 vs. 2.4+/-1.2, p<0.001). ADR was performed using the CrossBoss catheter in 246 of 458 (53.7%) and the Stingray system in 251 ADR cases (54.8%). Compared with non-ADR cases, ADR cases had lower technical (86.9% vs. 91.8%, p=0.005) and procedural success (85.0% vs. 90.7%, p=0.002), but similar risk for MACE (2.9% vs. 2.2%, p=0.42). ADR was associated with longer procedure and fluoroscopy time, and higher patient air kerma dose and contrast volume (all p<0.001). After excluding retrograde cases, ADR and antegrade wire escalation (AWE) had similar technical success (92.7% vs. 94.2%, p=0.43), procedural success (91.8% vs. 94.1%, p=0.23), and MACE (2.1% vs. 0.6%, p=0.12). CONCLUSIONS: ADR is used relatively frequently in contemporary CTO PCI, especially for challenging lesions and after failure of other strategies. ADR is associated with similar success rates and risk for complications as compared with AWE, and is important for achieving high procedural success.

Cardiology / Cardiovascular Research
Daubert MA, Yow E, Dunn G, Barnhart H, Douglas P, Udelson J, O'Connor C, **Goldstein S**, and **Sabbah H**. Effects of a novel tetrapeptide in heart failure with reduced ejection fraction (HFREF): A phase I randomized, placebo-controlled trial of elamipretide *J Am Coll Cardiol* 2016; 67(13):1283. PMID: Not assigned. Abstract

M.A. Daubert

Background: Elamipretide is a novel tetrapeptide that targets mitochondrial dysfunction and has the potential to augment cardiac function in HFrEF. Methods: To assess the safety of elamipretide, 36 subjects with EF ≤ 35% and stable NYHA Class II-III were randomized (2:1) to a 4-hr IV infusion of elamipretide in 3 ascending doses (cohort 1: 0.005 mg/kg/hr; cohort 2: 0.05 mg/kg/hr; cohort 3: 0.25mg/kg/hr) or saline. Clinical, lab and blinded echo assessments were performed at baseline, mid- and end-infusion and 6-, 8-, 12- and 24-hrs post-infusion. Change from baseline was compared between each cohort and pooled placebo subjects. Results: Subjects were 62(±10) years, 78% male, baseline EF 29%, and 77% had ischemic cardiomyopathy. There were no serious adverse events (AEs) in any elamipretide cohort. There were 4 non-serious AEs in 3 subjects; dyspnea and tachycardia led to discontinuation in 1 subject in cohort 2. Blood pressure and heart rate remained stable in all cohorts. No significant differences were seen in cohorts 1 or 2. Compared to placebo, elamipretide significantly reduced left ventricular (LV) volumes at end-infusion in cohort 3 and demonstrated a trend toward improvement in other echo parameters (Table). Conclusions: Single-dose elamipretide appears to be well tolerated in HFrEF. Furthermore, there is evidence of decreased LV volumes in the highest dose cohort at end-infusion. Further study of multiple-dose elamipretide is needed to determine long-term safety and clinical efficacy. (Table presented).

Cardiology / Cardiovascular Research
Eng MH, **Greenbaum A**, **Wang DD**, **Wyman J**, **Nemeh H**, **Paone G**, and **O'Neill W**. Transseptal delivery for mitral valve in valve procedures using an apical rail: Technique description and initial results *J Am Coll Cardiol* 2016; 67(13):335. PMID: Not assigned. Abstract

M.H. Eng, Henry Ford Hospital, Detroit, United States

Background: Prior surgical mitral rings or prosthetic valves may degenerate. Re-operation may be prohibitive, thus requiring an alternative such as transcatheter mitral valve replacement (TMVR). Using a transseptal route with an apical access as a rail; we performed TMVR in 11 patients. Methods: From 12/2013 - 8/2015, 11 consecutive patients with degenerated mitral valve repair or valve replacement received TMVR. Patients were assessed for Valve Academic Research Consortium-2 (VARC-2) complications up to their latest clinical follow up. Results: There was 100% procedural success. 8 of 11 patients utilized an apical rail and all apical rail cases employed a nitinol-based occluder device for hemostasis. There was 1 major bleeding event (Bleeding Academic Research Consortium 3a) and no subsequent bleeding events despite the use of oral anti-coagulants upon discharge. Mean follow-up was 150 days [IQR 40-123 days]. There were 2 late adverse outcomes, a non-cardiac related death (628 days) and a stroke (382 days). The mean mitral gradient decreased from 9.5 +/- 3.4 mmHg to 5.5 +/- 2.6 mmHg (p<0.01). Only 1 patient

was found to have ≥moderate regurgitation post-TMVR and none had left ventricular outflow tract obstruction. Conclusions: TMVR with an approach using transseptal access combined with an apical rail is feasibile and prospective studies comparing to the tranaspical route should be considered. (Table Presented).

Cardiology / Cardiovascular Research

Gibbs J, Mansour M, **Mawri S**, **Nasr Y**, **Sudasena D**, and **Ananthasubramaniam K**. The value of additional testing after non-diagnostic stress echocardiography in patients presenting with chest pain: A single-center analysis *J Am Coll Cardiol* 2016; 67(13):520. PMID: Not assigned. Abstract

J. Gibbs, Henry Ford Hospital, Detroit, United States

Background: Stress echocardiography (SE) is an important tool in the risk stratification and prognosis of patients with suspected coronary artery disease (CAD). Data regarding outcomes of patients with non-diagnostic SE are mixed. There is significant downstream resource utilization with additional testing in patients with non-diagnostic SE. We sought to evaluate whether downstream test utilization impacts subsequent hospitalizations or adverse cardiac events in patients with non-diagnostic SE. Methods: We retrospectively identified patients presenting to the observation unit for chest pain who underwent SE between Jan, 2011 and Dec, 2012. Patients who underwent dobutamine or exercise stress testing were included if they failed to achieve 85% of predicted maximal heart rate (PMHR) and had no detectable ischemia. Demographic and clinical risk factors for CAD were collected, as well as downstream test utilization and adverse cardiac events. A multivariable logistical regression analysis was used to evaluate whether additional testing impacted 12-month adverse cardiac events. Results: A total of 490 patients were included in the study. Of those, 112 (23%) underwent additional testing. Patients with further testing were more likely to be older, male, have hypertension or diabetes, and to have known CAD. Patients were more likely to undergo further testing if they performed worse on their initial SE (6.6 vs 7.6 METS, 67.1 vs 73.9% PMHR, $p<0.05$), or if they initially underwent dobutamine SE (45.5% vs 32.5%, $p<0.05$). There was no significant difference in 12-month adverse cardiac events for patients receiving further testing or not. Patients with additional testing did have increased odds of hospital readmission (OR 3.63, $p=0.003$). Conclusions: SE remains an important tool in the evaluation of patients presenting with chest pain. Our study demonstrates that the use of further cardiac testing after non-diagnostic SE is not associated with improved outcomes at 12-months, but is associated with hospital readmission and resultant cost. A strategy employing selective additional testing and good follow-up may improve cost-efficacy.

Cardiology / Cardiovascular Research

Gupta RC, **Sing-Gupta V**, **Palaniyandi S**, and **Sabbah HN**. Reduced aldehyde dehydrogenase-2 activity and protein level in left ventricular myocardium of dogs with chronic heart failure *J Am Coll Cardiol* 2016; 67(13):1498. PMID: Not assigned. Abstract

R.C. Gupta, Henry Ford Hospital, Detroit, United States

Background: Reactive aldehydes such as 4-hydroxy-2-nonenal (4HNE) are generated in the failing heart and contribute to cardiomyocyte injury and death and to progressive global LV dysfunction. Aldehyde dehydrogenase-2 (ALDH2) plays a pivotal role in detoxifying mitochondrial (MITO) reactive aldehydes. The present study examined the activity, protein level and mRNA expression of ALDH2 in left ventricular (LV) myocardium of dogs with chronic heart failure (HF) (LV ejection fraction ~30%). Methods: Studies were performed in LV tissue from 7 HF dogs produced by intracoronary microembolizations and 7 normal (NL) dogs. Isolated MITO fractions were prepared using a subcellular fractionation kit. ALDH2 activity was measured using a colorimetric ALDH2 assay kit and expressed as nmol NADH formed/min/mg protein. Protein levels of ALDH2 and porin, a MITO protein not altered in HF, were determined by Western blotting coupled to chemiluminescence and band intensities were expressed in densitometric units (du). mRNA expression of ALDH2 and GAPDH, an internal control, was measured in isolated RNA using real-time PCR and expressed as fold change. Results: No changes in protein level of porin was observed between NL and HF dogs (0.24 ± 0.02 vs. 0.22 ± 0.01 du). Compared to NL dogs, ALDH2 activity was significantly decreased (93.3 ± 3.5 vs. 44.5 ± 2.9 nmol NADH/min/mg, $p<0.05$) as were protein levels (1.01 ± 0.05 vs. 0.53 ± 0.02 du, $p<0.05$) in LV myocardium of HF dogs. Furthermore, ALDH2 mRNA level normalized to GAPDH was reduced 4 folds in failing hearts compared to NL hearts. Conclusions: Compared to NL dogs, activity and expression of ALDH2 are reduced in LV myocardium of HF dogs. This abnormality may contribute to the observed increase in levels of oxidative stress in the failing heart. ALDH2 represents a potential therapeutic target for attenuating the adverse effects of oxidative stress in HF.

Cardiology / Cardiovascular Research

Gupta RC, **Sing-Gupta V**, and **Sabbah HN**. Bendavia (elamipretide) restores phosphorylation of cardiac myosin binding protein c on serine 282 and improves left ventricular diastolic function in dogs with heart failure *J Am Coll Cardiol* 2016; 67(13):1443. PMID: Not assigned. Abstract

R.C. Gupta, Henry Ford Hospital, Detroit, United States

Background: Cardiac myosin binding protein-C (cMyBPC) modulates cross-bridge cycling rates via alterations in its phosphorylation. cMyBPC at serine 282 is dephosphorylated in heart failure (HF), a maladaptation implicated in LV diastolic dysfunction and HF with preserved ejection fraction (HFpEF). We showed that chronic therapy with Bendavia (BEN, Elamipretide), improves LV systolic and diastolic function and normalizes mitochondrial function in HF dogs. This study examined the effects of BEN on LV protein levels of cMyBPC and cMyBPC-S282 in HF dogs with reduced EF (HFrEF) that also manifest diastolic dysfunction. Methods: Studies were performed in LV tissue from 14 HF dogs randomized to 3 months therapy with s.c. injections of BEN (0.5 mg/kg once daily, n=7) or saline (HF-control, n=7) and from 6 normal (NL) dogs. cMyBPC and cMyBPC-S282 were measured by Western blotting coupled to chemiluminescence and band intensity expressed in densitometric units (du). Results: Data are shown in table. cMyBPC level were unchanged among study groups. Compared to NL, cMyBPC-S282 was significantly decreased in HF-controls as was the ratio cMyBPC-S282/cMyBPC. BEN significantly increased levels of cMyBPC-S282 and the ratio cMyBPC-S282/cMyBPC compared to HF-controls. Conclusions: Therapy with BEN restores near normal levels of cMyBPC-S282 in LV of HF dogs. This likely contributed to improved LV relaxation. The findings suggest that BEN may be useful in the treating HFrEF and HFpEF. (Table presented).

Cardiology / Cardiovascular Research

Hachey B, Kontos M, Newby LK, Peacock WF, and **McCord J**. Trends in cardiac biomarker protocols and troponin cut-points *J Am Coll Cardiol* 2016; 67(13):467. PMID: Not assigned. Abstract

B. Hachey, Henry Ford Hospital, Detroit, United States

Background: Various combinations of creatine kinase (CK)-MB, myoglobin and/or Cardiac Troponin I or T (cTnI/cTnT) have been used for evaluation of possible acute coronary syndrome (ACS). The current recommendation is to use the 99th percentile of cTnI/cTnT as the sole marker for diagnosis of acute myocardial infarction. Adoption of this recommendation in the US has not been well characterized. Methods: We retrospectively analyzed cardiac marker protocols collected from 829 US hospitals undergoing Chest Pain Center Accreditation through the Society of Cardiovascular Patient Care from 2009-2014. Data were obtained via a self-reported survey that addressed cardiac marker(s), sampling time periods and cut-points used for evaluation of possible ACS. Results: The combination of cTnI or cTnT with CK-MB was the most common strategy employed (Figure). However, the use of cTnI or cTnT as the sole marker increased over time (15 to 38%) as did use of the 99th percentile for cTnI/cTnT (30 to 60%) (Figure). Conclusions: Despite current recommendations, there remains considerable variation in cardiac marker testing strategies used in US hospitals for evaluation of possible ACS. Although increasing, fewer than 40% of hospitals used a cTn alone strategy, and only 49% used the recommended 99th percentile cTn cut-point. (Figure Presented).

Cardiology / Cardiovascular Research

Jain T, **Nowak R**, **Hudson M**, **Frisoli T**, **Jacobsen G**, **Tabaku M**, and **McCord J**. Short and long-term prognostic utility of the heart score in patients presenting to the emergency department with undifferentiated chest pain *J Am Coll Cardiol* 2016; 67(13):513. PMID: Not assigned. Abstract

T. Jain, Heart and Vascular Institute, Henry Ford Hospital, Detroit, United States

Background: The HEART score (HS) is a risk-stratification tool that was developed for patients evaluated for possible acute coronary syndrome (ACS) in the Emergency Department (ED). It incorporates elements of the history, ECG, age, risk factors and troponin levels. We sought to determine the short-term and long-term prognostic utility of the HS. Methods: A retrospective single-center analysis of 947 consecutive patients evaluated for possible ACS in ED in 1999 was conducted. Patients were followed for major adverse cardiac events (MACE) at 30 days: death, acute myocardial infarction (AMI), or revascularization procedure. All-cause mortality was assessed at 5 years. The HS was compared to the thrombolysis in myocardial infarction (TIMI) score. Results: At 30 days, 14 % (135/947) of patients had a MACE: 48 deaths (5%), 84 AMIs (9%) and 48 (5%) revascularization procedures. The MACE rate in patients with a HS ≤ 3 was 0.6 % (1/175) involving a revascularization procedure, 9.5% (53/557) in patients with a HS between 4 and 6 and 38% (81/215) with HS ≥ 7. The C-statistic for the HS was 0.82 and 0.68 for the TIMI score for predicting 30-day MACE, $p< 0.05$. Patients with a HS ≤ 3 had a significantly lower 5-year mortality rate as compared to those with a TIMI score 0 (10.6% vs 20.5%, $p=0.02$). Conclusions: The HS is not only a valuable risk-stratification

tool in predicting short-term MACE but also long-term mortality in patients presenting to the ED evaluated for possible ACS. The prognostic utility of the HS was superior to the TIMI score. (Figure presented).

Cardiology / Cardiovascular Research
Jain T, **Shah J**, **Shah S**, and **Modi S**. Heart within a heart *J Cardiovasc Ultrasound* 2016; 24(1):60-63. PMID: 27081446. Full Text

Department of Internal Medicine, Henry Ford Hospital, Detroit, MI, USA.
Department of Cardiology, Henry Ford Hospital, Detroit, MI, USA.

Device based closure of the left atrial appendage (LAA) has emerged as a viable approach for stroke prevention in atrial fibrillation (AF) patients with contraindications to chronic oral anticoagulation. One of the most feared complications is device related thrombus formation. We present a 66-year-old male with chronic AF who developed a life-threatening intracranial bleed on oral anti-coagulation. He subsequently underwent LAA closure using an Amplatzer muscular ventricular septal defect closure device for stroke prevention. However, he was found to have a large thrombus attached to the device a year later. We present a review of the various LAA closure devices, importance of periodic surveillance via echocardiography and management options to prevent this complication. Also, the case highlights the importance of contrast-enhance echocardiography in diagnosis of LAA closure device thrombus.

Cardiology / Cardiovascular Research
Lanfear DE, Levy WC, Stehlik J, Estep JD, Rogers JG, Shah KB, Boyle AJ, Chuang J, Farrar DJ, and Starling RC. Accuracy of seattle heart failure model and heartmate II risk score in non-inotrope dependent advanced heart failure patients: Insights from the roadmap study *J Heart Lung Transplant* 2016; 35(4):S109. PMID: Not assigned. Abstract

D.E. Lanfear, Henry Ford Hospital, Detroit, United States

Purpose: In advanced heart failure (HF) patients (pts) not on inotropes, optimal timing for left ventricular assist device (LVAD) is unclear. Validated methods exist for predicting survival in HF (Seattle HF model-SHFM), and after LVAD (HeartMate II Risk Score-HMRS), but utility in this patient group is not established. Methods: ROADMAP is a prospective, 41-center, non-randomized study of 200 NYHA Class IIIB/IV pts not on inotropes who met FDA indications for LVAD, comparing the effectiveness of HeartMate II LVAD support vs Optimal Medical Management (OMM). We tested SHFM predicted survival compared to observed in the OMM arm (n= 103), and HMRS vs observed in all LVAD pts (n= 111). We also assessed calibration for each score. Risk strata cutoffs were from the original works. Results: Of 103 OMM pts, 18 had a delayed LVAD due to clinical deterioration. SHFM predicted survival by intention to treat (AUC= 0.71, p< 0.001), but not when considering delayed LVADs as treatment failures (AUC= 0.56, p= 0.097), underestimating risk in lower risk groups (figure, left). In this relatively lower risk LVAD cohort, the HMRS overestimated risk (figure, right) showing marginal discrimination at 3 months (AUC= 0.71, p= 0.23) and 1 year (AUC= 0.62, p= 0.037. Conclusion: In non-inotrope advanced HF pts in ROADMAP, the SHFM was predictive of mortality but underestimated the risk of deterioration to rescue LVAD, while the HMRS overestimated post-LVAD mortality. Improved risk stratification is needed for these patients. (Figure Presented).

Cardiology / Cardiovascular Research
McIlvennan CK, **Bryce K**, Lindenfeld J, Allen LA, and **Lanfear DE**. Assessment of cognitive function prior to and after implantation of left ventricular assist device *J Heart Lung Transplant* 2016; 35(4):S165-S166. PMID: Not assigned Abstract

C.K. McIlvennan, University of Colorado, Aurora, United States

Purpose: Placement of a left ventricular assist device (LVAD) for end-stage heart failure improves survival and quality of life, but it remains uncertain if cognitive function improves. The Montreal Cognitive Assessment (MoCA) is a simple, validated cognitive evaluation tool. We assessed whether cognitive function changes after LVAD implantation. Methods: Data was collected on 147 consecutive patients undergoing LVAD at two hospitals (2011-2015) where MoCA testing prior to implant was part of evaluation. Patients who had repeat MoCA testing post-LVAD (n= 90) were analyzed. Change in MoCA score (Δ MoCA) was tested using paired t-test. Baseline characteristics (age, race, gender, INTERMACS, etiology, indication, site) were tested for association with Δ MoCA by t-test, chi-square as appropriate. Results: The cohort had a mean age of 57 (±12.9), 66% destination therapy (n= 59), and a mean time to repeat MoCA of 149 days. Mean baseline MoCA was 23.1 (±3.8), and was not associated with any baseline characteristics. MoCA score increased after LVAD implantation; the average change was +1.6 (±3.7) points (p <

0.0001) and varied substantially across the cohort (range -11 to +12, Figure). Change in MoCA did not differ by any baseline characteristic (all p > 0.1). Conclusion: Cognitive function assessed by MoCA improves statistically after LVAD implant but the small magnitude may not be clinically significant. It seems unlikely to expect major improvements in cognitive function after LVAD for most patients. (Figure Presented).

Cardiology / Cardiovascular Research

Muller CC, **McCord J**, **Michaels A**, **Nowak R**, Giannitsis E, Body R, Christ M, Lindahl B, DeFilippi C, Christenson R, Bendig G, **Jacobsen G**, and Mueller C. Symptoms predictive of acute myocardial infarction in the troponin era: Analysis from the TRAPID-AMI study *J Am Coll Cardiol* 2016; 67(13):518. PMID: Not assigned. Abstract

C.C. Muller, Henry Ford Hospital, Detroit, United States

Background: The TRAPID-AMI study was an Emergency Department (ED) multicenter trial evaluating a rapid "rule-out" acute myocardial infarction (AMI) protocol over 1 hour using changes in high-sensitivity cardiac troponin (cTn) T∗ (Roche Diagnostics). We studied which symptoms were predictive of AMI, as part of a sub-study of TRAPID-AMI. Methods: There were 1,282 patients evaluated in EDs for possible AMI from 12 centers in Europe, USA, and Australia from 2011 to 2013. The diagnosis of AMI was centrally adjudicated by 2 independent cardiologists in accordance with the universal definition of AMI, using all available clinical information and serial measurements of cTnI-Ultra (Siemens Healthcare). A total of 26 symptom variables were prospectively obtained. Multivariable logistic regression analysis was done; Odds Ratios (OR) with 95% confidence intervals (CI) were calculated. Results: There were 213/1282 (17%) AMIs. Independent predictors of AMI are shown (Figure). The presence of more predictors increased the risk of an AMI. In the entire group 131 (10%) had radiation to right arm/shoulder, 897 (70%) had chest pressure, 385 (30%) worsened with activity, and 448 (35%) had radiation to left arm/shoulder. Duration of symptoms was not predictive of AMI. There were no symptoms that were independently predictive of not having AMI. Conclusions: In a multicenter trial there were only 4 symptoms that were independently associated with the diagnosis of AMI. ∗510(K) submitted to FDA, but not yet approved in the U.S. (Figure presented).

Cardiology / Cardiovascular Research

Raymond T, **Mawri S**, **Jacobsen G**, **Selektor Y**, **Velez M**, **Williams C**, **Nemeh H**, **Borgi J**, **Morgan J**, **Lanfear D**, and **Tita C**. The incidence of spontaneous intracranial hemorrhage is associated with infection in patients with mechanical circulatory support *J Heart Lung Transplant* 2016; 35(4):S246. PMID: Not assigned. Abstract

T. Raymond, Henry Ford Hospital, Detroit, United States

Purpose: Intracranial hemorrhage (ICH) is a well-known catastrophic complication in patients with left ventricular assist devices (LVADs). The cause of non-traumatic ICH in patients with LVADs is likely multifactorial and has been inadequately studied. We anecdotally noted frequent presence of infection in this setting and sought to quantify it and assess outcomes. Methods: We retrospectively studied 223 consecutive patients who had continuous flow (CF) LVADs implanted between March 2007 and March 2014. Patients who suffered a non-traumatic ICH were selected for further data collection. The presence or absence of infection at time of ICH, defined by CDC criteria, was collected, along with patient characteristics and outcomes. The rate of infection among ICH patients was compared to published historical cohorts. Characteristics and outcomes were compared using the Wilcoxon rank sum test, chi-square test or Fischer exact test, as indicated. Results: Eighteen LVAD patients with non-traumatic ICH (13 parenchymal, 3 subarachnoid, 2 subdural) were identified. Median duration of support at the time of ICH was 700 days. The average INR was 3.3 ± 3.0 and platelet count was 171.2 ± 69.6. These did not differ between infected and non-infected groups (INR 4.5 ± 3.7 vs 2.8 ± 2.7, p = 0.225; platelets 193 ± 76.5 vs 162.2 ± 67.8, p = 0.37). Bacteremia was present on admission in 9/18 patients (50%), and chronic driveline infection in 4/18 patients (22.2%). The presence of any infection at the time of presentation for ICH was 66.7%. This is significantly higher when compared to the overall infection rate in the HMII DT trial/HMII arm of 36%, (p = 0.007). Compared to survivors, patients who died during the hospitalization had a greater degree of leukocytosis (WBC 15.1 ± 6.0 vs. 10.2 ± 5.6, p = 0.049). Admission INR level, platelet count and LDH level did not impact in-hospital mortality (survivors vs non-survivors: INR 2.9 ± 2.8 vs 3.8 ± 3.4, p = 0.885; platelet count 157.4 ± 47.4 vs 186.8 ± 89.3, p = 0.885; LDH level 466.5 ± 355.4 vs 232.3 ± 71.4, p = 0.166). Conclusion: There is a high incidence of infection in CF LVAD patients presenting with ICH and these patients appear to do worse. Early administration of antibiotics should be considered in these patients. Additional studies are warranted to explore causation and potential impact of early antibiotic treatment on patients' survival.

Cardiology / Cardiovascular Research

Rezik M, and **Mattina D**. Severe cardiomyopathy secondary to anti-TNF therapy for crohn's disease *J Am Coll Cardiol* 2016; 67(13):1042. PMID: Not assigned. Abstract

M. Rezik, Henry Ford Hospital, Detroit, United States

Background: Tumor necrosis factor-alpha inhibitors are a popular and effective therapy for inflammatory bowel disease and other inflammatory conditions. Despite a substantial amount of evidence, cardiomyopathy is a widely unrecognized adverse effect of these medications. Case: A 57-year-old male presented with a two-week history of dyspnea and productive cough. History included hypertension, asthma and crohn's disease. His symptoms had been worsening despite inhaler use and were especially pronounced when lying down at night. Physical exam was unremarkable without abnormal cardiac or pulmonary findings. Decision Making: ECG was significant for left ventricular hypertrophy and lateral T-wave inversions and troponin was elevated at 1.97. The patient was admitted and treated for a non-ST elevated myocardial infarction. Echocardiogram revealed an enlarged and severe hypokinetic left ventricle with 12% ejection fraction and diastolic filling dysfunction. Cardiac catheterization revealed mild non-obstructive disease. Given the presenting symptoms, a cardiac MRI was obtained and showed no evidence of viral myocarditis or other infiltrative process. On further review, it was noted that he had been started on adalimumab four months prior to presentation for treatment of his crohn's disease. Literature review revealed reports of heart failure after therapy and subsequent recovery after discontinuation. The adalimumab was discontinued and he was started on conventional heart failure therapy. Upon follow-up, the patient reported virtual resolution of symptoms. Repeat echocardiogram showed an improved ejection fraction of 20%. Conclusions: Cardiomyopathy is an important yet unfamiliar adverse effect of adalimumab and other TNF-alpha inhibitors. Physicians must be aware of this complication and patients on therapy should be monitored for symptoms of new or worsening heart failure.

Cardiology / Cardiovascular Research

Sabbah HN, **Gupta RC**, and Emanuele M. Vepoloxamer (purified sodium-free poloxamer-188) improves LV systolic function in dogs with advanced heart failure and protects failing cardiomyocytes from calcium overload *J Heart Lung Transplant* 2016; 35(4):S141. PMID: Not assigned. Abstract

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

Purpose: Ca2+ overload occurs in cardiomyocytes (CMs) of the failing heart and contributes to loss of CMs and to progressive LV dysfunction. Vepoloxamer (VEPO), purified sodium-free poloxamer-188, is a rheologic agent that improves microvascular blood flow and potentially repairs damaged cell membranes. We examined the effects of multiple acute i.v. infusions of VEPO on LV function in dogs with heart failure (HF) (LV ejection fraction, EF∼30%) and tested the hypothesis that the membrane reparative properties of VEPO attenuates Ca2+overload in CMs by preventing unregulated Ca2+ entry into the cells. Methods: 14 dogs were randomized to 2, 2 hr infusions of VEPO (450 mg/ kg, n= 7) or v/v saline (control, n= 7) given 3 weeks (W) apart. LV EF and plasma nt-pro BNP were measured at baseline, at end of infusion and at 1, 2 and 3W after each infusion. The change (Δ) between baseline and each study time point (treatment effect) was calculated. Separately, freshly isolated CMs from 6 HF control dogs were incubated for 2 hrs with VEPO (4.5 mg/ml) or saline and then treated with 10 μM Fura-2 AM for 1 hr and resuspended in 1.0 mM extracellular Ca2+ for 2 hrs to flourometrically assess intracellular Ca2+ concentration. Results: VEPO increased EF by 6.0±0.7%∗ at 2hrs; 7.0±0.7%∗% at 1W; 4.5±0.5%∗ at 2W; 1.0±0.6% at 3W; 6.0±1.3%∗ at 4W; 6.0±1.4%∗ at 5W; 5.9±1.3%∗ at 6W (∗= p< 0.05 vs. control) and reduced BNP by 910±92∗ pg/ ml at 2hrs; 328±103∗ pg/ml at 2W; 333±60∗ pg/ml at 4W;235±48∗ pg/ml at 6W (∗= p< 0.05 vs. control). Treatment of isolated CMs with VEPO reduced intracellular Ca2+ compared to saline (2.32±0.05 vs. 3.14±0.32 relative flourometric units, p< 0.05) thus inhibiting unregulated Ca2+ entry into CMs. Conclusion: VEPO relieves Ca2+overload in failing CMs. Multiple short i.v. infusions of VEPO, pulsed at 3W intervals, elicit progressive improvement in LV systolic function. The results support development of VEPO for pulsed treatment in patients with advanced HF and those on waiting lists for heart transplantation or LVADs requiring i.v. therapy.

Cardiology / Cardiovascular Research

Sabbah HN, **Gupta RC**, Sing-Gupta V, **Zhang K**, and Emanuele M. Multiple intravenous infusions of vepoloxamer (purified poloxamer-188) elicit progressive improvements in plasma biomarkers in dogs with advanced heart failure *J Am Coll Cardiol* 2016; 67(13):1551. PMID: Not assigned. Abstract

H.N. Sabbah

Background: Ca2+ overload occurs in heart failure (HF) leading to cardiomyocyte dysfunction and death. Vepoloxamer (VEPO), purified poloxamer-188, is a rheological agent that improves microvascular blood flow and

repairs damaged cell membranes and has been shown to prevent unregulated Ca2+ entry into failing cardiomyocytes thus limiting Ca2+ overload. We examined the effects of multiple acute i.v. infusion of VEPO on LV systolic function and plasma biomarkers in HF dogs (LV ejection fraction, EF~30%). Methods: 14 HF dogs were randomized to 2, 2 hours infusions of VEPO (450 mg/kg, n=7) or normal saline (control, n=7) given 3 weeks apart. Dogs were followed for 3 weeks after each infusion (total follow-up 6 weeks). LV EF, plasma n-terminal-pro brain natriuretic peptide (nt-pro BNP) and troponin-I (Tn-I) were measured at baseline, at 1, 2 and 3 weeks after each infusion. Plasma biomarkers were measured using commercially available ELISA assays. The change between baseline and each study timepoint (treatment effect, Δ) was calculated. Results: Data shown in table. Saline had no effect on EF, nt-pro BNP or Tn-I. Compared to saline control, VEPO increased EF, and progressively reduced nt-pro BNP and Tn-I. The benefits were sustained for up to 3 weeks after the 2nd infusion of VEPO. Conclusions: Pulsed therapy with i.v. VEPO improves LV systolic function, lowers nt-pro BNP and reduces Tn-I, a measure of ongoing cardiomyocyte death. The results support the development of pulsed VEPO therapy for treatment of advanced HF. (Table Presented).

Cardiology / Cardiovascular Research

Sabbah HN, **Gupta RC**, Sing-Gupta V, **Zhang K**, and Emanuele M. Vepoloxamer (purified poloxamer-188) restores integrity of cardiomyocyte calcium cycling proteins in left ventricular myocardium of dogs with advanced heart failure *J Am Coll Cardiol* 2016; 67(13):1449. PMID: Not assigned. Abstract

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

Background: Ca2+ overload occurs in failing cardiomyocytes (CMs) and contributes to abnormalities of Ca2+ cycling proteins (CCP). Vepoloxamer (VEPO), purified poloxamer-188, is a rheological agent that repairs damaged cell membranes which prevents unregulated Ca2+ entry into CMs thus limiting Ca2+ overload. We showed that multiple 2 hr i.v. infusions of VEPO in heart failure (HF) dogs improves LV systolic function with benefits persisting up to 3 weeks after each infusion. This study examined the effects of multiple infusions of VEPO on CMs CCP in LV tissue of HF dogs (LV ejection fraction, EF~30%). Methods: Studies were performed in 14 HF dogs randomized to 2, 2 hr infusions of VEPO (450 mg/kg, n=7) or saline (Control, n=7) given 3 weeks apart. Tissue samples obtained 3 weeks after the 2nd infusion were used. Ca2+-ATPase activity was measured by calorimetrically. Phosphorylated (p) phospholamban at serine-16 (p-PLB-s16), p-ryanodine receptors at serine-2808 (p-RYR-s2808) and p-sodium-calciumexchanger 1 (p-NCX-1) were measured using specific antibodies and Western blotting. LV tissue from 7 normal (NL) dogs was used for comparisons. Results: Ca2+-ATPase activity and p-PLB-s16 level were reduced and p-RYR-s2808 and p-NCX-1 levels increased in HF-Controls compared to NL (Table). VEPO treatment partially normalized activity and protein levels (Table). Conclusions: By limiting unregulated Ca2+ entry, VEPO attenuated Ca2+ overload in CMs and improved CCP leading to improved LV function. (Table presented).

Cardiology / Cardiovascular Research

Shah R, **Singh G**, **Lahiri M**, **Patel R**, and **Schuger C**. Central nervous system mediated cardiac asystole in setting of paraneoplastic N-methyl-D-aspartate receptor antibody encephalitis *J Am Coll Cardiol* 2016; 67(13):1253. PMID: Not assigned. Abstract

R. Shah, Henry Ford Health System, Detroit, United States

Background: Sinus bradycardia (SB) and sinus node arrest (SNA) with absence of escape are features of hyper-vagotonia and are seen with central nervous system pathology affecting the balance between sympathetic and parasympathetic systems. Case: A 37-year-old female with no history presented with fever and hallucinations. She developed status epilepticus requiring intubation and episodes of abrupt sinus tachycardia (ST), SB, and recurrent asystole. Vaginal ultrasound demonstrated bilateral ovarian masses suggestive of teratomas. Cerebrospinal fluid revealed elevated titer of antibodies to N-methyl-D-Aspartate (NMDA) receptor. The patient had frequent and unprovoked episodes of extreme SB with prolonged, hemodynamically-unstable, asystolic episodes, immediately followed by ST. Decision Making: ECG and telemetry demonstrated: ST, SB, non-conducted p waves, and SNA with >8 second pauses; bradycardia coincided with hypotension. An active fixation transvenous pacing right ventricular lead connected to an external pacemaker was placed. Patient required frequent pacing until she underwent oopherectomy with removal of teratomas and plasmapheresis for anti-NMDA receptor encephalitis. Autonomic instability and cardiac dysrhythmia resolved without need for permanent pacing. Conclusions: This case demonstrates a rare, reversible, and under recognized cause of paraneoplastic-mediated cardiac rhythm dysfunction in the setting of anti-N-methyl-D-Aspartate receptor encephalitis. (Figure presented).

Cardiology / Cardiovascular Research
Srivastava AV, and **Ananthasubramaniam K**. Guiding coronary revascularization using PET stress myocardial perfusion imaging: The proof is in the pudding *J Nucl Cardiol* 2016;PMID: 27033351. Article Request Form

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Cardiology / Cardiovascular Research
Wang DD, **Eng M**, **Myers E**, **Forbes M**, **Karabon P**, **Greenbaum A**, and **O'Neill W**. Inferior and posterior: Utilization of 3D print and computer aided design to spatially map optimal transseptal crossing point for left atrial appendage occlusion with the watchman device *J Am Coll Cardiol* 2016; 67(13):323. PMID: Not assigned. Abstract

D.D. Wang, Henry Ford Hospital, Detroit, United States

Background: Traditional left atrial appendage (LAA) occlusion with the Watchman device utilizes 2D transesophageal guidance. There is little data available on optimal location for transseptal crossing for successful LAA occlusion. This study sought to investigate if 3D print (3DP) and computer aided design (CAD) could better define optimal transseptal puncture site to obtain maximal coaxiality for successful LAA occlusion. Methods: 4/2015-9/2015, 20 patients underwent Watchman LAA device implantation. All patients underwent preprocedural CT scan of the LAA. 3DP models and CAD generations were made of each patient with attention to the fossa ovalis, and LAA ostium. On a 3D x, y, z coordinate grid system, the center of the fossa ovalis was localized, along with the coordinates of the ostium of the LAA (Figure 1). Height differences were obtained and horizontal distances were obtained by vector mapping. Results: Of the 20 patients, 9 had 3DP models and CAD simulations available for retrospective analysis. Using a Sign test, the ostium of the LAA was located inferior to the center of the fossa ovalis 100% of the cases ($p<0.01$). Bench testing of all nine 3d prints demonstrated greatest ease in obtaining ex-vivo device coaxiality of catheter to LAA blood flow with inferior and posterior septal crossing. Conclusions: Inferior and posterior transseptal crossing provides operators with greatest ability to obtain catheter and hence LAA device coaxiality for successful Watchman implantation. (Figure Presented).

Cardiology / Cardiovascular Research
Xuereb L, **Kaur B**, **Akrawe S**, **Nemeh HW**, **Borgi J**, **Lanfear DE**, **Williams CT**, **Paone G**, and **Morgan JA**. Does preoperative atrial fibrillation increase the incidence of thromboembolic complications in patients supported with long-term LVADs? *J Heart Lung Transplant* 2016; 35(4):S130-S131. PMID: Not assigned. Abstract
L. Xuereb, Cardiac Surgery, Henry Ford Hospital, Detroit, United States

Purpose: We reviewed our nine year experience of continuous flow left ventricular assist devices (LVADs) to determine the impact of preoperative atrial fibrillation (AF) on stroke, device thrombosis, and survival. Methods: Between March 2006 and May 2015, 231 patients underwent implantation of 240 CF LVADs - 127 (52.9%) as bridge to transplant (BTT) and 113 (47.1%) as destination therapy (DT). Effect of AF on postoperative outcomes was assessed by using Kaplan Meier survival and Cox proportional hazard regression. Results: There were 78 (32.5%) patients with preoperative AF with a mean age of 55.7 + 11.4 years. There was a similar incidence of stroke in patients with and without AF - 12.8% versus 16.0%, respectively ($p= 0.803$). The incidence of device exchange for thrombosis was also similar in both groups (3.9% vs. 3.7%; $p= 0.999$). Survival was similar, with 1-month, 6-month, 12-month, and 24-month survivals of 96.2%, 91.7%, 84.5%, and 69.2%, respectively, for AF patients, versus 93.1%, 85.0%, 79.4%, and 74.1%, respectively, for non-AF patients ($p= 0.424$). Preoperative AF was not a significant independent predictor of survival using Cox proportional hazard regression (HR 1.08, 95% CI 0.66-1.76). Conclusion: Preoperative AF was associated with a similar incidence of postoperative stroke, device thrombosis, and survival. Based on these data, it seems unnecessary to perform a left atrial appendage ligation or alter postoperative anticoagulation in patients with AF undergoing LVAD implantation. (Table presented).

Cardiology / Cardiovascular Research
Xuereb L, **Kaur B**, **Akrawe S**, **Rashty J**, **Nemeh HW**, **Borgi J**, **Lanfear DE**, **Williams CT**, **Paone G**, and **Morgan JA**. Reoperation for bleeding does not adversely impact long-term outcomes in LVAD recipients *J Heart Lung Transplant* 2016; 35(4):S249. PMID: Not assigned. Abstract

L. Xuereb, Cardiac Surgery, Henry Ford Hospital, Detroit, United States

Purpose: We reviewed our nine year experience with continuous flow LVADs to determine the impact of reoperation for bleeding on outcomes. Methods: Between March 2006 and May 2015, 231 patients underwent implantation of 240 CF LVADs - 127 (52.9%) as bridge to transplant (BTT) and 113 (47.1%) as destination therapy (DT). Effect of reoperation for bleeding on outcomes was assessed. Results: Bleeding requiring reoperation occurred in 33 (13.8%) patients, 42.4% had a prior sternotomy, and 30.3% had previous temporary mechanical support. Survival was 95.2%, 85.7%, 84.5%, and 66.2%, respectively, at 30-days, 6-months, 12-months, and 24-months for patients who required reoperation, versus 92.1%, 88.0%, 80.4%, and 76.1%, respectively, for patients who did not (p= 0.237). The incidence of postoperative infection, stroke, right ventricular failure, renal failure, and/or device thrombosis was similar (p= NS). Conclusion: Reoperation for bleeding did not adversely impact survival or development of other LVAD-related complications. It therefore may be prudent to re-explore a bleeding patient early to limit transfusions and avoid potential consequences, such as right ventricular failure and prolonged ventilation. (Table Presented).

Cardiology / Cardiovascular Research

Xuereb L, **Kaur B**, **Akrawe S**, **Rashty J**, **Nemeh HW**, **Borgi J**, **Tita C**, **Selektor Y**, **Velez M**, **Lanfear DE**, **Williams CT**, **Paone G**, and **Morgan JA**. Drive line infections are not associated with an increased incidence of thromboembolic complications in patients on continuous flow LVAD support *J Heart Lung Transplant* 2016; 35(4):S246. PMID: Not assigned. Abstract

L. Xuereb, Cardiac Surgery, Henry Ford Hospital, Detroit, United States

Purpose: We reviewed our single institutional experience of continuous flow left ventricular assist devices (LVADs) to determine the impact of driveline (DL) infections on the incidence of thromboembolic complications. Methods: Between March 2006 and May 2015, 231 patients underwent implantation of 240 LVADs - 127 (52.9%) as bridge to transplant and 113(47.1%) as destination therapy. Effect of DL infections on stroke, pump thrombosis, and survival was assessed. Results: There were 24 (10.0%) patients who developed a DL infection, 6 (25%) were female, and 11 (45.8%) destination therapy patients. Freedom from stroke was similar for patients with and without DL infections - 92.5% vs. 91.0% at 6 months, 77.0% vs. 87.0% at 1 year, and 70.5% vs. 81.0% at 2 years; p= 0.273. The incidence of pump thrombosis was also similar - 4.2% vs. 3.7%%; p= 0.999. Survival was similar between the groups with 1-month, 6-month, 1-year, and 2-year survivals of 100.0%, 100.0%, 94.7%, and 94.7%, respectively, for DL infection patients, versus 93.5%, 85.8%, 79.6%, and 69.8%, respectively, for patients without DL infections (p= 0.259). DL infection was not a significant predictor of survival in Cox proportional hazard regression (HR 1.58, p= 0.277). Conclusion: Drive line infections were not associated with a higher incidence of thromboembolic complications. Based on these data, it does not appear necessary to raise anticoagulation target goals in the setting of a DL infection. (Figure Presented).

Cardiology / Cardiovascular Research

Yadav P, **Eng M**, **Divine G**, **Wang DD**, **Arjomand-Fard H**, **Wyman J**, **Isley M**, **Borgi J**, **Paone G**, **Greenbaum A**, and **O'Neill W**. Outcomes of impella assisted percutaneous balloon aortic valvuloplasty in very high risk severe aortic stenosis patients *J Am Coll Cardiol* 2016; 67(13):404. PMID: Not assigned. Abstract

P. Yadav, Henry Ford Hospital, Detroit, United States

Background: Limited data available suggests poor outcomes with high risk Percutaneous Balloon Aortic Valvuloplasty (PBAV) in patients with severe aortic stenosis and coexistent severe left ventricular dysfunction, recent decompensated heart failure or severe coronary artery disease. Methods: Retrospective analysis of patients with severe aortic stenosis who underwent high risk PBAV with hemodynamic support with Impella (Abiomed). Time to death was assessed with Kaplan-Meier estimates and by hazard ratios estimated by univariate Cox regression models Results: 28 patients, mean age 79 ± 8.6 years, STS mortality risk 13 ± 12%, average NYHA class 3.7, left ventricular ejection fraction 29% ± 17%, mean creatinine 2.1 ± 1.9 mg/dL, mean GFR 52 ± 28. Successful PBAV performed with rapid pacing in 100% cases. Impella removed in 68% of the patients at the end of the case. Overall, survival was 75% at 30 days and 63% at 1 year. Earlier death associated with: higher STS (HR=1.07, p=0.002), higher mean creatinine (HR=1.33, p=0.020) and lower GFR (HR=0.97, p=0.015). When Impella placed sequentially after PBAV (n=12), 50% of the patients survived to 30 days (4 patients had intraprocedural cardiac arrest). If Impella placed first with simultaneous support during BAV (n=16) 94% patients alive at 30 days with no intraprocedural cardiac arrest. (HR for simultaneous support=0.36, p=0.115) Conclusions: Hemodynamic support with Impella in high risk PBAV patient showed survival higher than reported in the limited literature. (Figure Presented).

Center for Health Policy and Health Services Research

Coleman KJ, Stewart C, Waitzfelder BE, Zeber JE, Morales LS, Ahmed AT, **Ahmedani BK**, Beck A, Copeland LA, Cummings JR, Hunkeler EM, Lindberg NM, Lynch F, Lu CY, Owen-Smith AA, Trinacty CM, Whitebird RR, and Simon GE. Racial-ethnic differences in psychiatric diagnoses and treatment across 11 health care systems in the mental health research network *Psychiatr Serv* 2016:appips201500217. PMID: 27079987. Full Text

Dr. Coleman is with the Department of Research and Evaluation, Kaiser Permanente Southern California, Pasadena (e-mail: karen.j.coleman@kp.org). Dr. Stewart and Dr. Simon are with the Group Health Research Institute, Group Health Cooperative, Seattle. Dr. Waitzfelder and Dr. Trinacty are with the Center for Health Research, Kaiser Permanente Hawaii, Honolulu. Dr. Zeber and Dr. Copeland are with Health Services Research and Development, U.S. Department of Veterans Affairs, Temple, Texas, and the Center for Applied Health Research, Baylor Scott and White Health, Temple, Texas. Dr. Morales is with the Center for Health Equity, Diversity and Inclusion, University of Washington, Seattle. Dr. Ahmed is with Kaiser Permanente Northern California, Permanente Medical Group, San Francisco. Dr. Ahmedani is with the Center for Health Policy and Health Services Research, Henry Ford Health System, Detroit. Dr. Beck is with the Institute for Health Research, Kaiser Permanente Colorado, Denver. Dr. Cummings is with the Department of Health Policy and Management, Rollins School of Public Health, Emory University, Atlanta. Ms. Hunkeler is with the Division of Research, Kaiser Permanente Northern California, Oakland. Dr. Lindberg and Dr. Lynch are with the Center for Health Research, Kaiser Permanente Northwest, Portland, Oregon. Dr. Lu is with Harvard Medical School and Harvard Pilgrim Health Care Institute, Boston. Dr. Owen-Smith is with the School of Public Health, Georgia State University, Atlanta. Dr. Whitebird is with the School of Social Work, University of St. Thomas/St. Catherine University, St. Paul, Minnesota.

OBJECTIVE: The objective of this study was to characterize racial-ethnic variation in diagnoses and treatment of mental disorders in large not-for-profit health care systems. METHODS: Participating systems were 11 private, not-for-profit health care organizations constituting the Mental Health Research Network, with a combined 7,523,956 patients age 18 or older who received care during 2011. Rates of diagnoses, prescription of psychotropic medications, and total formal psychotherapy sessions received were obtained from insurance claims and electronic medical record databases across all health care settings. RESULTS: Of the 7.5 million patients in the study, 1.2 million (15.6%) received a psychiatric diagnosis in 2011. This varied significantly by race-ethnicity, with Native American/Alaskan Native patients having the highest rates of any diagnosis (20.6%) and Asians having the lowest rates (7.5%). Among patients with a psychiatric diagnosis, 73% (N=850,585) received a psychotropic medication. Non-Hispanic white patients were significantly more likely (77.8%) than other racial-ethnic groups (odds ratio [OR] range .48-.81) to receive medication. In contrast, only 34% of patients with a psychiatric diagnosis (N=548,837) received formal psychotherapy. Racial-ethnic differences were most pronounced for depression and schizophrenia; compared with whites, non-Hispanic blacks were more likely to receive formal psychotherapy for their depression (OR=1.20) or for their schizophrenia (OR=2.64). CONCLUSIONS: There were significant racial-ethnic differences in diagnosis and treatment of psychiatric conditions across 11 U.S. health care systems. Further study is needed to understand underlying causes of these observed differences and whether processes and outcomes of care are equitable across these diverse patient populations.

Center for Health Policy and Health Services Research

Lu M, **Li J**, **Rupp LB**, Holmberg SD, Moorman AC, Spradling PR, Teshale EH, **Zhou Y**, Boscarino JA, Schmidt MA, **Lamerato LE**, Trinacty C, **Trudeau S**, and **Gordon SC**. Hepatitis C treatment failure is associated with increased risk of hepatocellular carcinoma *J Viral Hepat* 2016;PMID: 27028626. Full Text

Department of Public Health Sciences, Henry Ford Health System, Detroit, MI, USA.
Center for Health Policy and Health Services Research, Henry Ford Health System, Detroit, MI, USA.
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Center for Health Research, Geisinger Health System, Danville, PA, USA.
Center for Health Research, Kaiser Permanente-Northwest, Portland, OR, Portland.
Center for Health Research, Kaiser Permanente-Hawai'i, Waipahu, HI, USA.
Division of Gastroenterology and Hepatology, Henry Ford Health System, Detroit, MI, USA.

Sustained virological response (SVR) to antiviral therapy for hepatitis C (HCV) reduces risk of hepatocellular carcinoma (HCC), but there is little information regarding how treatment failure (TF) compares to lack of treatment. We evaluated the impact of treatment status on risk of HCC using data from the Chronic Hepatitis Cohort Study (CHeCS-an observational study based in four large US health systems, with up to 7 years of follow-up on patients). Multivariable analyses were used to adjust for bias in treatment selection, as well as other covariates, followed by sensitivity analyses. Among 10 091 HCV patients, 3681 (36%) received treatment, 2099 (57%) experienced treatment failure (TF), and 1582 (43%) of these achieved sustained virological response (SVR). TF patients

demonstrated almost twice the risk of HCC than untreated patients [adjusted hazard ratio (aHR) = 1.95, 95% confidence interval (CI) 1.50-2.53]; this risk persisted across all stages of fibrosis. Several sensitivity analyses validated these results. Although African Americans were at increased risk of treatment failure, they were at lower risk for HCC and all-cause mortality compared to White patients. SVR patients had lower risk of HCC than TF patients (aHR = 0.48, CI 0.31-0.73), whereas treatment - regardless of outcome - reduced all-cause mortality (aHR = 0.45, CI 0.34-0.60 for SVR patients; aHR = 0.78, CI 0.65-0.93 for TF patients).

Dermatology
Rosen T, and **Stein Gold LF**. Antifungal drugs for onychomycosis: Efficacy, safety, and mechanisms of action *Semin Cutan Med Surg* 2016; 35(3 Suppl 3):S51-55. PMID: 27074700. Article Request Form

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In 1996, oral terbinafine joined itraconazole and fluconazole on the short list of systemic medications that could be used to treat onychomycosis (although fluconazole was not approved for this indication by the US Food and Drug Administration [FDA], it was commonly used for this purpose). In 1999, ciclopirox was the first topical treatment to be FDA approved. The addition of the topical antifungal agents efinaconazole and tavaborole in 2014 expanded the roster of medications available to more effectively manage onychomycosis in a wide range of patients, including those for whom comorbid conditions, concomitant medications, or patient preference limited the use of systemic antifungals.

Dermatology
Stein Gold LF. Understanding onychomycosis resolving diagnostic dilemmas *Semin Cutan Med Surg* 2016; 35(3 Suppl 3):S48-50. PMID: 27074698. Article Request Form

Director of Dermatology Research Henry Ford Health System Detroit, Michigan.

No scientifically rigorous, large, prospective studies have been done to document the true prevalence of onychomycosis; the reported rates vary mainly by climate and by population, but the overall prevalence in the United States is estimated to be at least 10%. Advanced age and diabetes are the most commonly reported risk factors for onychomycosis. The differential diagnosis of onychomycosis is lengthy, and visual inspection alone is not sufficient for a definitive diagnosis-direct microscopic examination of a wet-mount preparation with 10% to 20% potassium hydroxide is the first-line diagnostic test.

Dermatology
Stein Gold LF. Topical therapies for psoriasis: Improving management strategies and patient adherence *Semin Cutan Med Surg* 2016; 35(2 Suppl 2):S36-44; quiz S45. PMID: 27074696. Article Request Form

Director of Dermatology Research Henry Ford Health System Detroit, Michigan.

Psoriasis is a chronic disease that has a substantial effect on quality of life of patients and often needs long-term treatment. Topical treatments for psoriasis include corticosteroids, vitamin D derivatives, tazarotene, anthralin, tacrolimus, pimecrolimus, and newer formulations of tar. Although many of these treatments are effective, they must be prescribed appropriately and used consistently for a period of weeks to months before clinical evidence of improvement can be seen and patients perceive that the treatment is working. As such, medication dosage/schedule, choice of vehicle, and especially patient adherence to medication are key factors for a treatment to be effective. Addressing patient preferences about treatments and concerns about treatment-related toxicities and managing their expectations represent additional aspects of patient care. Therapies such as calcipotriene and betamethasone dipropionate (Cal/BD) fixed combination foam and new drugs and vehicles continuously enhance the treatment landscape for psoriasis. Because adherence to topical treatment can be a major difficulty, keeping the treatment regimen simple and using new and sophisticated treatment vehicles that are acceptable to patients can likely improve treatment outcomes.

Dermatology
Stein Gold LF. Introduction *Semin Cutan Med Surg* 2016; 35(2 Suppl 2):S35. PMID: 27074694.
Article Request Form

Director of Dermatology Research Henry Ford Health System Detroit, Michigan.

Dermatology
Zabetian S, **Friedman BJ**, and **McHargue C**. A case of idiopathic granulomatous mastitis associated with erythema nodosum, arthritis, and reactive cough *JAAD Case Rep* 2016; 2(2):125-127. PMID: 27051851. Full Text

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

Diagnostic Radiology
Morrison J, Jahangiri Y, Vance L, **McVinnie D**, and Farsad K. Characterization of iodide-induced sialadenitis: Pooled cohort analysis of case reports *J Vasc Interv Radiol* 2016; 27(3):S120-S121. PMID: Not assigned. Abstract

J. Morrison, Dotter Interventional Institute, Portland, United States

Purpose: To characterize the findings, associations, and outcomes of iodide-induced sialadenitis (IIS) using the largest known cohort of pooled case reports. Materials: Published reports of IIS with intravascular iodinated contrast were searched in Medline. Two unpublished cases from the authors' institutions were also included. Variables were compared using Wilcoxon rank-sum and Chi2 tests. Factors associated with resolution time were evaluated with uni- and multivariate regression analysis. Results: 43 articles were found describing 52 patients with IIS, for a total of 54 patients (Table). Median age was 62 years (range 8-81; 60.4% male). No association was seen between renal function and course of IIS. There was no association with contrast volume or osmolarity. Steroid premedication was not protective. On regression analysis, time to onset (P=0.017) and tenderness at presentation (P=0.005) were significant predictors of longer time-to-resolution. Recurrence occurred in 16 cases (29.6%) with repeat iodinated contrast exposure. All cases were self-limited. Conclusions: IIS is a rare, self-limited adverse reaction from iodinated contrast administration unrelated to renal function or contrast dose, and unresponsive to steroid premedication. Recurrence is likely very high with repeat exposure. (Table Presented).

Emergency Medicine
Hourmozdi JJ, **Markin A**, **Johnson B**, **Fleming PR**, and **Miller JB**. Routine chest radiography is not necessary after ultrasound-guided right internal jugular vein catheterization *Crit Care Med* 2016;PMID: 27035241. Full Text

1Department of Emergency Medicine, Henry Ford Hospital, Detroit, MI. 2Department of Internal Medicine, Henry Ford Hospital, Detroit, MI.

OBJECTIVES: Central venous catheter placement is a common procedure performed on critically ill patients. Routine postprocedure chest radiographs are considered standard practice. We hypothesize that the rate of clinically relevant complications detected on chest radiographs following ultrasound-guided right internal jugular vein catheterization is exceedingly low. DESIGN: Retrospective chart review. SETTING: Adult ICUs, emergency departments, and general practice units at an academic tertiary care hospital system. PATIENTS: All 1,322 ultrasound-guided right internal jugular vein central venous catheter attempts at an academic tertiary care hospital system over a 1-year period. INTERVENTIONS: None. MEASUREMENTS AND MAIN RESULTS: Data from standardized procedure notes and postprocedure chest radiographs were extracted and individually reviewed to verify the presence of pneumothorax or misplacement, and any intervention performed for either complication. The overall success rate of ultrasound-guided right internal jugular vein central venous catheter placement was 96.9% with an average of 1.3 attempts. There was only one pneumothorax (0.1% [95% CI, 0-0.4%]), and the rate of catheter misplacement requiring repositioning or replacement was 1.0% (95% CI, 0.6-1.7%). There were no arterial placements found on chest radiographs. Multivariate regression analysis showed no correlation between high-risk patient characteristics and composite complication rate. CONCLUSIONS: In a large teaching hospital system, the overall rate of clinically relevant complications detected on chest radiographs following ultrasound-guided right internal jugular vein catheterization is exceedingly low. Routine chest radiograph after this common procedure is an unnecessary use of resources and may delay resuscitation of critically ill patients.

Emergency Medicine
Jain T, **Nowak R**, **Hudson M**, **Frisoli T**, **Jacobsen G**, **Tabaku M**, and **McCord J**. Short and long-term prognostic utility of the heart score in patients presenting to the emergency department with undifferentiated chest pain *J Am Coll Cardiol* 2016; 67(13):513. PMID: Not assigned. Abstract

T. Jain, Heart and Vascular Institute, Henry Ford Hospital, Detroit, United States
Background: The HEART score (HS) is a risk-stratification tool that was developed for patients evaluated for possible acute coronary syndrome (ACS) in the Emergency Department (ED). It incorporates elements of the history, ECG, age, risk factors and troponin levels. We sought to determine the short-term and long-term prognostic utility of the HS. Methods: A retrospective single-center analysis of 947 consecutive patients evaluated for possible ACS in ED in 1999 was conducted. Patients were followed for major adverse cardiac events (MACE) at 30 days: death, acute myocardial infarction (AMI), or revascularization procedure. All-cause mortality was assessed at 5 years. The HS was compared to the thrombolysis in myocardial infarction (TIMI) score. Results: At 30 days, 14 % (135/947) of patients had a MACE: 48 deaths (5%), 84 AMIs (9%) and 48 (5%) revascularization procedures. The MACE rate in patients with a HS ≤ 3 was 0.6 % (1/175) involving a revascularization procedure, 9.5% (53/557) in patients with a HS between 4 and 6 and 38% (81/215) with HS ≥ 7. The C-statistic for the HS was 0.82 and 0.68 for the TIMI score for predicting 30-day MACE, $p< 0.05$. Patients with a HS ≤ 3 had a significantly lower 5-year mortality rate as compared to those with a TIMI score 0 (10.6% vs 20.5%, p=0.02). Conclusions: The HS is not only a valuable risk-stratification tool in predicting short-term MACE but also long-term mortality in patients presenting to the ED evaluated for possible ACS. The prognostic utility of the HS was superior to the TIMI score. (Figure presented).

Emergency Medicine
Muller CC, **McCord J**, **Michaels A**, **Nowak R**, Giannitsis E, Body R, Christ M, Lindahl B, DeFilippi C, Christenson R, Bendig G, **Jacobsen G**, and Mueller C. Symptoms predictive of acute myocardial infarction in the troponin era: Analysis from the TRAPID-AMI study *J Am Coll Cardiol* 2016; 67(13):518. PMID: Not assigned. Abstract

C.C. Muller, Henry Ford Hospital, Detroit, United States

Background: The TRAPID-AMI study was an Emergency Department (ED) multicenter trial evaluating a rapid "rule-out" acute myocardial infarction (AMI) protocol over 1 hour using changes in high-sensitivity cardiac troponin (cTn) T∗ (Roche Diagnostics). We studied which symptoms were predictive of AMI, as part of a sub-study of TRAPID-AMI. Methods: There were 1,282 patients evaluated in EDs for possible AMI from 12 centers in Europe, USA, and Australia from 2011 to 2013. The diagnosis of AMI was centrally adjudicated by 2 independent cardiologists in accordance with the universal definition of AMI, using all available clinical information and serial measurements of cTnI-Ultra (Siemens Healthcare). A total of 26 symptom variables were prospectively obtained. Multivariable logistic regression analysis was done; Odds Ratios (OR) with 95% confidence intervals (CI) were calculated. Results: There were 213/1282 (17%) AMIs. Independent predictors of AMI are shown (Figure). The presence of more predictors increased the risk of an AMI. In the entire group 131 (10%) had radiation to right arm/shoulder, 897 (70%) had chest pressure, 385 (30%) worsened with activity, and 448 (35%) had radiation to left arm/shoulder. Duration of symptoms was not predictive of AMI. There were no symptoms that were independently predictive of not having AMI. Conclusions: In a multicenter trial there were only 4 symptoms that were independently associated with the diagnosis of AMI. ∗510(K) submitted to FDA, but not yet approved in the U.S. (Figure presented).

Endocrinology
Bossick AS, Peters RM, Burmeister C, Kakumanu N, **Shill JE**, and **Cassidy-Bushrow AE**. Antenatal inflammation and gestational diabetes mellitus risk among pregnant African-American women *J Reprod Immunol* 2016; 115:1-5. PMID: 27061480. Full Text

Department of Public Health Sciences, Henry Ford Health System, Detroit, MI 48202, USA.
College of Nursing, Wayne State University, Detroit, MI 48202, USA.
Department of Medicine, Division of Endocrinology, Diabetes and Metabolism, Michigan State University, East Lansing, MI 48824, USA.
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Although inflammation is associated with risk of gestational diabetes mellitus (GDM), little is known if there is an association between inflammation and GDM in African-American women, a group at higher risk for GDM complications. In the present study, we aimed to determine if selected inflammatory cytokines (i.e. TNF-alpha, hs-

CRP, IL-6, IL-10, IL-6/IL-10 ratio, IL-1beta) measured in the 2nd trimester, were associated with GDM risk in 185 pregnant African-American women. GDM was defined as a physician-documented GDM diagnosis, a fasting glucose between 92 and 125mg/dl, or evidence of glucose intolerance (defined using the 3-h glucose tolerance test). A total of 18 women (9.7%) had GDM. After covariate adjustment, C-reactive protein, measured at a mean 21.2+/-3.7 weeks gestation, was statistically significantly associated with GDM development (P=0.025); for every one-unit increase in log-transformed C-reactive protein, the odds of GDM increased by 5.3. Results were similar using a principal component analysis approach. This study provides evidence that higher levels of 2nd trimester C-reactive protein is associated with increased risk of GDM in African-American women. Further research is needed to examine whether C-reactive protein may be a useful early-pregnancy screen for evaluating potential GDM risk in African-American women.

Endocrinology

Lahiri SW. Management of type 2 diabetes in the setting of morbid obesity: How can weight gain be prevented or reversed? *Clin Diabetes* 2016; 34(2):115-120. PMID: 27092024. Article Request Form

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

Gastroenterology

Lu M, **Li J**, **Rupp LB**, Holmberg SD, Moorman AC, Spradling PR, Teshale EH, **Zhou Y**, Boscarino JA, Schmidt MA, **Lamerato LE**, Trinacty C, **Trudeau S**, and **Gordon SC**. Hepatitis C treatment failure is associated with increased risk of hepatocellular carcinoma *J Viral Hepat* 2016;PMID: 27028626. Full Text

Department of Public Health Sciences, Henry Ford Health System, Detroit, MI, USA.
Center for Health Policy and Health Services Research, Henry Ford Health System, Detroit, MI, USA.
Division of Viral Hepatitis, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention, Atlanta, GA, USA.
Center for Health Research, Geisinger Health System, Danville, PA, USA.
Center for Health Research, Kaiser Permanente-Northwest, Portland, OR, Portland.
Center for Health Research, Kaiser Permanente-Hawai'i, Waipahu, HI, USA.
Division of Gastroenterology and Hepatology, Henry Ford Health System, Detroit, MI, USA.

Sustained virological response (SVR) to antiviral therapy for hepatitis C (HCV) reduces risk of hepatocellular carcinoma (HCC), but there is little information regarding how treatment failure (TF) compares to lack of treatment. We evaluated the impact of treatment status on risk of HCC using data from the Chronic Hepatitis Cohort Study (CHeCS-an observational study based in four large US health systems, with up to 7 years of follow-up on patients). Multivariable analyses were used to adjust for bias in treatment selection, as well as other covariates, followed by sensitivity analyses. Among 10 091 HCV patients, 3681 (36%) received treatment, 2099 (57%) experienced treatment failure (TF), and 1582 (43%) of these achieved sustained virological response (SVR). TF patients demonstrated almost twice the risk of HCC than untreated patients [adjusted hazard ratio (aHR) = 1.95, 95% confidence interval (CI) 1.50-2.53]; this risk persisted across all stages of fibrosis. Several sensitivity analyses validated these results. Although African Americans were at increased risk of treatment failure, they were at lower risk for HCC and all-cause mortality compared to White patients. SVR patients had lower risk of HCC than TF patients (aHR = 0.48, CI 0.31-0.73), whereas treatment - regardless of outcome - reduced all-cause mortality (aHR = 0.45, CI 0.34-0.60 for SVR patients; aHR = 0.78, CI 0.65-0.93 for TF patients).

Global Health Initiative

AJ P, **R M**, **I T**, **JM Z**, and PJ H. Applying the United Nations Sustainable Development Goals in the United States as a Framework for Local Action in Low-Income Communities: A Workshop Forum for Sustainable Development in Detroit, Michigan *Twelfth International Conference on Environmental, Cultural, Economic, and Social Sustainability* 2016;PMID: Not assigned - Abstract.

Global Health Initiative

Dankerlui D, **Parke D**, **Prentiss T**, **Zervos J**, **Plum A**, **Tamler I**, **Kaljee L**, and **P K**. Henry ford health system global health initiative's 'research training to research project model.' *CUGH Global Health Conference* 2016;PMID: Not assigned - Abstract.

Global Health Initiative
Kaljee L, and Rick S. Zimmerman (Editor) RJDE, Jon K. Andrus (Editor), Everold N. Hosein (Editor). Implementation of public health innovations in developing countries *Introduction to global health promotion. San Francisco, CA: Jossey-Bass* 2016;PMID: Not assigned, Book Chapter. Article Request Form

Global Health Initiative
Kilgore PE, Salim AM, **Zervos MJ**, and Schmitt HJ. Pertussis: Microbiology, disease, treatment, and prevention *Clin Microbiol Rev* 2016; 29(3):449-486. PMID: 27029594. Article Request Form

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Medical and Scientific Affairs, Pfizer Vaccines, Paris, France Department of Pediatrics, Johannes Gutenberg-University, Mainz, Germany.

Pertussis is a severe respiratory infection caused by Bordetella pertussis, and in 2008, pertussis was associated with an estimated 16 million cases and 195,000 deaths globally. Sizeable outbreaks of pertussis have been reported over the past 5 years, and disease reemergence has been the focus of international attention to develop a deeper understanding of pathogen virulence and genetic evolution of B. pertussis strains. During the past 20 years, the scientific community has recognized pertussis among adults as well as infants and children. Increased recognition that older children and adolescents are at risk for disease and may transmit B. pertussis to younger siblings has underscored the need to better understand the role of innate, humoral, and cell-mediated immunity, including the role of waning immunity. Although recognition of adult pertussis has increased in tandem with a better understanding of B. pertussis pathogenesis, pertussis in neonates and adults can manifest with atypical clinical presentations. Such disease patterns make pertussis recognition difficult and lead to delays in treatment. Ongoing research using newer tools for molecular analysis holds promise for improved understanding of pertussis epidemiology, bacterial pathogenesis, bioinformatics, and immunology. Together, these advances provide a foundation for the development of new-generation diagnostics, therapeutics, and vaccines.

Global Health Initiative
W. B, and **Parke D**. Official development assistance and women's rights: How aid donor characteristics affect women's rights improvement in recipient countries *Asian Women* 2016; 32(1):1-29. PMID: Not assigned.
Article Request Form

Abstract: How does official development assistance (ODA) affect women's rights in aid-receiving countries? We argue that ODA allows those donor countries who have more respect for women's rights and who have the intention of spreading the norm of gender equality to successfully influence recipient countries, and thus improve women's rights in aid-recipient countries. We argue that this is possible because aid is equipped with technical assistance, donor conditionality, and donor-recipient collaborative projects that can be tailored to address a specific policy objective and that are ripe with opportunities for transfers of technical know-how and synergistic exchanges of local and global norms. We further contend that the effect of foreign aid on the improvement of women's rights is conditional on donors' respect for women's rights at home: foreign aid from countries with more equal women's rights has a stronger positive effect than that from countries with less equal women's rights. We illustrate the plausibility of our theoretical argument in the context of a case of aid projects in Bangladesh and use statistical analysis to test our argument more systematically. We show that aid in general, and aid from France and the Nordic countries - those with better provision of women's rights at home among major aid donors - in particular exert positive effects on improving women's rights in recipient countries from 1981 to 2011, after controlling for political, socio-economic, and regional factors.

Hematology, Oncology and the Josephine Ford Cancer Institute
Afifi S, **Michael A**, and Lesokhin A. Immunotherapy: A new approach to treating multiple myeloma *Ann Pharmacother* 2016;PMID: 27083916. Full Text

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Josephine Ford Cancer Center, Henry Ford Hospital, Brownstown Township, MI, USA.

Memorial Sloan Kettering Cancer Center, New York, NY, USA.

OBJECTIVE: To review the clinical pharmacology, efficacy, and safety of daratumumab and elotuzumab for the treatment of relapsed refractory multiple myeloma (RRMM). DATA SOURCES: A literature search of MEDLINE, PubMed, the US National Institutes of Health Clinicaltrials.gov, the Food and Drug administration, and relevant meeting abstracts was conducted using the termsdaratumumab, elotuzumab, multiple myeloma, anti-CD38, HuMax-CD38, HuLuc63, SLAMF7, andanti-CS1 STUDY SELECTION/DATA EXTRACTION: Human and animal studies describing the pharmacology, pharmacokinetics, efficacy, and safety of daratumumab and elotuzumab for MM were identified. DATA SYNTHESIS: Daratumumab (anti-CD38) and elotuzumab (anti-CS1) have been recently FDA approved for the treatment of RRMM after showing efficacy in clinical trials. Elotuzumab approval was based on phase III data, and daratumumab gained accelerated approval based on phase I/II trials. Daratumumab has demonstrated significant single-agent activity, with an overall response rate (ORR) of 36% in patients with a median of 4 prior lines of therapy. Elotuzumab has not been shown to have single-agent activity. But the efficacy of both these antibodies in combination with lenalidomide and dexamethasone in RRMM showed an ORR exceeding 80%. Tolerability of elotuzumab and daratumumab seems to be acceptable, with the most common adverse event being infusion reactions. CONCLUSION: Daratumumab and elotuzumab have shown encouraging results in RRMM that led to their FDA approval. Both are well tolerated with minimal toxicities. Phase III clinical trials will define optimal combination and place in therapy of daratumumab and elotuzumab.

Hematology, Oncology and the Josephine Ford Cancer Institute
Ali HY, Munir K, Braun T, Griggs JJ, Silver SM, Gorski DH, Breslin TM, and Henry NL. Appropriate use of the 21-gene recurrence score (RS) assay across Michigan *Cancer Research* 2016; 76(4)PMID: Not assigned. Abstract

H.Y. Ali

Background: The 21-gene RS assay is used to assess prognosis and to predict response to adjuvant chemotherapy in patients with early stage hormone receptor positive, Her2 negative invasive breast cancer. The National Comprehensive Cancer Network (NCCN) first recommended consideration of testing of appropriate patients with the RS assay in 2008. We examined trends in the use of testing with the RS assay in hospitals across Michigan from 2006 through 2013 using data from the Michigan Breast Oncology Quality Initiative (MiBOQI), a Blue Cross Blue Shield of Michigan/Blue Care Network-sponsored quality initiative Methods: Demographic, pathologic, and treatment data for women with breast cancer treated at all 25 hospitals participating in MiBOQI were abstracted from the medical record. Patients were excluded if they had stage 0 or IV disease at diagnosis, received neoadjuvant therapy, had bilateral breast cancer, or had a prior history of breast cancer. The primary outcome was the percentage of patients eligible for testing according to NCCN criteria (version 2010) who underwent testing with the RS assay. Analyses were performed using the statistical software R, Version 3.0.1 Results: Of the 18,046 patients in the MiBOQI Registry from 2006-2013 who met inclusion and exclusion criteria, 7133 (39.5%) met the NCCN criteria for testing (eligible). The rate of testing increased from 2006 to 2013 in both the eligible and ineligible cohorts, and varied by site Testing of the eligible cohort was statistically significantly associated with younger age, lower tumor grade, and lack of nodal involvement. Overall, 73.4% of patients whose tumors were tested with the RS assay met the NCCN criteria for testing and were deemed appropriately tested. This rate of appropriate testing ranged from 60.8% to 85.4% across sites. Of all patients who underwent testing, 498 (9.3%) had 1 or more positive lymph nodes (>0.2 cm). Receipt of chemotherapy was lower in eligible patients who were tested compared to those not tested (25.5% vs 29.9%, $p<0.001$). Of the 2387 eligible patients with RS < 18, 117 (5.5%) received chemotherapy, which ranged from 0% - 13.6% across the 25 sites. Of the 341 patients with RS > 30, 56 (9.8%) did not receive treatment with chemotherapy, which ranged from 0% - 50% across the sites. Of the 1192 patients with RS 18-30, 502 (45.7%) received chemotherapy, ranging from 14.5% for RS 18 to 72.5% for RS 30 Conclusions: In sites across Michigan the majority of patients whose tumors were tested with the RS assay were in accordance with the NCCN guidelines, although there was considerable variability across sites. The rate of testing for patients who do not meet the NCCN criteria is increasing. There is very low inappropriate use of the recurrence score for making chemotherapy treatment decisions. (Table Presented).

Hematology, Oncology and the Josephine Ford Cancer Institute
Farhan S, **Peres E**, and **Janakiraman N**. Cytomegalovirus and effect on early chimerism in patients with myeloid disorders undergoing stem cell transplantation using reduced toxicity ablative conditioning regimen *Bone Marrow Transplant* 2016; 51:S328. PMID: Not assigned. Abstract

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Introduction: The influence of cytomegalovirus (CMV) on the chimerism in reduced toxicity ablative conditioning SCT in myeloid disorders is ill defined. A recent report published in Blood by Sellar et al showed that in patients who received alemtuzumab-based regimen, the group of patients who were recipient positive (R+)/ Donor negative (D-) had CMV-specific T cells that are exclusively of recipient origin and significantly influenced the chimerism status toward recipients. To explore the impact of CMV in recipients and donors on early chimerism, we undertook a retrospective analysis of patients with myeloid disorders who received four days of fludarabine and busulfan with or without anti-thymocyte globulin (ATG) at our center in the last 10 years. Material (or patients) and methods: Chimerism assay was performed using a quantitative fluorescence-based short tandem repeat-polymerase chain reaction (STR-PCR) with capillary electrophoresis for PCR product resolution. Results: 42 patients with myeloid disorders received fludarabine and busulfan x 4 doses. Of the 42 patients, 25 had ATG. There were 28 males and 14 females with a median age of 62 years. Median time to follow up was 8 months (0.8-54 months). Disease risk was considered advanced in 21, intermediate in 4 and early in 17. Total Recipient cell chimerism showed increase recipient chimerism in 5/11 (45%) of R+D- vs 2/6 (33.3%) of R-D- in the group of patients who received ATG, P = 1.0, with a mean of recipient chimerism at day 100 of 20.4% in the R+Dgroup compared to 17% in the R-D- group. In the group who did not get ATG, recipient chimerism increase was 3/4 (75%) in the R+D- patients compared to 4/4 (100%) in patients who were R-, P = 1.0. The mean of recipient chimerism at day 100 in the R+D- no ATG group was 23.25% with a median of 12% while the mean and median at day 100 in the R- no ATG group were 35.25% and 19.5% respectively (P = 0.573). When looking at the increase in recipient chimerism in the group of patients who were R+D-, in those who got ATG it was 45% increase vs 75% increase in those who did not get ATG (P = 0.569) with a median of 12% vs 0% respectively (P = 0.49). Also increase of recipient chimerism was 33.3% in patients who were R- and got ATG vs 100% in R- no ATG patients (P = 0.076)with median at day 100 of 0 vs 19.5% (P = 0.098). Conclusion: In this small cohort from a single center, we found that in patients with myeloid disorders who received reduced toxicity ablative conditioning regimen and ATG, there was no statistically significant increase in recipient chimersim in the R+D- group compared to R-D- group. This is different from what Sellar et al found in a small group of patients who received alemtuzumab. These results may indicate a difference between ATG and alemtuzumab in the effect of CMV on the recipient chimerism, which need to be studied further in a larger retrospective or prospective study. This is especially important in myeloid disorders since persistent or increase in recipient chimerism may identify high-risk patient cohorts who may benefit from additional therapeutic interventions.

Hematology, Oncology and the Josephine Ford Cancer Institute

Henry NL, **Ali H**, Braun T, Munir K, Silver SM, Griggs JJ, Breslin TM, and **Gorski DH**. Use across Michigan of the 21-gene recurrence score (RS) assay in lymph node positive patients with breast cancer *Cancer Research* 2016; 76(4)PMID: Not assigned. Abstract

N.L. Henry

Background: Standard of care for women with lymph node positive breast cancer includes treatment with chemotherapy. The 21-gene RS assay is indicated to assess prognosis and to predict response to adjuvant chemotherapy in patients with early stage hormone receptor-positive, HER2-negative invasive breast cancer. Findings from the SWOG S8814 clinical trial, published in 2010, suggested utility for using the RS assay for treatment decision making in node-positive patients in order to withhold chemotherapy. The Center for Medicare and Medicaid Services subsequently approved coverage for the use of the RS assay in women with up to 3 involved lymph nodes, and the National Comprehensive Cancer Network recently recommended consideration of testing in this population. We examined trends in the use of testing of patients with node positive breast cancer with the RS assay in hospitals across Michigan from 2006 through 2013 using data from the Michigan Breast Oncology Quality Initiative (MiBOQI), a Blue Cross Blue Shield of Michigan/Blue Care Network-sponsored quality initiative Methods: Demographic, pathologic, and treatment data for women with breast cancer treated at all 25 hospitals participating in MiBOQI were abstracted from the medical record. Patients were excluded if they had stage 0 or IV disease at diagnosis, received neoadjuvant therapy, had bilateral breast cancer, or had a prior history of breast cancer. The primary endpoint was the percentage of patients with lymph node positive, hormone receptor-positive, HER2-negative breast cancer who underwent testing with the RS assay. Analyses were performed using the statistical software R, Version 3.0.1 Results: Of the 30,992 patients included in the MiBOQI Registry from 2006-2013, 2526 (10.7%) had hormone receptor positive, HER2 negative, lymph node positive disease and met the eligibility criteria. The rate of testing with the RS assay in this patient cohort increased from 0% in 2006 to 32.5% in 2013, including an increase from 15.4% in 2010 to 28.3% in 2011. Median age of the tested cohort was 60 (range 26-87). On multivariate analysis, testing was statistically significantly associated with older age, smaller tumor size, 1-3 involved lymph nodes, and lower Charlson Comorbidity Index. Receipt of chemotherapy was lower in those patients who underwent testing compared with those not tested (40.0% vs 82.0%, $p<0.001$). Chemotherapy was administered to 105 (27.4%) of the patients with RS < 18, 91 (51.4%) of the patients with RS 18-30, and 49 (92.4%) of the patients with RS > 30 Conclusions: Use of the RS assay for assessment of women with involved lymph nodes is increasing over time, primarily in older patients and patients with lower risk disease, and is associated with decreased treatment with chemotherapy. Results of the

ongoing SWOG S1007 clinical trial, which is assessing the impact of use of the RS assay on breast cancer outcomes, are eagerly awaited.

Hematology, Oncology and the Josephine Ford Cancer Institute
Hwang C, Sethi S, Heilbrun LK, **Gupta NS**, **Chitale DA**, Sakr WA, **Menon M**, **Peabody JO**, Smith DW, Sarkar FH, and Heath EI. Anti-androgenic activity of absorption-enhanced 3, 3'-diindolylmethane in prostatectomy patients *Am J Transl Res* 2016; 8(1):166-176. PMID: 27069550. Full Text

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Consumption of cruciferous vegetables is associated with a decreased risk of developing prostate cancer. Antineoplastic effects of cruciferous vegetables are attributable to bioactive indoles, most prominently, 3, 3'-diindolylmethane (DIM). In addition to effects on proliferation and apoptosis, DIM acts as an antiandrogen in prostate cancer cell lines. This study characterized the effects of prostatic DIM on the androgen receptor (AR) in patients with prostate cancer. Men with localized prostate cancer were treated with a specially formulated DIM capsule designed for enhanced bioavailability (BR-DIM) at a dose of 225 mg orally twice daily for a minimum of 14 days. DIM levels and AR activity were assessed at the time of prostatectomy. Out of 28 evaluable patients, 26 (93%) had detectable prostatic DIM levels, with a mean concentration of 14.2 ng/gm. The mean DIM plasma level on BR-DIM therapy was 9.0 ng/mL; levels were undetectable at baseline and in follow-up samples. AR localization in the prostate was assessed with immunohistochemistry. After BR-DIM therapy, 96% of patients exhibited exclusion of the AR from the cell nucleus. In contrast, in prostate biopsy samples obtained prior to BR-DIM therapy, no patient exhibited AR nuclear exclusion. Declines in PSA were observed in a majority of patients (71%). Compliance was excellent and toxicity was minimal. In summary, BR-DIM treatment resulted in reliable prostatic DIM levels and anti-androgenic biologic effects at well tolerated doses. These results support further investigation of BR-DIM as a chemopreventive and therapeutic agent in prostate cancer.

Hematology, Oncology and the Josephine Ford Cancer Institute
Modi D, **Hwang C**, Mamdani H, Kim S, Gayar H, Vaishampayan U, Joyrich R, and Heath EI. Radium-223 in heavily pretreated metastatic castrate-resistant prostate cancer *Clin Genitourin Cancer* 2016;PMID: 27053499. Full Text

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BACKGROUND: Radium-223 is a bone-targeting radiopharmaceutical that extends survival in mCRPC. Postapproval data are limited, and the value of biochemical and radiologic monitoring during radium therapy is unknown. PATIENTS AND METHODS: We conducted a retrospective study of 29 patients with mCRPC who received radium-223 at 1 of 3 participating institutions between August 2013 and December 2014. Trend of PSA, radiographic changes, and association of biochemical and clinical variables with PSA trend were measured. RESULTS: The median age of patients was 70 years, 79% of patients (N = 23) were European Americans, and 17% of patients (N = 5) were African Americans. Twenty patients (69%) had received at least 3 lines of prior therapies. Some 38% of patients (N = 11) received all 6 cycles of radium-223. Twenty patients (69%) had an increase in PSA during radium therapy, and 4 patients (14%) had a decline in PSA levels. Five patients had visceral metastases on computed tomography imaging performed during the course of radium-223. CONCLUSIONS: Radium therapy in mCRPC was associated with an increase in PSA in the majority of these heavily pretreated patients. The development of visceral

disease was not uncommon, suggesting a need for follow-up computed tomography monitoring during radium-223 therapy. The significance of early increases in PSA and pain with radium-223 is still uncertain. Although pain and PSA flare have been reported in patients who subsequently have a dramatic response to therapy, we observed that a PSA increase or pain flare correlates to an improvement in bone scans only in a minority of patients.

Hematology, Oncology and the Josephine Ford Cancer Institute

Nabi S, **Kahlon P**, Bozorgnia F, Arshad A, Saleem A, and **Kuriakose P**. Analyzing relationship between monoclonal gammopathy of undetermined significance (MGUS) with different types of neuropathy: An observational study *Indian J Hematol Blood Transfus* 2016; 32(2):186-192. PMID: 27065581. Full Text

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To analyze multiple variables, including immunoglobulin subtypes in patients with monoclonal gammopathy of undetermined significance (MGUS) and different types of neuropathy. This was a retrospective, single center study done in a tertiary care hospital in the United States. The data was collected for years 2001-2011. Inclusion criteria were the presence of MGUS and neuropathy. Exclusion criteria were the presence of other factors such as diabetes, vitamin B12 deficiency, alcoholism etc. which can cause neuropathy. Patients with IgM MGUS were compared with patients having Non-IgM MGUS. A total of 281 patients were analyzed in this study. The average age at the time of diagnosis of MGUS and neuropathy was 68 years. The most common type of neuropathy was sensorimotor peripheral neuropathy (46 %). The most common location of neuropathy was the lower extremities (68 %). Among our patients, 52 % had their neuropathy symptoms for 1-5 years before presenting to the clinic. When IgM MGUS was compared with Non-IgM MGUS, a statistically significant difference was found in terms of race (White vs. Others, OR 4.43, 95 % CI 2.13, 9.19, $p < 0.001$) and survival status (OR 1.98, 95 % CI 1.01, 3.90, $p = 0.046$). Patients with MGUS are prone to develop different types of neuropathies. Caucasians are more likely to have IgM MGUS as compared to other races. IgM MGUS is generally related to worse outcomes as compared to Non-IgM MGUS. Medical therapies, including gabapentin and pregabalin are effective treatments and the response rate can be as high as 80-90 % with these medications.

Hematology, Oncology and the Josephine Ford Cancer Institute

Rana S, Blowers EC, **Tebbe C**, Contreras JI, Radhakrishnan P, Kizhake S, Zhou T, Rajule RN, Arnst JL, **Munkarah AR**, **Rattan R**, and Natarajan A. Isatin derived spirocyclic analogues with alpha-methylene-gamma-butyrolactone as anticancer agents: A structure-activity relationship study *J Med Chem* 2016;PMID: 27077228. Article Request Form

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Design, synthesis, and evaluation of alpha-methylene-gamma-butyrolactone analogues and their evaluation as anticancer agents is described. SAR identified a spirocyclic analogue 19 that inhibited TNFalpha-induced NF-kappaB activity, cancer cell growth and tumor growth in an ovarian cancer model. A second iteration of synthesis and screening identified 29 which inhibited cancer cell growth with low-muM potency. Our data suggest that an isatin-derived spirocyclic alpha-methylene-gamma-butyrolactone is a suitable core for optimization to identify novel anticancer agents.

Hypertension and Vascular Research

Karuppagounder V, Giridharan VV, Arumugam S, Sreedhar R, **Palaniyandi SS**, Krishnamurthy P, Quevedo J, Watanabe K, Konishi T, and Thandavarayan RA. Modulation of macrophage polarization and HMGB1-TLR2/TLR4 cascade plays a crucial role for cardiac remodeling in senescence-accelerated prone mice *PLoS One* 2016; 11(4):e0152922. PMID: 27070323. Full Text

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The aim of this study was to investigate the role of macrophage polarization in aging heart. Macrophage differentiation is pathogenically linked to many inflammatory and immune disorders. It is often preceded by myocardial inflammation, which is characterized by increased cardiac damage and pro-inflammatory cytokine levels. Therefore, we investigated the hypothesis that senescence accelerated-prone (SAMP8) mice cardiac tissue would develop macrophage polarization compared with senescence-resistant control (SAMR1) mice. Both SAMP8 and SAMR1 mice were sacrificed when they became six month old. We evaluated, histo-pathological changes and modifications in protein expression by Western blotting and immuno-histochemical staining for M1 and M2 macrophage markers, high mobility group protein (HMG)B1 and its cascade proteins, pro-inflammatory factors and inflammatory cytokines in cardiac tissue. We observed significant upregulation of HMGB1, toll-like receptor (TLR)2, TLR4, nuclear factor (NF)kappaB p65, tumor necrosis factor (TNF)alpha, cyclooxygenase (COX)2, interferon (IFN)gamma, interleukin (IL)-1beta, IL-6 and M1 like macrophage specific marker cluster of differentiation (CD)68 expressions in SAMP8 heart. In contrast, M2 macrophage specific marker CD36, and IL-10 expressions were down-regulated in SAMP8 mice. The results from the study demonstrated that, HMGB1-TLR2/TLR4 signaling cascade and induction of phenotypic switching to M1 macrophage polarization in SAMP8 mice heart would be one of the possible reasons behind the cardiac dysfunction and thus it could become an important therapeutic target to improve the age related cardiac dysfunction.

Hypertension and Vascular Research
Sreedhar R, Giridharan VV, Arumugam S, Karuppagounder V, **Palaniyandi SS**, Krishnamurthy P, Quevedo J, Watanabe K, Konishi T, and Thandavarayan RA. Role of MAPK-mediated endoplasmic reticulum stress signaling in the heart during aging in senescence-accelerated prone mice *Biofactors* 2016;PMID: 27087487. Full Text

Department of Clinical Pharmacology, Faculty of Pharmaceutical Sciences, Niigata University of Pharmacy and Applied Life Sciences, Niigata City, Japan.
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International Collaborative Research Center, Changchun University of Chinese Medicine, Jingyue Economic Development District, Changchun, China.

Heart failure is typically related to aging as there is a definite relationship between age-related changes in the heart and the pathogenesis of heart failure. We have previously reported the involvement of p38 mitogen-activated protein kinase protein in cardiac function using animal models of heart failure. To further understand its relationship with aging-induced heart failure, we have compared its expression in the hearts of senescence accelerated-prone (SAMP8) mice and their control (SAMR1) with normal aging behavior. We have identified its activation along with reduced expression of 14-3-3eta protein in SAMP8 mice hearts than in SAMR1 mice. To reveal the downstream signaling, we have measured the endoplasmic reticulum stress marker proteins along with some inflammatory and apoptosis markers and identified a significant increase in SAMP8 mice hearts than that of SAMR1. In addition, we have performed comet assay and revealed a significant DNA damage in the cardiomyocytes of SAMP8 mice when compared with SAMR1 mice. All these results demonstrate the role of 14-3-3eta protein and the downstream mitogen-activated protein kinase-mediated endoplasmic reticulum stress, and apoptosis and DNA damage in aging-induced cardiac malfunction in SAMP8 mice. Thus targeting this signaling might be effective in treating age-related cardiac dysfunction.

Infectious Diseases
Plum AJ, Mucha R, Tamler I, Zervos JM, Hammer PJ. Applying the United Nations Sustainable Development Goals in the United States as a Framework for Local Action in Low-Income Communities: A Workshop Forum for Sustainable Development in Detroit, Michigan *Twelfth International Conference on Environmental, Cultural, Economic, and Social Sustainability* 2016;PMID: Not assigned - Abstract.

Infectious Diseases

Dankerlui D, **Parke D**, **Prentiss T**, **Zervos J**, **Plum A**, **Tamler I**, **Kaljee L**, and **P K**. Henry ford health system global health initiative's 'research training to research project model.' *CUGH Global Health Conference* 2016;PMID: Not assigned - Abstract.

Infectious Diseases

Kilgore PE, Salim AM, **Zervos MJ**, and Schmitt HJ. Pertussis: Microbiology, disease, treatment, and prevention *Clin Microbiol Rev* 2016; 29(3):449-486. PMID: 27029594. Article Request Form

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Medical and Scientific Affairs, Pfizer Vaccines, Paris, France Department of Pediatrics, Johannes Gutenberg-University, Mainz, Germany.

Pertussis is a severe respiratory infection caused by Bordetella pertussis, and in 2008, pertussis was associated with an estimated 16 million cases and 195,000 deaths globally. Sizeable outbreaks of pertussis have been reported over the past 5 years, and disease reemergence has been the focus of international attention to develop a deeper understanding of pathogen virulence and genetic evolution of B. pertussis strains. During the past 20 years, the scientific community has recognized pertussis among adults as well as infants and children. Increased recognition that older children and adolescents are at risk for disease and may transmit B. pertussis to younger siblings has underscored the need to better understand the role of innate, humoral, and cell-mediated immunity, including the role of waning immunity. Although recognition of adult pertussis has increased in tandem with a better understanding of B. pertussis pathogenesis, pertussis in neonates and adults can manifest with atypical clinical presentations. Such disease patterns make pertussis recognition difficult and lead to delays in treatment. Ongoing research using newer tools for molecular analysis holds promise for improved understanding of pertussis epidemiology, bacterial pathogenesis, bioinformatics, and immunology. Together, these advances provide a foundation for the development of new-generation diagnostics, therapeutics, and vaccines.

Infectious Diseases

Shukla BS, Shelburne S, **Reyes K**, Kamboj M, Lewis JD, Rincon SL, Reyes J, Carvajal LP, Panesso D, Sifri CD, **Zervos MJ**, Pamer EG, Tran TT, Adachi J, Munita JM, Hasbun R, and Arias CA. Influence of MIC in Clinical Outcomes of Enterococcus faecium Bacteremia Treated with Daptomycin: Is It Time to Change the Breakpoint? *Clin Infect Dis* 2016;PMID: 27045126. Full Text

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BACKGROUND: Daptomycin has become a key front-line antibiotic for multidrug-resistantE. faeciumbloodstream infections (BSIs). We previously showed thatE. faeciumstrains with daptomycin MICs in the higher end of susceptibility frequently harbor mutations in genes associated with daptomycin resistance. We postulate that patients withE. faeciumBSIs exhibiting daptomycin MICs of 3-4 microg/mL and treated with daptomycin are more likely to have worse clinical outcomes than those exhibiting daptomycin MICs</=2 microg/mL. METHODS: We conducted a multicenter (4 sites) retrospective cohort study (2010 - 2015) that included adult patients withE. faeciumBSI for whom initial isolates, follow-up blood culture data, and daptomycin administration data were available. A central laboratory performed standardized daptomycin MIC testing for all isolates. The primary outcome was microbiologic failure, defined as clearance of bacteremia occurring >/=4 days after the index blood culture. The secondary outcome was all-cause in-hospital mortality. RESULTS: A total of 62 patients were included. Thirty-one patients (50%) were infected with isolates exhibiting daptomycin MICs of 3-4 microg/mL. Overall, 34 (55%) patients had microbiologic failure and 25 (40%) died during hospitalization. On a multivariate logistic regression model, daptomycin MICs of 3-4 microg/mL (OR 4.7 [1.37-16.12], p=0.014) and immunosuppression (OR 5.32 [1.20-23.54], p=0.028) were significantly associated with microbiologic failure, while initial daptomycin dose of >/=8 mg/kg was not significantly associated with evaluated outcomes. CONCLUSION: Daptomycin MICs of 3-4 microg/mL in the initialE. faeciumblood isolate predicted microbiological failure of DAP therapy suggesting that modification in the daptomycin breakpoint for enterococci should be considered.

Internal Medicine

Gibbs J, Mansour M, **Mawri S**, **Nasr Y**, **Sudasena D**, and **Ananthasubramaniam K**. The value of additional testing after non-diagnostic stress echocardiography in patients presenting with chest pain: A single-center analysis *J Am Coll Cardiol* 2016; 67(13):520. PMID: Not assigned. Abstract

J. Gibbs, Henry Ford Hospital, Detroit, United States

Background: Stress echocardiography (SE) is an important tool in the risk stratification and prognosis of patients with suspected coronary artery disease (CAD). Data regarding outcomes of patients with non-diagnostic SE are mixed. There is significant downstream resource utilization with additional testing in patients with non-diagnostic SE. We sought to evaluate whether downstream test utilization impacts subsequent hospitalizations or adverse cardiac events in patients with non-diagnostic SE. Methods: We retrospectively identified patients presenting to the observation unit for chest pain who underwent SE between Jan, 2011 and Dec, 2012. Patients who underwent dobutamine or exercise stress testing were included if they failed to achieve 85% of predicted maximal heart rate (PMHR) and had no detectable ischemia. Demographic and clinical risk factors for CAD were collected, as well as downstream test utilization and adverse cardiac events. A multivariable logistical regression analysis was used to evaluate whether additional testing impacted 12-month adverse cardiac events. Results: A total of 490 patients were included in the study. Of those, 112 (23%) underwent additional testing. Patients with further testing were more likely to be older, male, have hypertension or diabetes, and to have known CAD. Patients were more likely to undergo further testing if they performed worse on their initial SE (6.6 vs 7.6 METS, 67.1 vs 73.9% PMHR, p<0.05), or if they initially underwent dobutamine SE (45.5% vs 32.5%, p<0.05). There was no significant difference in 12-month adverse cardiac events for patients receiving further testing or not. Patients with additional testing did have increased odds of hospital readmission (OR 3.63, p=0.003). Conclusions: SE remains an important tool in the evaluation of patients presenting with chest pain. Our study demonstrates that the use of further cardiac testing after non-diagnostic SE is not associated with improved outcomes at 12-months, but is associated with hospital readmission and resultant cost. A strategy employing selective additional testing and good follow-up may improve cost-efficacy.

Internal Medicine

Hachey B, Kontos M, Newby LK, Peacock WF, and **McCord J**. Trends in cardiac biomarker protocols and troponin cut-points *J Am Coll Cardiol* 2016; 67(13):467. PMID: Not assigned. Abstract

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Background: Various combinations of creatine kinase (CK)-MB, myoglobin and/or Cardiac Troponin I or T (cTnI/cTnT) have been used for evaluation of possible acute coronary syndrome (ACS). The current recommendation is to use the 99th percentile of cTnI/cTnT as the sole marker for diagnosis of acute myocardial infarction. Adoption of this recommendation in the US has not been well characterized. Methods: We retrospectively analyzed cardiac marker protocols collected from 829 US hospitals undergoing Chest Pain Center Accreditation through the Society of Cardiovascular Patient Care from 2009-2014. Data were obtained via a self-reported survey that addressed cardiac marker(s), sampling time periods and cut-points used for evaluation of possible ACS. Results: The combination of cTnI or cTnT with CK-MB was the most common strategy employed (Figure). However, the use of cTnI or cTnT as the sole marker increased over time (15 to 38%) as did use of the 99th percentile for cTnI/cTnT (30 to 60%) (Figure).

Conclusions: Despite current recommendations, there remains considerable variation in cardiac marker testing strategies used in US hospitals for evaluation of possible ACS. Although increasing, fewer than 40% of hospitals used a cTn alone strategy, and only 49% used the recommended 99th percentile cTn cut-point. (Figure Presented).

Internal Medicine
Hourmozdi JJ, **Markin A**, **Johnson B**, **Fleming PR**, and **Miller JB**. Routine chest radiography is not necessary after ultrasound-guided right internal jugular vein catheterization *Crit Care Med* 2016;PMID: 27035241. Full Text

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OBJECTIVES: Central venous catheter placement is a common procedure performed on critically ill patients. Routine postprocedure chest radiographs are considered standard practice. We hypothesize that the rate of clinically relevant complications detected on chest radiographs following ultrasound-guided right internal jugular vein catheterization is exceedingly low. DESIGN: Retrospective chart review. SETTING: Adult ICUs, emergency departments, and general practice units at an academic tertiary care hospital system. PATIENTS: All 1,322 ultrasound-guided right internal jugular vein central venous catheter attempts at an academic tertiary care hospital system over a 1-year period. INTERVENTIONS: None. MEASUREMENTS AND MAIN RESULTS: Data from standardized procedure notes and postprocedure chest radiographs were extracted and individually reviewed to verify the presence of pneumothorax or misplacement, and any intervention performed for either complication. The overall success rate of ultrasound-guided right internal jugular vein central venous catheter placement was 96.9% with an average of 1.3 attempts. There was only one pneumothorax (0.1% [95% CI, 0-0.4%]), and the rate of catheter misplacement requiring repositioning or replacement was 1.0% (95% CI, 0.6-1.7%). There were no arterial placements found on chest radiographs. Multivariate regression analysis showed no correlation between high-risk patient characteristics and composite complication rate. CONCLUSIONS: In a large teaching hospital system, the overall rate of clinically relevant complications detected on chest radiographs following ultrasound-guided right internal jugular vein catheterization is exceedingly low. Routine chest radiograph after this common procedure is an unnecessary use of resources and may delay resuscitation of critically ill patients.

Internal Medicine
Jain T, **Nowak R**, **Hudson M**, **Frisoli T**, **Jacobsen G**, **Tabaku M**, and **McCord J**. Short and long-term prognostic utility of the heart score in patients presenting to the emergency department with undifferentiated chest pain *J Am Coll Cardiol* 2016; 67(13):513. PMID: Not assigned. Abstract

T. Jain, Heart and Vascular Institute, Henry Ford Hospital, Detroit, United States

Background: The HEART score (HS) is a risk-stratification tool that was developed for patients evaluated for possible acute coronary syndrome (ACS) in the Emergency Department (ED). It incorporates elements of the history, ECG, age, risk factors and troponin levels. We sought to determine the short-term and long-term prognostic utility of the HS. Methods: A retrospective single-center analysis of 947 consecutive patients evaluated for possible ACS in ED in 1999 was conducted. Patients were followed for major adverse cardiac events (MACE) at 30 days: death, acute myocardial infarction (AMI), or revascularization procedure. All-cause mortality was assessed at 5 years. The HS was compared to the thrombolysis in myocardial infarction (TIMI) score. Results: At 30 days, 14 % (135/947) of patients had a MACE: 48 deaths (5%), 84 AMIs (9%) and 48 (5%) revascularization procedures. The MACE rate in patients with a HS ≤ 3 was 0.6 % (1/175) involving a revascularization procedure, 9.5% (53/557) in patients with a HS between 4 and 6 and 38% (81/215) with HS ≥ 7. The C-statistic for the HS was 0.82 and 0.68 for the TIMI score for predicting 30-day MACE, p< 0.05. Patients with a HS ≤ 3 had a significantly lower 5-year mortality rate as compared to those with a TIMI score 0 (10.6% vs 20.5%, p=0.02). Conclusions: The HS is not only a valuable risk-stratification tool in predicting short-term MACE but also long-term mortality in patients presenting to the ED evaluated for possible ACS. The prognostic utility of the HS was superior to the TIMI score. (Figure presented).

Internal Medicine
Jain T, **Shah J**, **Shah S**, and **Modi S**. Heart within a heart *J Cardiovasc Ultrasound* 2016; 24(1):60-63. PMID: 27081446. Full Text

Department of Internal Medicine, Henry Ford Hospital, Detroit, MI, USA.
Department of Cardiology, Henry Ford Hospital, Detroit, MI, USA.

Device based closure of the left atrial appendage (LAA) has emerged as a viable approach for stroke prevention in atrial fibrillation (AF) patients with contraindications to chronic oral anticoagulation. One of the most feared complications is device related thrombus formation. We present a 66-year-old male with chronic AF who developed a life-threatening intracranial bleed on oral anti-coagulation. He subsequently underwent LAA closure using an Amplatzer muscular ventricular septal defect closure device for stroke prevention. However, he was found to have a large thrombus attached to the device a year later. We present a review of the various LAA closure devices, importance of periodic surveillance via echocardiography and management options to prevent this complication. Also, the case highlights the importance of contrast-enhance echocardiography in diagnosis of LAA closure device thrombus.

Internal Medicine

Muller CC, **McCord J**, **Michaels A**, **Nowak R**, Giannitsis E, Body R, Christ M, Lindahl B, DeFilippi C, Christenson R, Bendig G, **Jacobsen G**, and Mueller C. Symptoms predictive of acute myocardial infarction in the troponin era: Analysis from the TRAPID-AMI study *J Am Coll Cardiol* 2016; 67(13):518. PMID: Not assigned. Abstract

C.C. Muller, Henry Ford Hospital, Detroit, United States

Background: The TRAPID-AMI study was an Emergency Department (ED) multicenter trial evaluating a rapid “rule-out” acute myocardial infarction (AMI) protocol over 1 hour using changes in high-sensitivity cardiac troponin (cTn) T∗ (Roche Diagnostics). We studied which symptoms were predictive of AMI, as part of a sub-study of TRAPID-AMI. Methods: There were 1,282 patients evaluated in EDs for possible AMI from 12 centers in Europe, USA, and Australia from 2011 to 2013. The diagnosis of AMI was centrally adjudicated by 2 independent cardiologists in accordance with the universal definition of AMI, using all available clinical information and serial measurements of cTnI-Ultra (Siemens Healthcare). A total of 26 symptom variables were prospectively obtained. Multivariable logistic regression analysis was done; Odds Ratios (OR) with 95% confidence intervals (CI) were calculated. Results: There were 213/1282 (17%) AMIs. Independent predictors of AMI are shown (Figure). The presence of more predictors increased the risk of an AMI. In the entire group 131 (10%) had radiation to right arm/shoulder, 897 (70%) had chest pressure, 385 (30%) worsened with activity, and 448 (35%) had radiation to left arm/shoulder. Duration of symptoms was not predictive of AMI. There were no symptoms that were independently predictive of not having AMI. Conclusions: In a multicenter trial there were only 4 symptoms that were independently associated with the diagnosis of AMI. ∗510(K) submitted to FDA, but not yet approved in the U.S. (Figure presented).

Internal Medicine

Nabi S, **Kahlon P**, Bozorgnia F, Arshad A, Saleem A, and **Kuriakose P**. Analyzing relationship between monoclonal gammopathy of undetermined significance (MGUS) with different types of neuropathy: An observational study *Indian J Hematol Blood Transfus* 2016; 32(2):186-192. PMID: 27065581. Full Text

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To analyze multiple variables, including immunoglobulin subtypes in patients with monoclonal gammopathy of undetermined significance (MGUS) and different types of neuropathy. This was a retrospective, single center study done in a tertiary care hospital in the United States. The data was collected for years 2001-2011. Inclusion criteria were the presence of MGUS and neuropathy. Exclusion criteria were the presence of other factors such as diabetes, vitamin B12 deficiency, alcoholism etc. which can cause neuropathy. Patients with IgM MGUS were compared with patients having Non-IgM MGUS. A total of 281 patients were analyzed in this study. The average age at the time of diagnosis of MGUS and neuropathy was 68 years. The most common type of neuropathy was sensorimotor peripheral neuropathy (46 %). The most common location of neuropathy was the lower extremities (68 %). Among our patients, 52 % had their neuropathy symptoms for 1-5 years before presenting to the clinic. When IgM MGUS was compared with Non-IgM MGUS, a statistically significant difference was found in terms of race (White vs. Others, OR 4.43, 95 % CI 2.13, 9.19, $p < 0.001$) and survival status (OR 1.98, 95 % CI 1.01, 3.90, $p = 0.046$). Patients with MGUS are prone to develop different types of neuropathies. Caucasians are more likely to have IgM MGUS as compared to other races. IgM MGUS is generally related to worse outcomes as compared to Non-IgM MGUS. Medical therapies, including gabapentin and pregabalin are effective treatments and the response rate can be as high as 80-90 % with these medications.

Internal Medicine

Rahman M. Pulmonary hypertension inappropriately who group classified secondary to mass effect *J Am Coll Cardiol* 2016; 67(13):1105. PMID: Abstract

M. Rahman, Henry Ford Hospital, Detroit, United States

Background: Pulmonary Artery Hypertension (PAH) classification is important before initiating phosphodiesterase inhibitor therapy, which can treat Group 1 but acutely worsen Group 2. Case: 41-year-old woman with no medical or surgical history presented with a syncopal episode and complained of progressive dyspnea over 1 year. Her physical exam showed normal normal lung sounds, a loud P2, a grade 2 tricuspid murmur without other signs of right heart failure: peripheral edema, ascites, an elevated jugular venous pressure or an S3 gallop. Decision Making: Echocardiography showed severely elevated pulmonary artery pressure of 129 mm Hg, severely dilated right atrium, right ventricular hypertrophy and moderate tricuspid regurgitation. We proceeded to hemodynamic catheterization that confirmed elevated right-sided pressures, extremely elevated pulmonary capillary wedge pressure (PCWP) but low normal left ventricular end diastolic pressure (LVEDP) with an increased PCWP-LVEDP gradient. Mitral Stenosis was suspected and transeptal access for direct catheter measurement of gradient across mitral valve was initially planned, however, such elevated right sided pressures, transeptal access would result in a permanent atrial septal defect and a right to left shunt. Cardiology was consulted. Echo images and PCWP tracings were reviewed. On echo there was minimal flow acceleration, normal left atrium, and appropriately coapting valves. Her tracing showed an inappropriate waveform, likely secondary to under wedging as such high pulmonary arterial pressures are difficult to completely occlude. Her CT thorax showed that the right atrium impinges on the right pulmonary vein resulting in presentation similar to pulmonary venous occlusive disease. CT angiogram confirmed the significant extrinsic compression causing higher PCWP. Patient was started on Sildenafil during that hospitalization with repeat echo three months later showing improved right heart parameters and decreased pulmonary pressures. Conclusions: When there is discordance amongst diagnostic exam and clinical presentation, primary review of data is integral to help classify PAH and determine appropriate treatment.

Internal Medicine

Raymond T, **Mawri S**, **Jacobsen G**, **Selektor Y**, **Velez M**, **Williams C**, **Nemeh H**, **Borgi J**, **Morgan J**, **Lanfear D**, and **Tita C**. The incidence of spontaneous intracranial hemorrhage is associated with infection in patients with mechanical circulatory support *J Heart Lung Transplant* 2016; 35(4):S246. PMID: Not assigned. Abstract

T. Raymond, Henry Ford Hospital, Detroit, United States

Purpose: Intracranial hemorrhage (ICH) is a well-known catastrophic complication in patients with left ventricular assist devices (LVADs). The cause of non-traumatic ICH in patients with LVADs is likely multifactorial and has been inadequately studied. We anecdotally noted frequent presence of infection in this setting and sought to quantify it and assess outcomes. Methods: We retrospectively studied 223 consecutive patients who had continuous flow (CF) LVADs implanted between March 2007 and March 2014. Patients who suffered a non-traumatic ICH were selected for further data collection. The presence or absence of infection at time of ICH, defined by CDC criteria, was collected, along with patient characteristics and outcomes. The rate of infection among ICH patients was compared to published historical cohorts. Characteristics and outcomes were compared using the Wilcoxon rank sum test, chi-square test or Fischer exact test, as indicated. Results: Eighteen LVAD patients with non-traumatic ICH (13 parenchymal, 3 subarachnoid, 2 subdural) were identified. Median duration of support at the time of ICH was 700 days. The average INR was 3.3 ± 3.0 and platelet count was 171.2 ± 69.6. These did not differ between infected and non-infected groups (INR 4.5 ± 3.7 vs 2.8 ± 2.7, p = 0.225; platelets 193 ± 76.5 vs 162.2 ± 67.8, p = 0.37). Bacteremia was present on admission in 9/18 patients (50%), and chronic driveline infection in 4/18 patients (22.2%). The presence of any infection at the time of presentation for ICH was 66.7%. This is significantly higher when compared to the overall infection rate in the HMII DT trial/HMII arm of 36%, (p = 0.007). Compared to survivors, patients who died during the hospitalization had a greater degree of leukocytosis (WBC 15.1 ± 6.0 vs. 10.2 ± 5.6, p = 0.049). Admission INR level, platelet count and LDH level did not impact in-hospital mortality (survivors vs non-survivors: INR 2.9 ± 2.8 vs 3.8 ± 3.4, p = 0.885; platelet count 157.4 ± 47.4 vs 186.8 ± 89.3, p = 0.885; LDH level 466.5 ± 355.4 vs 232.3 ± 71.4, p = 0.166). Conclusion: There is a high incidence of infection in CF LVAD patients presenting with ICH and these patients appear to do worse. Early administration of antibiotics should be considered in these patients. Additional studies are warranted to explore causation and potential impact of early antibiotic treatment on patients' survival.

Internal Medicine
Rezik M, and **Mattina D**. Severe cardiomyopathy secondary to anti-TNF therapy for crohn's disease *J Am Coll Cardiol* 2016; 67(13):1042. PMID: Not assigned. Abstract

M. Rezik, Henry Ford Hospital, Detroit, United States

Background: Tumor necrosis factor-alpha inhibitors are a popular and effective therapy for inflammatory bowel disease and other inflammatory conditions. Despite a substantial amount of evidence, cardiomyopathy is a widely unrecognized adverse effect of these medications. Case: A 57-year-old male presented with a two-week history of dyspnea and productive cough. History included hypertension, asthma and crohn's disease. His symptoms had been worsening despite inhaler use and were especially pronounced when lying down at night. Physical exam was unremarkable without abnormal cardiac or pulmonary findings. Decision Making: ECG was significant for left ventricular hypertrophy and lateral T-wave inversions and troponin was elevated at 1.97. The patient was admitted and treated for a non-ST elevated myocardial infarction. Echocardiogram revealed an enlarged and severe hypokinetic left ventricle with 12% ejection fraction and diastolic filling dysfunction. Cardiac catheterization revealed mild non-obstructive disease. Given the presenting symptoms, a cardiac MRI was obtained and showed no evidence of viral myocarditis or other infiltrative process. On further review, it was noted that he had been started on adalimumab four months prior to presentation for treatment of his crohn's disease. Literature review revealed reports of heart failure after therapy and subsequent recovery after discontinuation. The adalimumab was discontinued and he was started on conventional heart failure therapy. Upon follow-up, the patient reported virtual resolution of symptoms. Repeat echocardiogram showed an improved ejection fraction of 20%. Conclusions: Cardiomyopathy is an important yet unfamiliar adverse effect of adalimumab and other TNF-alpha inhibitors. Physicians must be aware of this complication and patients on therapy should be monitored for symptoms of new or worsening heart failure.

Internal Medicine
Salem D, and **Alchakaki A**. Treatment of severe ace inhibitor angioedema: Current and future therapies *Consultant* 2016; 56(2):134-137. PMID: Not assigned. Article Request Form

For many years, corticosteroids, antihistamines, and epinephrine have been used to treat severe angioedema related to therapy with angiotensinconverting enzyme inhibitors (ACEIs). However, no clear evidence exists to support these therapies in patients who present with ACEIinduced angioedema. Moreover, no clear guidelines are practiced or applied in U.S. hospitals, in contrast with a number of European countries. Despite that the newer medications ecallantide and icatibant have demonstrated efficacy in treating hereditary angioedema, few recent randomized clinical trials have been published investigating the benefits of these agents in treating ACEI angioedema. This literature review summarizes the most recent studies and evidence in the approach to ACEI angioedema treatment for primary care providers.

Nephrology
Neyra JA, Canepa-Escaro F, **Yee J**, and **Yessayan L**. The authors reply *Crit Care Med* 2016; 44(1):e53-54. PMID: 26672946. Full Text

Division of Nephrology, University of Texas Southwestern Medical Center, Dallas, TXDepartment of Internal Medicine, Asante Health System, Grants Pass, ORDivision of Nephrology and Hypertension, Henry Ford Hospital, Detroit, MIDivision of Nephrology and Hypertension and Division of Pulmonary and Critical Care Medicine, Henry Ford Hospital, Detroit, MI; for the Acute Kidney Injury in Critical Illness Study Group.

Nephrology
Provenzano R, Besarab A, Sun CH, Diamond SA, Durham JH, Cangiano JL, Aiello JR, **Novak JE**, Lee T, Leong R, Roberts BK, Saikali KG, Hemmerich S, Szczech LA, Yu KP, and Neff TB. Oral hypoxia-inducible factor prolyl hydroxylase inhibitor roxadustat (fg-4592) for the treatment of anemia in patients with ckd *Clin J Am Soc Nephrol* 2016;PMID: 27094610. Full Text

St. John Hospital and Medical Center, Detroit, Michigan;
FibroGen, Inc., San Francisco, California;
Apex Research of Riverside, Riverside, California;
San Antonio Kidney Disease Center, San Antonio, Texas;
Palmetto Nephrology, Professional Association, Orangeburg, South Carolina;
Nephrology Private Practice, San Juan, Puerto Rico;
Mountain Kidney and Hypertension Associates, Professional Association, Asheville, North Carolina; and.

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BACKGROUND AND OBJECTIVES: Roxadustat (FG-4592), an oral hypoxia-inducible factor prolyl hydroxylase inhibitor that stimulates erythropoiesis, regulates iron metabolism, and reduces hepcidin, was evaluated in this phase 2b study for safety, efficacy, optimal dose, and dose frequency in patients with nondialysis CKD. DESIGN, SETTING, PARTICIPANTS, & MEASUREMENTS: The 145 patients with nondialysis CKD and hemoglobin </=10.5 g/dl were randomized into one of six cohorts of approximately 24 patients each with varying roxadustat starting doses (tiered weight and fixed amounts) and frequencies (two and three times weekly) followed by hemoglobin maintenance with roxadustat one to three times weekly. Treatment duration was 16 or 24 weeks. Intravenous iron was prohibited. The primary end point was the proportion of patients achieving hemoglobin increase of >/=1.0 g/dl from baseline and hemoglobin of >/=11.0 g/dl by week 17 (16 weeks of treatment). Secondary analyses included mean hemoglobin change from baseline, iron utilization, and serum lipids. Safety was evaluated by frequency/severity of adverse events. RESULTS: Of the 145 patients enrolled, 143 were evaluable for efficacy. Overall, 92% of patients achieved hemoglobin response. Higher compared with lower starting doses led to earlier achievement of hemoglobin response. Roxadustat-induced hemoglobin increases were independent of baseline C-reactive protein levels and iron repletion status. Overall, over the first 16 treatment weeks, hepcidin levels decreased by 16.9% (P=0.004), reticulocyte hemoglobin content was maintained, and hemoglobin increased by a mean (+/-SD) of 1.83 (+/-0.09) g/dl (P<0.001). Overall mean total cholesterol level was reduced by a mean (+/-SD) of 26 (+/-30) mg/dl (P<0.001) after 8 weeks of therapy, independent of the use of statins or other lipid-lowering agents. No drug-related serious adverse events were reported. CONCLUSIONS: In patients with nondialysis CKD who were anemic, various starting dose regimens of roxadustat were well tolerated and achieved anemia correction with reduced serum hepcidin levels. After anemia correction, hemoglobin was maintained by roxadustat at various dose frequencies without intravenous iron supplementation.

Neurology
Girotra T, Baki N, and **Grover K**. Rituximab for refractory myasthenia gravis in a pregnant patient *Neurology* 2016; 86(16)PMID: Not assigned. Abstract

T. Girotra, Henry Ford Hospital, Detroit, United States

Objective: To report the first ever case of successful pregnancy outcome in a patient who received Rituximab infusion for refractory Myasthenia Gravis Background: Rituximab (RTX) is a chimeric Immunoglobulin G1 monoclonal anti-CD-20 antibody. Traditionally, RTX has been used for hematological malignancies and autoimmune disorders. Recently, there have been reports which have shown benefit of RTX in refractory Myasthenia Gravis (MG). There is little data available regarding safety of RTX during pregnancy. Method: 23 years-old female suffering from refractory MG (non-responsive to thymectomy, plasmapharesis, intravenous immunoglobilins and mycophenolate) was started on RTX infusion (375 mg/m2) with daily pyridostigmine maintenance. After two infusions, she demonstrated a favorable response. She conceived six months after the second infusion. Result: Pregnancy was complicated by Pre-Eclempsia at 39 weeks. Spontaneous vaginal delivery of a healthy 3039 g boy at 39 weeks. Post-partum period was complicated by a single eclemptic seizure which responded to intravenous magnesium. Baby showed no evidence of weakness or immunosuppression on follow up visits. Conclusion: We present the first case of a successful pregnancy in a patient treated with RTX infusion for refractory MG. Auto-reactive B cells are appropriate candidates for targeted drug therapy as they play an important role in the pathogenesis of MG. RTX global drug safety database contains only 153 pregnancy outcomes out of which none of them were MG patients. There were 90 live births with 22 preterm deliveries, 33 spontaneous abortions, 1 still birth and 1 maternal death. There were higher rates of preterm deliveries and first trimester losses compared to general population. There were two reports of congenital anomalies (club foot and cardiac malformation). Despite lack of strong evidence of teratogenesis, limited cohort size prevents drawing conclusions regarding safety of RTX. It is still recommended to use effective contraception during and for 12 months after treatment.

Neurology
Greer DM, **Varelas PN**, and Wijdicks EF. American academy of neurology guidelines and the neurologic determination of death-reply *JAMA Neurol* 2016;PMID: 27065178. Full Text

Department of Neurology, Yale University School of Medicine, New Haven, Connecticut.
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Neurology
Kassis H, **Shehadah A**, **Li C**, **Zhang Y**, **Cui Y**, **Roberts C**, **Sadry N**, **Liu X**, **Chopp M**, and **Zhang ZG**. Class IIa histone deacetylases affect neuronal remodeling and functional outcome after stroke *Neurochem Int* 2016; 96:24-31. PMID: 27103167. Article Request Form

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We have previously demonstrated that stroke induces nuclear shuttling of class IIa histone deacetylase 4 (HDAC4). Stroke-induced nuclear shuttling of HDAC4 is positively and significantly correlated with improved indices of neuronal remodeling in the peri-infarct cortex. In this study, using a rat model for middle cerebral artery occlusion (MCAO), we tested the effects of selective inhibition of class IIa HDACs on functional recovery and neuronal remodeling when administered 24hr after stroke. Adult male Wistar rats (n = 15-17/group) were subjected to 2 h MCAO and orally gavaged with MC1568 (a selective class IIa HDAC inhibitor), SAHA (a non-selective HDAC inhibitor), or vehicle-control for 7 days starting 24 h after MCAO. A battery of behavioral tests was performed. Lesion volume measurement and immunohistochemistry were performed 28 days after MCAO. We found that stroke increased total HDAC activity in the ipsilateral hemisphere compared to the contralateral hemisphere. Stroke-increased HDAC activity was significantly decreased by the administration of SAHA as well as by MC1568. However, SAHA significantly improved functional outcome compared to vehicle control, whereas selective class IIa inhibition with MC1568 increased mortality and lesion volume and did not improve functional outcome. In addition, MC1568 decreased microtubule associated protein 2 (MAP2, dendrites), phosphorylated neurofilament heavy chain (pNFH, axons) and myelin basic protein (MBP, myelination) immunoreactivity in the peri-infarct cortex. Quantitative RT-PCR of cortical neurons isolated by laser capture microdissection revealed that MC1568, but not SAHA, downregulated CREB and c-fos expression. Additionally, MC1568 decreased the expression of phosphorylated CREB (active) in neurons. Taken together, these findings demonstrate that selective inhibition of class IIa HDACs impairs neuronal remodeling and neurological outcome. Inactivation of CREB and c-fos by MC1568 likely contributes to this detrimental effect.

Neurology
Kaveeshvar H, Kashouty R, and **Loomba V**. Spontaneous carotid dissection in a patient after incidental amphetamine salt overdose presenting as cluster like headache *Neurology* 2016; 86(16)PMID: Not assigned. Abstract

H. Kaveeshvar, Henry Ford Hospital, Detroit, United States

Objective: To highlight cluster like headache can be due to very serious underlying pathology which should not be overlooked Background: Cluster headache has been documented to be the first presenting symptom of an internal carotid dissection. Furthermore, an abrupt increase in blood pressure has been linked to a spontaneous carotid dissection. There are no previous cases reports linking overdose of prescribed amphetamines salts to carotid dissection. Methods: Case Report Results: We present a case report of a 29-year-old man who overdosed on his prescribed attention deficit hyperactivity disorder medication and subsequently developed an internal carotid dissection, which initially manifested as a cluster headache Conclusions: Amphetamines have been linked to ischemic and hemorrhagic strokes in several studies, mainly in young patients. This case provides awareness of this potential complication of amphetamine salt prescription as well as serves to remind physicians of the potential of cluster headache as the presenting symptom of a carotid dissection.

Neurology
Lewitt P, Freed M, Leinonen M, Sedkov A, and Murck H. Effect of patient characteristics on motor function in response to 35-50 mg of inhaled levodopa (CVT-301) in patients with Parkinson's disease: Results from a phase 2b study *Neurology* 2016; 86(16)PMID: Not assigned. Abstract

P. Lewitt, Henry Ford Hospital, Wayne State University, School of Medicine, West Bloomfield, United States

Objective: To examine whether the response to an inhaled levodopa formulation (CVT-301; 35 and 50 mg) is dependent on baseline patient characteristics. Background: Many patients with Parkinson's disease (PD) treated with levodopa experience motor fluctuations (OFF episodes) after a period of good motor control. CVT-301, levodopa inhalation powder formulation, is under development for rapid relief of OFF episodes. In a phase 2b study, oral

levodopa dosage at baseline ranged from 250-1800 mg/day. CVT-301 significantly improved UPDRS (Unified Parkinson's Disease Rating Scale) Part 3 relative to placebo; treatment effect was evident at 10 minutes, the earliest time point assessed. Design/Methods: Data were derived from a phase 2b study (CVT-301-003; NCT01777555). CVT-301 and placebo were self-administered up to 3 times/day. Dose was escalated from 35 mg (weeks 1 and 2) to 50 mg (weeks 3 and 4). Baseline characteristics, including gender, PD stage (Hoehn & Yahr; H&Y), dyskinesia, and daily OFF time, were examined for possible influence on UPDRS Part 3 changes in CVT-301 versus placebo (end of week 4). Tolerability was assessed. Additional analyses will be performed. Results: Eighty-six patients were randomized 1:1 to CVT-301 or placebo; 66.3[percnt] male, 33.7[percnt] female, mean age 62.4 years (range 37-79). At week 4, the mean change in UPDRS Part 3 was -10.02 (CVT-301) versus -3.07 (placebo), treatment effect of -6.95; P<0.001. The difference in UPDRS Part 3 score between CVT-301 and placebo was independent of gender (male, P=0.03; female, P<0.001), H&Y (<2.5, P=0.04; ≥2.5, P<0.001), daily OFF time (<4 hours, P=0.04; ≥4 hours, P<0.001), and presence of dyskinesia (YES, P=0.004; NO, trend with P=0.07). CVT-301 was tolerated during the 4-week study. Conclusions: Antiparkinsonian efficacy, defined by change in motor function, did not vary as a function of the demographic and clinical characteristics tested.

Neurology
LeWitt P, Niyazov A, Sedkov A, Murck H, and Guo A. Patients' experience of Parkinson's disease following treatment with inhaled Levodopa: Results from a phase 2b study *Neurology* 2016; 86(16)PMID: Not assigned. Abstract

P. LeWitt, Henry Ford Hospital, Wayne State University, School of Medicine, West Bloomfield, United States

Objective: To report patient experiences from a clinical trial regarding Parkinson's disease (PD) control following treatment with inhaled levodopa. Background: CVT-301, an inhaled levodopa powder formulation, is being investigated for treatment of OFF episodes in patients with PD. Data from a phase 2b study of CVT-301 showed improvement in motor function and in daily OFF time. Patient Global Impression of Change (PGI-C), a patient-reported outcome, was included in this study. Design/Methods: This was a randomized, double-blind, placebo-controlled study in patients with PD experiencing >2hours/day OFF time. CVT-301 or placebo was used as an adjunct to usual PD medications for OFF symptoms for 4 weeks. Two doses were studied (35 mg [dosing level 1 (DL1), weeks 1-2]; 50 mg [dosing level 2 (DL2), weeks 3-4]). PGI-C ratings were measured at DL1 (end of week 2) and DL2 (end of week 4) to assess the effect of CVT-301 on patient impression of Parkinsonian control. PGI-C ratings were compared between placebo and CVT-301 using chi-square test. PGI-C ratings per baseline demographics and clinical characteristics were explored. Safety and tolerability were assessed. Results: Eighty-six patients with PD were randomized 1:1 to CVT-301 or placebo. Seventy-nine and 74 patients completed the PGI-C at DL1 and DL2, respectively. The majority of patients reported an improved impression of Parkinsonian control with CVT-301 (DL1:65.0[percnt]; DL2:71.8[percnt]), whereas less than half reported improvements with placebo (DL1:43.6[percnt]; DL2:45.7[percnt]). Compared with placebo, treatment with CVT-301 was associated with a significantly favorable impression of PD at DL2 (71.8[percnt]vs45.7[percnt], P=0.0225) and a directional favorable impression (65.0[percnt]vs43.6[percnt], P=0.0561) at DL1. Baseline demographic and clinical characteristics did not impact PGI-C ratings. CVT-301 was generally tolerated during the 4-week trial. Conclusions: Most patients reported an improved PGI-C rating with CVT-301, an inhaled levodopa, supportive of the positive findings in motor function and daily OFF time.

Neurology
LeWitt PA, and **Fahn S**. Levodopa therapy for Parkinson disease: A look backward and forward *Neurology* 2016; 86(14 Suppl 1):S3-s12. PMID: 27044648. Full Text
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From the Department of Neurology (P.A.L.), Henry Ford Hospital; Department of Neurology (P.A.L.), Wayne State University School of Medicine, Detroit, MI; and Department of Neurology (S.F.), Columbia University Medical Center, New York, NY.

Although levodopa is widely recognized as the most effective therapy for Parkinson disease (PD), its introduction 5 decades ago was preceded by several years of uncertainty and equivocal clinical results. The translation of basic neuroscience research by Arvid Carlsson and Oleh Hornykiewicz provided a logical pathway for treating PD with levodopa. Yet the pioneering clinicians who transformed PD therapeutics with this drug-among them Walther Birkmayer, Isamu Sano, Patrick McGeer, George Cotzias, Melvin Yahr, and others-faced many challenges in determining whether the concept and the method for replenishing deficient striatal dopamine was correct. This article reviews highlights in the early development of levodopa therapy. In addition, it provides an overview of emerging drug delivery strategies that show promise for improving levodopa's pharmacologic limitations.

Neurology
LeWitt PA, Hauser RA, Grosset DG, Stocchi F, Saint-Hilaire MH, Ellenbogen A, Leinonen M, Hampson NB, DeFeo-Fraulini T, Freed MI, and Kieburtz KD. A randomized trial of inhaled levodopa (CVT-301) for motor fluctuations in Parkinson's disease *Mov Disord* 2016;PMID: 27090868. Full Text

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Institute of Neurological Sciences, Glasgow, United Kingdom.
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Boston University School of Medicine, Boston, Massachusetts, USA.
Quest Research Institute and Michigan Institute for Neurological Disorders, Farmington Hills, Michigan, USA.
4Pharma AB, Stockholm, Sweden.
Virginia Mason Medical Center, Seattle, Washington, USA.
Acorda Therapeutics, Chelsea, Massachusetts, USA.
Clintrex LLC, Rye, New York, USA.

BACKGROUND: Although levodopa is the most effective oral PD therapy, many patients experience motor fluctuations, including sudden loss of dose effect and delayed benefit. CVT-301 is a levodopa inhalation powder with the potential for rapid onset of action. The objective of this study was to evaluate CVT-301 self-administered by PD patients to relieve OFF episodes. METHODS: PD patients with >/=2 hours per day of OFF time despite oral levodopa >/=4 times per day were randomized to CVT-301 or placebo for 4 weeks, to be used up to 3 times per day for OFF episodes. After 2 weeks, the study-drug dose was escalated from 35 to 50 mg. The primary end point was mean change in UPDRS Part III score from a predose OFF state to the average of postdose scores obtained at 10, 20, 30, and 60 minutes, as assessed in-clinic at the end of week 4. Home diaries were recorded. RESULTS: Eighty-six patients used the study drug at an average frequency of 2.1 times per day for CVT-301 and for placebo. At 4 weeks, least-squares mean change in UPDRS Part III score favored CVT-301 by 7.0 points (P < 0.001). A treatment effect was evident at 10 minutes. At 4 weeks, least-squares mean OFF-time change from baseline favored CVT-301 by 0.9 hours per day (P = 0.045). The most frequently reported adverse events in the CVT-301 group were dizziness, cough, and nausea, each in 7% (3 of 43 patients). CONCLUSIONS: CVT-301 self-administered during OFF episodes provided rapid improvement of motor function, and daily OFF time was significantly reduced at the higher dose. CVT-301 was generally safe and well-tolerated. (c) 2016 The Authors. Movement Disorders published by Wiley Periodicals, Inc. on behalf of International Parkinson and Movement Disorder Society.

Neurology
Maturu S, **Dayyoub T**, **Schultz L**, **Snyder J**, **Wasade V**, Elsayed M, **Gaddam S**, **Mahmood N**, **Constantinou J**, **Barkley G**, **Spanaki-Varelas M**, and **Zillgitt A**. Outcomes of genetic generalized epilepsy at a comprehensive epilepsy center *Neurology* 2016; 86(16)PMID: Not assigned. Abstract

S. Maturu, Henry Ford Hospital, Detroit, United States

Objective: This study aimed to provide a review of clinical outcomes for patients with genetic generalized epilepsy (GGE) from a diverse population in Metro-Detroit, Michigan. Background: The prognosis of GGE and its electroclinical syndromes remains poorly understood despite comprising approximately 20[percnt] of all epilepsy cases. The available data is comprised of methodological heterogeneity and often population homogeneity. Furthermore, the data is limited in its scope of prognostic factors regarding specific GGE electroclinical syndromes. Methods: A retrospective search of the Henry Ford Health System database was done from 1999 to 2012 on ICD-9 codes 345.10 or 345.11 for patients with a diagnosis of GGE. Inclusion criteria included a diagnosis of GGE or EEG with generalized epileptiform discharges 3 Hz (or both), age > 6 y, and treatment with at least 1 seizure medication. The associations of seizure freedom, initial and current seizure types, seizure freedom at 6 months and 1 year, and EEG findings were assessed using chi-square and two sample t-tests. Results: A total of 137 patients were analyzed. Nearly half were on 2 or more seizure medications at last follow-up, with an average of 3.8 seizure medication trials before arriving at their current seizure medication regimen. The primary outcome was seizure freedom at last follow-up. Of the 137 patients, 60 (44[percnt]) were seizure free at their last follow-up. Comparisons of the seizure types revealed a statistically significant difference in seizure freedom between patients with absence and GTCS and patients with absence, myoclonic, and GTCS. Conclusions: A substantial portion of patients were unable to achieve prolonged seizure freedom despite multiple seizure medication trials. Early seizure control within 1 year is predictive of long-term seizure freedom. In addition patients with a presumed diagnosis of JAE tended to have a more favorable outcome than those with JME.

Neurology
Mehta C, Jones M, Cuero MR, **Wellwood J**, **Rehman M**, **Mitsias P**, and **Varelas P**. Intracranial hemorrhage on warfarin: Time to reversal is of the essence *Neurology* 2016; 86(16)PMID: Not assigned. Abstract

C. Mehta

Background: Anticoagulation reversal is recommended for patients with intracerebral hemorrhage (ICH) on vitamin K antagonists or novel anticoagulants. Guidelines vary and standardized protocols are inconsistent. While our institution has guidelines indicating appropriate products for reversal, no specific timeline is indicated. ICH volume is known to increase by approximately 38[percnt] within the first 3 hours. Increase in hemorrhage size may be heightened in patients on anticoagulation without timely reversal. Objective: Identify a specified window for reversal of Vitamin K antagonists, in which ICH volume remained below the average growth in a control population on follow up imaging. Methods: Retrospective chart review of patients at Henry Ford Hospital from 2013-2014 with the diagnosis of ICH. Patients were excluded if they did not have follow up scans, if they underwent surgical intervention which precluded calculation of hemorrhage volume on subsequent scans, or had < 1cc initial hemorrhage volume. Results: Forty-five control patients were identified: Mean age 66.8 (44-92), GCS on admission 11 (3-15), ICH volume on admission 20.28cc, ICH volume on repeat scan 23.94cc, change in ICH volume 23.94[percnt], and time between initial and stability scans was 1150 minutes. Eleven patients on vitamin K antagonists (warfarin) were identified who underwent reversal with 4-factor prothrombin complex concentrate. Mean age 74.3 (58-88), GCS on admission 11 (315), ICH volume on admission 31.81cc, ICH volume on repeat scan 42.42cc, and time between initial and stability scans was 630 minutes. Mean time to PCC drug administration 221 minutes (52-805). Patients who had PCC administered before 195 minutes had a mean change in ICH volume of 16.95[percnt]. Patients who had reversal completed after the 195 minute mark had an mean change in ICH volume of 60.28[percnt]. (P value= 0.0032). Conclusions: We propose a “recommended reversal time” of less than 200 minutes for Vitamin K antagonists.

Neurology
Naqvi I, **Katramados A**, and Agarwal R. Arachnoid cyst with intracystic hemorrhage in a child: Need for vigilance and prompt treatment *Neurology* 2016; 86(16)PMID: Not assigned. Abstract

I. Naqvi, Henry Ford Hospital, Detroit, United States

Intracranial arachnoid cysts (AC) constitute one percent of all intracranial lesions, most frequently identified in children and mostly located in the middle cranial fossa. They are typically asymptomatic benign non communicating collections of cerebrospinal fluid that occur in relation to the subarachnoid space. Up to 27 per cent cases may be complicated by subacute or chronic subdural hematoma (SDH) or intracranial hemorrhage with minor head trauma, reportedly up to 16 weeks post trauma. Neurological symptoms can be acute and non-localizing. Most common are severe headache and vomiting, or seizures; and can be more subtle such as cognitive, emotional and memory decline from compression of adjacent tissue causing temporal lobe hypoplasia. Treatment is evacuation of SDH, and cystectomy with communication between cyst and cerebral cistern has also been proposed. We report a case of a 7 year old boy admitted with acute bilateral arm paresthesia, in the setting of possible prior head and neck trauma during trampoline play. He frequented the Emergency Department twice in the preceding month with new onset headaches, emesis and neck pain. Physical examination was pain limited, and non-focal. CT C spine did not show signs of trauma. The following day, the patient developed diplopia and was sent for MRI brain which showed large anterior and middle cranial fossa AC with bleed causing significant mass effect and herniation. He was taken for urgent SDH evacuation with drain placement. Post-operatively he rapidly improved back to full baseline functionality. This case highlights the diagnostic difficulties of AC with intracystic hemorrhage, particularly in children with unusual and delayed presentation. It also indicates need for close follow up among patients with AC and minor head trauma.

Neurology
Nazem-Zadeh MR, **Bowyer SM**, **Moran JE**, **Davoodi-Bojd E**, **Zillgitt A**, Weiland BJ, **Bagher-Ebadian H**, **Mahmoudi F**, Elisevich K, and **Soltanian-Zadeh H**. MEG Coherence and DTI Connectivity in mTLE *Brain Topogr* 2016;PMID: 27060092. Full Text

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Magnetoencephalography (MEG) is a noninvasive imaging method for localization of focal epileptiform activity in patients with epilepsy. Diffusion tensor imaging (DTI) is a noninvasive imaging method for measuring the diffusion properties of the underlying white matter tracts through which epileptiform activity is propagated. This study investigates the relationship between the cerebral functional abnormalities quantified by MEG coherence and structural abnormalities quantified by DTI in mesial temporal lobe epilepsy (mTLE). Resting state MEG data was analyzed using MEG coherence source imaging (MEG-CSI) method to determine the coherence in 54 anatomical sites in 17 adult mTLE patients with surgical resection and Engel class I outcome, and 17 age- and gender- matched controls. DTI tractography identified the fiber tracts passing through these same anatomical sites of the same subjects. Then, DTI nodal degree and laterality index were calculated and compared with the corresponding MEG coherence and laterality index. MEG coherence laterality, after Bonferroni adjustment, showed significant differences for right versus left mTLE in insular cortex and both lateral orbitofrontal and superior temporal gyri ($p < 0.017$). Likewise, DTI nodal degree laterality, after Bonferroni adjustment, showed significant differences for right versus left mTLE in gyrus rectus, insular cortex, precuneus and superior temporal gyrus ($p < 0.017$). In insular cortex, MEG coherence laterality correlated with DTI nodal degree laterality ([Formula: see text] in the cases of mTLE. None of these anatomical sites showed statistically significant differences in coherence laterality between right and left sides of the controls. Coherence laterality was in agreement with the declared side of epileptogenicity in insular cortex (in 82 % of patients) and both lateral orbitofrontal (88 %) and superior temporal gyri (88 %). Nodal degree laterality was also in agreement with the declared side of epileptogenicity in gyrus rectus (in 88 % of patients), insular cortex (71 %), precuneus (82 %) and superior temporal gyrus (94 %). Combining all significant laterality indices improved the lateralization accuracy to 94 % and 100 % for the coherence and nodal degree laterality indices, respectively. The associated variations in diffusion properties of fiber tracts quantified by DTI and coherence measures quantified by MEG with respect to epileptogenicity possibly reflect the chronic microstructural cerebral changes associated with functional interictal activity. The proposed methodology for using MEG and DTI to investigate diffusion abnormalities related to focal epileptogenicity and propagation may provide a further means of noninvasive lateralization.

Neurology

Patel AA, **Mahajan A**, Benjo A, Pathak A, Kar J, Jani VB, Annapureddy N, Agarwal SK, Sabharwal MS, Simoes PK, Konstantinidis I, Yacoub R, Javed F, El Hayek G, Menon MC, and Nadkarni GN. A nationwide analysis of outcomes of weekend admissions for intracerebral hemorrhage shows disparities based on hospital teaching status *Neurohospitalist* 2016; 6(2):51-58. PMID: 27053981. Full Text

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Division of Rheumatology, Department of Internal Medicine, Vanderbilt University Medical Center, Nashville, TN, USA.
Division of Cardiology, Department of Internal Medicine, University of Arkansas Medical Sciences, Little Rock, AR, USA.
Department of Internal Medicine, St. Luke's Roosevelt Medical Center at Mount Sinai, New York, NY, USA.
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BACKGROUND AND PURPOSE: With the "weekend effect" being well described, the Brain Attack Coalition released a set of "best practice" guidelines in 2005, with the goal to uniformly provide standard of care to patients with stroke. We attempted to define a "weekend effect" in outcomes among patients with intracranial hemorrhage (ICH) over the last decade, utilizing the Nationwide Inpatient Sample (NIS) data. We also attempted to analyze the trend of such an effect. MATERIALS AND METHODS: We determined the association of ICH weekend admissions with hospital outcomes including mortality, adverse discharge, length of stay, and cost compared to weekday admissions using multivariable logistic regression. We extracted our study cohort from the NIS, the largest all-payer data set in the United States. RESULTS: Of 485 329 ICH admissions from 2002 to 2011, 27.5% were weekend admissions. Overall, weekend admissions were associated with 11% higher odds of in-hospital mortality. When analyzed in 3-year groups, excess mortality of weekend admissions showed temporal decline. There was higher mortality with weekend admissions in nonteaching hospitals persisted (odds ratios 1.16, 1.13, and 1.09, respectively, for 3-year subgroups).

Patients admitted during weekends were also 9% more likely to have an adverse discharge (odds ratio 1.09; 95% confidence interval: 1.07-1.11; P < .001) with no variation by hospital status. There was no effect of a weekend admission on either length of stay or cost of care. CONCLUSION: Nontraumatic ICH admissions on weekends have higher in-hospital mortality and adverse discharge. This demonstrates need for in-depth review for elucidating this discrepancy and stricter adherence to standard-of-care guidelines to ensure uniform care.

Neurology
Sripathi N, and **Grover K**. Cardiac conduction defects in oculopharyngeal muscular dystrophy *Neurology* 2016; 86(16)PMID: Not assigned. Abstract

N. Sripathi, Henry Ford Hospital, Detroit, United States
Objective: To report association of cardiac conduction defects with Oculopharyngeal Muscular Dystrophy (OPMD) Background: OPMD is predominantly characterized by gradual development of ptosis with pharyngeal involvement that usually presents in fourth to sixth decades. Several extra-skeletal manifestations including deafness, endocrine disorders, smooth muscle involvement, peripheral neuropathy and impaired executive functions have been described. Cardiomyopathy or cardiac conduction defects have not been reported frequently. Goto described two Japanese patients with cardiomyopathy in 1977 with OPMD phenotype (J Neurol Neurosurg Psych 1977;40: 600). There is only one report of cardiomyopathy in a genetically confirmed OPMD siblings that was detected by echocardiography. Electrocardiography screening was normal in these two. Methods: Four male patients with OPMD, diagnosed by muscle biopsy in one (who refused genetic testing) and genetically confirmed GCN triplet repeat mutations in three with cardiac symptomatology were evaluated. Results: Ejection fractions at the time of evaluation were normal in all, and one went on to develop congestive heart failure. Cardiac arrhythmias detected were as follows: polymorphic Ventricular tachycardia and supraventricular tachycardia in 1, asymptomatic incomplete right bundle branch block in I and sinus bradycardia with first degree AV block in 2. Patient with polymorphic ventricular tachycardia required a single chamber AICD and another patient developed congestive heart failure. Conclusions: Our series along with the other emphasizes apparent association of Cardiomyopathy and cardiac conduction defects with OPMD, and these patients warrant screening with both echocardiography and electrocardiography.

Neurology
Tzagournissakis M, Spanaki C, Amoiridis G, Plaitakis A, and **Mitsias P**. Familial amyloidotic polyneuropathy in Crete, Greece *Neurology* 2016; 86(16)PMID: Not assigned. Abstract

M. Tzagournissakis, Neurology University, Hospital of Heraklion, Heraklion, Greece

Objective: To report the clinical, molecular, treatment and outcome data of all patients with FAP evaluated at the University Hospital of Crete, Greece. Background: Familial Amyloidotic Polyneuropathy (FAP) has been linked with multiple transthyretin (TTR) gene mutations and is encountered among different ethnic groups. Systematic study of FAP in this region has not been previously done. Methods: We studied 17 patients (9 women), members of 6 unrelated families. All patients underwent thorough clinical and laboratory investigation including rectal or nerve biopsy and molecular analysis. All patients had family history of polyneuropathy. Results: The mean age of disease onset was 30 years (range: 27 to 43). Symptoms were: paresthesias, progressive weakness of the lower extremities, urinary difficulties, diarrhea, postural dizziness and weight loss (n=17). The upper extremities were involved later in the disease course. Neurological findings were: loss of pain and temperature sensation in a glove and stocking distribution and distal weakness (n=17), orthostatic hypotension (n=15), and carpal tunnel syndrome (n=4). Cardiac complications were: arrhythmia (n=14), heart failure in the late phase of the disease (n=3). One patient presented with chronic renal failure treated with hemodialysis. Electromyography universally revealed denervation in the muscles of the lower extremities and slightly below normal conduction velocities. Rectal or sural nerve biopsy revealed the presence of amyloid deposit (n=17). On molecular analysis all patients were heterozygotes for the TTR Met30 mutation. 11/17 patients underwent orthotopic liver transplantation. 8/11 showed remarkable improvement, especially of autonomic symptoms and muscle strength. 2/11died of post-operative complications, one of intracerebral hemorrhage and one of unrelated cause. Conclusions: FAP encountered in Crete is due to Met30 mutation. Haplotype analysis that is in progress may help elucidate the origin of this mutation in relation to other populations. Orthotopic liver transplantation is the most effective treatment currently available for this disabling polyneuropathy.

Neurology
Wang H, Robinson J, **Varelas P**, Henderson G, Wijdicks E, and Greer D. Variability of brain death policies in the united states *Neurology* 2016; 86(16)PMID: Not assigned. Abstract

H. Wang, Yale School of Medicine, New Haven, United States

Objective: To assess how widely the updated 2010 American Academy of Neurology (AAN) practice parameters for brain death determination have been incorporated into hospital policies in the U.S. Background: Brain death is medically and legally accepted form of death in the US and worldwide. We previously showed that significant variability exists in individual institutional policies regarding brain death determination, leading to the 2010 update in US guidelines. We sought to evaluate if there has been adoption of these new guidelines, leading to decreased variability of brain death determination. Methods: We worked with organ procurement organizations to obtain individual US hospital policies pertaining to the determination of brain death. Policies were evaluated for summary statistics across 5 categories of data: 1) who is qualified to perform the determination, 2) what are the necessary prerequisites for testing, 3) details of the clinical examination, 4) details of apnea testing, and 5) details of ancillary testing. We compared this data with the standards in the AAN 2010 guideline update. Results: 508 unique hospital policies were obtained, representing the majority of hospitals that would be able to evaluate a brain dead patient in the US. Although improvement in compliance with the AAN guidelines was readily apparent, there remained significant variability across all categories of data. These included excluding the absence of hypotension (56[percnt]) and hypothermia (80[percnt]), specifying all aspects of the clinical examination and apnea testing, and specifying appropriate ancillary tests. Conclusions: Significant variability remains in US hospital policies for brain death determination. Hospitals should be encouraged to implement the updated 2010 guidelines to ensure 100[percnt] accurate and appropriate brain death determination.

Neurology
Yacoby-Zeevi O, Zawoznik E, Weinstock I, Nemas M, Caraco Y, **LeWitt P**, Oren S, and Shaltiel-Karyo R. Continuous subcutaneous administration of carbidopa enhances levodopa pharmacokinetics: A series of studies conducted in the pig, mouse and healthy volunteers *Neurology* 2016; 86(16)PMID: Not assigned. Abstract

O. Yacoby-Zeevi, Neuroderm, Rehovot, Israel

OBJECTIVE: To systematically evaluate the peripheral and central pharmacokinetics of levodopa during continuous subcutaneous carbidopa delivery. BACKGROUND: Although commercially available levodopa formulations include carbidopa or benserazide for dopa-decarboxylase inhibition, little is known how carbidopa delivery affects the pharmacokinetics of oral levodopa. METHODS: We conducted a series of pharmacokinetic studies in pigs, mice, and humans to characterize effects of continuous subcutaneous carbidopa delivery co-administered with oral levodopa/carbidopa (IR-LD/CD) compared to oral IR-LD/CD on levodopa pharmacokinetics. The porcine and human studies compared peripheral levodopa pharmacokinetic parameters (area under the curves [AUC], peak plasma concentrations [Cmax] and plasma elimination half-life [t]) and the mouse studies compared brain levodopa and dopamine levels. RESULTS: In pigs receiving oral IR-LD/CD (125/25mg, TID), additional continuous subcutaneous carbidopa delivery (60mg/24h) significantly increased the levodopa t1/2 and AUC versus IR-LD/CD alone, and versus IR-LD/CD plus oral carbidopa at doses equivalent to those administered subcutaneously. In mice, continuous administration of carbidopa (0.5mg/24h) in addition to oral IR-LD/CD (1.2/0.3 mg BID) improved peripheral levodopa pharmacokinetics as well as brain dopamine concentrations, with no significant effect on brain levodopa levels. We also confirmed that carbidopa given at relatively high and constant rates of delivery does not inhibit levodopa decarboxylation to dopamine in the brain. In healthy human volunteers receiving oral IR-LD/CD (200/50mg BID), subcutaneous continuous administration of carbidopa (80mg/24h) increased the plasma levodopa t, Cmax and AUC by 17.4[percnt], 40.5[percnt] and 22.3[percnt], respectively, and reduced the Tmax by 22.0[percnt], (all $p<0.003$ versus IR-LD/CD plus saline infusion). CONCLUSIONS: This series of studies demonstrates that maintaining basal plasma concentrations of carbidopa are essential for attaining maximum plasma concentrations of levodopa and that small continuous dosing of subcutaneous carbidopa has a positive effect on levodopa pharmacokinetics.

Neurology
Zahoor S, **Kaveeshvar H**, and **Loomba V**. Pain as the presenting symptom of primary progressive multiple sclerosis *Neurology* 2016; 86(16)PMID: Not assigned. Abstract

S. Zahoor, Henry Ford Hospital, Detroit, United States

Objective: To highlight a case in which a patient had extensive treatment for chronic pain but not sufficient diagnostic evaluation to determine the underlying cause of symptoms. Background: To our knowledge, this is the first case

report of pain being the presenting symptom of primary progressive multiple sclerosis. Methods: Case Report Results: We present a case of a 32 year old female with a benign past medical history presenting for a multitude of chronic pain complaints and back pain. Prior to visiting our neurology clinic, patient had been to several different pain physicians and turned away due to suspicion of narcotic seeking behavior. She described her pain as being a constant throbbing and sharp bilateral pain. The pain started to effect her balance and her grip ability. She had followed with a pain physician who had prescribed her narcotics and various neuropathic pain medications which did not help as her condition worsened. When she finally arrived to neurology clinic she was noted to be hyper reflexic with diminished proprioception. An MRI cervical spine was performed which demonstrated multiple foci of increased T2 signal noted throughout the brain cervical cord, and thoracic cord, with suggestion of focal areas of cord atrophy, suggestive of demyelinating disease. CSF analysis was consistent with oligoclonal bands and IgG Index providing our patient with the likely diagnosis of primary progressive multiple sclerosis Conclusions: This case highlights the importance of taking a diagnostic approach to pain via a good neurologic exam. Our patient suffered through years of pain and increasing debility and finally coming to a diagnosis gave her a great sense of relief and prognostication.

Neurology
Zhang ZG, and **Chopp M**. Exosomes in stroke pathogenesis and therapy *J Clin Invest* 2016; 126(4):1190-1197. PMID: 27035810. Article Request Form

Stroke is one of the leading causes of death and disability worldwide. Stroke recovery is orchestrated by a set of highly interactive processes that involve the neurovascular unit and neural stem cells. Emerging data suggest that exosomes play an important role in intercellular communication by transferring exosomal protein and RNA cargo between source and target cells in the brain. Here, we review these advances and their impact on promoting coupled brain remodeling processes after stroke. The use of exosomes for therapeutic applications in stroke is also highlighted.

Nursing
Everson C. Clinical nurse educator's perspective *Aorn Journal* 2016; 103(3):325-326. PMID: Not assigned.
[Everson, Claire] Henry Ford Macomb Hosp, Clinton Township, MI USA. Article Request Form
Everson, C (reprint author), Henry Ford Macomb Hosp, Clinton Township, MI USA.

Obstetrics, Gynecology and Women's Health Services
Jaber S, Winer I, and **Rasool N**. Recurrent omental hemangiopericytoma: A therapeutic challenge *Case Rep Obstet Gynecol* 2016; 2016:2075157. PMID: 27088021. Full Text

Division of Gynecologic Oncology, Department of Women's Health Services, Henry Ford Hospital, Detroit, MI 48202, USA.
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Hemangiopericytomas are vascular tumors with a susceptibility to arise anywhere in the human body. We present a case of a 68-year-old female with primary omental hemangiopericytoma and a two-time recurrence managed with surgery and close follow-up. The first recurrence was at 52 months and the second at 37 months following the prior presentation. No adjuvant chemotherapy or radiation therapy was administered. Given the widespread nature of the cell of origin, routine follow-up postoperatively with interval imaging in order to detect recurrences is imperative. Pathologic tumor characteristics may determine potential for recurrence and may also assist in determining whether adjuvant treatment modalities should be included in the management plan. Review of the English literature reveals a total of 24 cases of omental hemangiopericytomas inclusive of the current report.

Obstetrics, Gynecology and Women's Health Services
Rana S, Blowers EC, **Tebbe C**, Contreras JI, Radhakrishnan P, Kizhake S, Zhou T, Rajule RN, Arnst JL, **Munkarah AR**, **Rattan R**, and Natarajan A. Isatin derived spirocyclic analogues with alpha-methylene-gamma-butyrolactone as anticancer agents: A structure-activity relationship study *J Med Chem* 2016;PMID: 27077228. Article Request Form

Division of Gynecology Oncology, Department of Women's Health and Josephine Ford Cancer Center, Henry Ford Hospital , Detroit, Michigan 48202, United States.

Design, synthesis, and evaluation of alpha-methylene-gamma-butyrolactone analogues and their evaluation as anticancer agents is described. SAR identified a spirocyclic analogue 19 that inhibited TNFalpha-induced NF-kappaB

activity, cancer cell growth and tumor growth in an ovarian cancer model. A second iteration of synthesis and screening identified 29 which inhibited cancer cell growth with low-muM potency. Our data suggest that an isatin-derived spirocyclic alpha-methylene-gamma-butyrolactone is a suitable core for optimization to identify novel anticancer agents.

Obstetrics, Gynecology and Women's Health Services
Sangha R, **Katukuri V**, **Palmer M**, and **Khangura RK**. Recurrence after robotic myomectomy: is it associated with use of GnRH agonist? *J Robot Surg* 2016;PMID: 27072151. Full Text

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Gonadotropin-releasing hormone (GnRH) agonist therapy is used before myomectomy to decrease the size of the fibroids, but its association with fibroid recurrence postoperatively remains unsettled. We undertook a retrospective study of robotic-assisted myomectomy (RM) patients at our academic medical center to determine symptomatic recurrence and reoperation rates in those who did versus did not receive preoperative GnRH therapy. Only patients, who had their index myomectomy at least 2 years prior to the chart review, were included in this study. Of 118 RM patients identified between January 2005 and December 2009, 17 patients (14.4 %) had symptomatic recurrence as early as 5 months to as late as 30 months postoperatively. The symptomatic recurrence group had significantly higher preoperative GnRH use (35 vs 9 % non-recurrence; p = 0.009). A total of 7.6 % of all patients underwent reoperation. GnRH agonist use was significantly higher in the reoperation group (56 vs 9 % no reoperation; p = 0.002). Cavity entry during the initial surgery was also more frequent in the reoperation group (56 vs 20 %; p = 0.030), whereas the presence of multiple fibroids, size of the largest leiomyoma, and uterine volume were not statistically different between groups. Our study is among the earliest to report RM reoperation rates in patients receiving preoperative GnRH therapy, showing that the role of GnRH agonist therapy to shrink myomas may not be beneficial when measured against risk of disease recurrence.

Obstetrics, Gynecology and Women's Health Services
Swain M, Jeudy M, and Pearlman MD. Controversies in screening mammography *Clin Obstet Gynecol* 2016; 59(2):351-361. PMID: 27101240. Full Text

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The utility and effectiveness of screening mammography in diagnosing breast cancer at earlier stages and reducing disease-specific mortality remain controversial especially as to when to start and stop routine mammographic screening, and whether mammograms should be performed annually or biennially in average-risk women. This manuscript will analyze the available moderate and high-quality data to analyze both the benefits (lives saved and life-years saved) and inconveniences/harms (additional views, extra biopsies/overdiagnosis, and overtreatment of ductal carcinoma in situ) of different mammography screening guidelines to assist the practitioner in counseling their patients in clinical practice.

Obstetrics, Gynecology and Women's Health Services
Wegienka G, **Kaur H**, **Sangha R**, and **Cassidy-Bushrow AE**. Maternal-cord blood vitamin d correlations vary by maternal levels *J Pregnancy* 2016; 2016:7474192. PMID: 27066272. Full Text

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Vitamin D levels of pregnant women and their neonates tend to be related; however, it is unknown whether there are any subgroups in which they are not related. 25-Hydroxyvitamin D [25(OH)D] was measured in prenatal maternal and child cord blood samples of participants (n = 241 pairs) in a birth cohort. Spearman correlations were examined within subgroups defined by prenatal and delivery factors. Cord blood as a percentage of prenatal 25(OH)D level was calculated and characteristics compared between those who did and did not have >/=25% and >/=50% of the maternal level and those who did and did not have a detectable 25(OH)D level. The correlation among Black children was lower than in White children. When the maternal 25(OH)D level was <15 ng/mL, the overall correlation was r = 0.16. Most children had a 25(OH)D cord blood level less than half of their mother's; 15.4% had a level that was <25% of their mother's. Winter birth and maternal level were associated with the level being less than 25%. Children with undetectable levels were more likely to be Black and less likely to be firstborn. These data suggest mothers may reduce their contribution to the fetus's 25(OH)D supply once their own level becomes low.

Opthalmology and Eye Care Services
Elfersy AJ, **Prinzi RA**, Peracha ZH, **Kim DD**, **Crandall DA**, **Darnley-Fisch DA**, and **Imami NR**. IOP elevation after cataract surgery: Results for residents and senior staff at henry ford health system *J Glaucoma* 2016;PMID: 27027228. Full Text

Department of Ophthalmology, Henry Ford Hospital, Detroit, MI.

PURPOSE: To determine the incidence of intraocular pressure (IOP) elevation on postoperative day 1 (POD1) after cataract surgery performed by resident surgeons compared with attending surgeons and to examine the influence of associated variables on the incidence of postoperative IOP elevation. PATIENTS AND METHODS: Retrospective review of 2472 consecutive 2.2 to 2.8 mm temporal clear corneal cataract extractions by phacoemulsification performed by either residents or attending surgeons at Henry Ford Health System. Fellow eyes were excluded, resulting in 1847 eyes. IOP measurements of >40, >30, and >23 mm Hg were noted along with incremental IOP elevations of >/=10 and 20 mm Hg over preoperative/baseline IOP. Associated variables included: age, sex, diabetes mellitus, hypertension, glaucoma, glaucoma suspect, uveitis, prior ocular trauma, and vitreous loss at surgery. RESULTS: Resident-performed cataract surgery was associated with statistically significant higher rates of IOP elevation in all categories and in all clinical situations known to be associated with postoperative IOP spike, that is, vitreous loss at surgery, prior ocular trauma, and preexisting glaucoma. CONCLUSIONS: The incidence of postoperative day 1 IOP elevation after phacoemulsification performed by resident surgeons was 2 to 5 times that of experienced cataract surgeons. Variables including vitreous loss at surgery, prior ocular trauma, preexisting glaucoma, glaucoma suspect status, and male sex were significant contributors. Consideration for prophylactic IOP lowering is advised in high-risk patients.

Opthalmology and Eye Care Services
Spaulding J, **Saraf S**, Essad K, and **Christianson M**. The first case of intracranial rosai dorfman disease *Neurology* 2016; 86(16)PMID: Not assigned. Abstract

J. Spaulding, Ophthalmology, Henry Ford Hospital, Detroit, United States

Objective: to report an interesting and informative case of an atypical presentation of a rare condition, Rosai Dorfman Disease (RDD) Background: RDD previously known as Sinus Histiocytosis with massive lymphadenopathy (SHML), is a rare, idiopathic disease seen mainly in children and young adults. It typically presents with painless lymphadenopathy, fever, leukocytosis, elevated erythrocyte sedimentation rate, and polyclonal hypergammaglobulinemia. To date only 5 cases of isolated epibulbar disease have been described in the literature. Case, Methods: An 80 year-old African-American woman presented with a history of a right orbital mass and complaints of worsening blurred vision and photophobia in the left eye. Her vision was NLP in the right and 20/60 in the left eye. She had a large, pink lesions under the superior bulbar conjunctiva of both eyes with concomitant cell and flare. MRI orbits, biopsies of right subconjunctival lesion and both retrobulbar lesions. Pathology showed histiocytes with abundant atypical reticular cytoplasm with phagocytosed lymphocytes. Immunohistochemical staining was S-100 positive, CD1a negative, and CD68 positive for histiocytes. Results: Enhancing soft tissue masses posterior to both globes, and masses in the cavernous sinus, cribriform plate, crista Galli, and interhemispheric fissure on either side of the falx, the left optic nerve sheath Conclusions: RDD is associated with massive cervical lymphadenopathy in 90[percnt] of patients, lymphadenopathy is also present inguinal (26[percnt]), axillary (24[percnt]), and mediastinal (15[percnt]). Up to 43[percnt] of patients presented with extranodal pathology, most frequently involving the skin, upper respiratory system, eyelid, orbit, bone, salivary glands, and the central nervous system. Our case is classified as RDD with orbital, uveal, epibulbar and intracranial involvement. The age of presentation is atypical, suggesting that RDD may masquerade as several entities and should be kept in the differential for patients with any combination of orbital masses, idiopathic uveitis, and subconjunctival lesions.

Orthopaedics
Gibson G, and **Yang M**. Gene editing in chondrocytes using crispr/cas9 *Osteoarthritis and Cartilage* 2016; 24:S2-S3. PMID: Not assigned. Abstract

[Gibson, G.; Yang, M.] Henry Ford Hosp, Detroit, MI 48202 USA.

Purpose: The capacity, simplicity of use and scope of the CRISPR/Cas9 system offers the ability to define the function and interaction of known genes as well as identify the function of previously uncharacterized genes. The development of permanent chondrocyte cell lines expressing Cas9 has enabled the adaptation of these techniques to define the genetic and epigenetic regulation chondrocyte function. Methods: The CRISPR/Cas9 system has been adapted to provide a cheap, simple system to edit the genome of both prokaryote and eukaryote cells. By delivery of

the nuclease Cas9 in combination with a specific targeting guide RNA (sgRNA) double-strand breaks can be created at the desired DNA locus. Subsequent error prone repair generates frequent insertions or deletions (indels) that result in gene disruption. The Cas9 gene is relatively large (158 kDa) and expression in chondrocytes, which are known for their particularly poor transfection efficiency, represents a significant challenge. A stable chondrocyte cell line expressing Cas9 (RCS/Cas9) was generated by transfection of rat chondrosarcoma cells that have a flipase recognition target FRT site in the eukaryotic translation factor 1a locus. Subsequent editing of a target locus in these cells required only transfection with a specific, small sgRNA gene construct. Further enrichment by FACS allowed easy single cell cloning with the target gene precisely edited. As proof of principle sgRNAs targeting Acan and miR-140 were separately transfected to create chondrocyte cell lines with no expression of Acan (AcanKO) or miR-140 (miR-140KO). The Acan sgRNA targeted the third exon of the Acan gene and contained a restriction enzyme (PstI) sequence. The miR-140 sgRNA targeted the seed sequence. Success of the editing process was determined by elimination of the restriction site and sequence analysis of multiple clones. Results: After FACS enrichment approximately 80% of the cells showed targeted mutation. 15 of the 16 cell clones targeted to mutate the Acan gene showed target site mutation. Sequence analysis of the mutation site in cloned cells showed indels expected cause loss of Acan gene and protein expression or miR-140 expression. The AcanKO and miR-140KO clones showed no change in cell growth. The AcanKO clones maintained the cartilage phenotype as demonstrated expression of chondrocyte marker genes, including, Col2a1, Col1a2, Matn1 and Comp. When injected subcutaneously in nude mice the RCS or RCS/Cas9 cell lines generated a chondrosarcoma with a fully cartilaginous matrix. In contrast the AcanKO cell line generated a much smaller tumor-like tissue with few chondrocyte-like cells and substantial infiltration of immune cells. The loss of miR-140 expression was consistent with the indel size and presence in the seed sequence. Expression of cartilage genes, Col2a1, Comp and Acan were reduced in the miR-140KO cells but this did not appear to be associated with loss of phenotype. Expression of the miR-140 host gene WWP2 was unaffected by the targeted mutations indicating that changes in cell function observed were not associated with changes in expression of the host gene. The mutations were shown to affect miRNA maturation. Gene array analysis surprisingly showed no change in those genes, Adamts5, Pdgfa, Dnpep, Sp1, Hdac4 and Igfpb1, previously suggested to be miR-140 targets. Conclusion: The cell line described and similar chondrocyte cell lines under development will enable utilization of the extensive and rapidly expanding scope of the CRISP/Cas9 system to characterize gene function in chondrocytes. Some of the capacities of the CRISPR/Cas9 system that include; the use of arrayed sgRNA libraries for the identification of genes essential for survival, proliferation or other specific chondrocyte functions such as suppression of terminal differentiation; and the identification of epigenomic mechanisms, including histone modification, for gene regulation will be discussed.

Orthopaedics

North WT, **Mehran N**, **Davis JJ**, **Silverton CD**, **Weir RM**, and **Laker MW**. Topical vs intravenous tranexamic acid in primary total hip arthroplasty: A double-blind, randomized controlled trial *J Arthroplasty* 2016; 31(4):928-929. PMID: 26783121. Full Text

Department of Adult Reconstructive Surgery, Henry Ford Hospital, Orthopaedic Surgery, Detroit, Michigan.

Otolaryngology – Head and Neck Surgery

Worsham MJ, **Chen KM**, **Chitale D**, **Stephen JK**, and **Divine G**. Differentially methylated miRNA methylomes of normal breast tissue from ER negative and ER positive breast cancer mimic their respective tumor phenotypes *Can Res* 2016; 76(4)PMID: Not assigned. Abstract

M.J. Worsham, Henry Ford Health System, Detroit, United States

Background: The unique structure and function of normal tissues is known to be regulated by epigenetic mechanisms. Understanding how normal cells in their respective tumor milieus might affect their susceptibility to become not only malignant but acquire breast cancer (BC) subtype-specific phenotypes, may determine tumor clinical behavior outcomes. The goal was to compare genome wide methylation profiles of non-coding miRNAs of breast cancer tissue and normal breast epithelium, respectively, from ER negative and ER positive tumors, and assess their miRNA methylomes in the context of tumor ER phenotypes as ER negative vs ER positive. Methods: Breast cancer tissue from 79 patients (40 ER-positive and 39 ER-negative) and normal tissue from 39 of these patients (19 ER-negative and 20-ER-positive) were assayed using the Illumina 450K bead array. A sub analysis focused on 2249 miRNA CpGs assigned to 615 unique miRNAs. M-values were computed as a logit function [(log (beta/ (1-beta))] of the methylation beta values. T-tests were used to compare the means of the M-values for the ER-positive and ER-negative groups. The t-test p-values were used to generate adaptive FDR (aFDR) levels and aFDRs of 0.05 or lower were considered to be statistically significant (Tier 1). Tier 1 CpGs were subsequently filtered to select only those with a mean beta ratio between ER-positive and ER-negative of under 0.5 or over 2.0 (Tier 2). The Tier 2 CpGs were further filtered to select only those with a mean beta difference of 0.2 or more (Tier 3). Results: In

the tumor cohort, 1224/2249 (54%) CpGs were differentially methylated between ER negative and ER positive BC at Tier 1 (aFDR 0.05 or lower). Of the 1224, 963 (78.7%) were hypermethylated, and 1035 (84.6%) were associated with the promoter region. The 1224, 24 and 2 CpGs were associated with 379, 22 and 2 genes for Tiers 1, 2 and 3, respectively. When the same analysis was performed on normal tissue only (19 ER-negative and 20-ER-positive) 76 of the 2249 CpGs had significant aFDR values and none of those met the Tier 2 or Tier 3 criteria. Seventy-one of the 76 (93.4%) where hypermethylated, and 65 (85.5%) were associated with the promoter region. The 76 significant Tier 1 (aFDR) differentially methylated CpGs were associated with 48 genes of which 43 were common to tumor Tier 1 differentially methylated miRNA genes, 10 were common to tumor Tier 2 genes, and 5 were restricted to normal tissue only. Conclusions Normal epithelial tissues demonstrated similar differential methylation directionality as their respective tumor counterparts (although to a lesser extent), favoring promoter region localization. Accordingly, the recognition of normal breast tissue-specific epigenetic propensities that align with their tumor phenotypes, suggest the possibility of progression markers specific for estrogen receptor status as well as markers not associated with progression. This provides insights into our view of possible links between epigenetic programming, progression continuums, and how hormonal receptor subtypes may be determined.

Otolaryngology – Head and Neck Surgery

Worsham MJ, **Chen KM**, **Datta I**, **Stephen JK**, **Chitale D**, and **Divine G**. Epigenetically altered microRNA mediated pathway dysregulation in ER negative breast cancer *Can Res* 2016; 76(4)PMID: Not assigned. Abstract

M.J. Worsham, Henry Ford Health System, Detroit, United States

Background: Micro RNAs (miRNA) are endogenous, small non-coding RNAs that control gene expression by directing their target mRNAs for degradation and/or posttranscriptional repression. Compared to mRNA signatures, miRNAs have better and stronger biomarker properties with 20 times more power in biomarker studies as compared to mRNAs (when comparing 20,000 mRNAs to ~1,000 miRNAs). Emerging evidence now supports the idea that DNA methylation is crucially involved in the dysregulation of miRNAs in cancer, representing a novel class of potential biomarkers for diagnosis, prediction of treatment, or prognosis. ER-negative breast cancer (BC) is an aggressive histological subtype with limited treatment options and very poor prognosis. Our long term objective is to derive a diagnostic, prognostic, and predictive ER-negative specific miRNA panel for detection of early cancer, recurrence/metastasis, and as potential therapeutic targets for better management of ER-negative BC. Methods: The initial discovery step profiled 39 primary ER negative and 40 ER positive BC cases using the Illumina Infinium HumanMethylation450 BeadChip followed by a subanalysis focusing on 2249 miRNA CpGs assigned to 615 unique miRNAs. T-tests were used to compare the means of the M-values for the ER-positive and ER-negative groups. The t-test p-values were used to generate adaptive FDR (aFDR) levels and aFDRs of 0.05 or lower were considered to be statistically significant (Tier 1). Tier 1 CpGs were subsequently filtered to select only those with a mean beta ratio between ER positive and ER negative of under 0.5 or over 2.0 (Tier 2). The Tier 2 CpGs were further filtered to select only those with a mean beta difference of 0.2 or more (Tier 3). Because miRNAs perform their important functions via their targets, the targets of miRNAs were assessed for functional enrichment analysis in IPA for biologic involvement. Results: Over half of the miRNA CpGs (1224/2249, 54%) were differentially methylated between ER negative and ER positive BC with significant aFDR levels. The 1224 CpGs at Tier 1 were associated with 379 miRNAs; the 24 and 2 CpGs for Tiers 2 and 3 with 22 and 2 miRNAs, respectively. The 22 miRNA genes were assigned to 4621 targets using online databases that predict miRNA targets. The degree of confidence that a target gene is associated with a miRNA is characterized in these databases as either “experimentally observed”, or just as “high” (predicted). Of these 4621 targets, 87 were designated as experimentally observed and were examined in IPA. Top pathways and networks designated by miRNA targets included the cell cycle G1/S checkpoint regulation canonical pathway, and the cell-to-cell interaction/cancer networks among others. MiRNA targets in top pathways and networks were circled back to their respective miRNAs revealing cooperatively mediated pathway dysregulation of ER negative BC. Conclusion: Aberrantly methylated miRNAs showed perturbation of biologically significant pathways and networks, suggesting that miRNAs mediate pathway dysregulation in a coordinated manner, strengthening the case for utility of miRNAs as viable biomarkers in ER negative BC.

Pathology

Hwang C, Sethi S, Heilbrun LK, **Gupta NS**, **Chitale DA**, Sakr WA, **Menon M**, **Peabody JO**, Smith DW, Sarkar FH, and Heath EI. Anti-androgenic activity of absorption-enhanced 3, 3'-diindolylmethane in prostatectomy patients *Am J Transl Res* 2016; 8(1):166-176. PMID: 27069550. Full Text

Department of Hematology/Oncology, Josephine Ford Cancer Institute, Henry Ford Health System Detroit, MI, USA. Department of Pathology, Karmanos Cancer Institute, Wayne State University School of Medicine Detroit, MI, USA. Department of Oncology, Karmanos Cancer Institute, Wayne State University School of Medicine Detroit, MI, USA. Department of Pathology, Josephine Ford Cancer Institute, Henry Ford Health System Detroit, MI, USA.

Department of Vattikuti Institute of Urology, Josephine Ford Cancer Institute, Henry Ford Health System Detroit, MI, USA.
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Department of Oncology, Karmanos Cancer Institute, Wayne State University School of MedicineDetroit, MI, USA.

Consumption of cruciferous vegetables is associated with a decreased risk of developing prostate cancer. Antineoplastic effects of cruciferous vegetables are attributable to bioactive indoles, most prominently, 3, 3'-diindolylmethane (DIM). In addition to effects on proliferation and apoptosis, DIM acts as an antiandrogen in prostate cancer cell lines. This study characterized the effects of prostatic DIM on the androgen receptor (AR) in patients with prostate cancer. Men with localized prostate cancer were treated with a specially formulated DIM capsule designed for enhanced bioavailability (BR-DIM) at a dose of 225 mg orally twice daily for a minimum of 14 days. DIM levels and AR activity were assessed at the time of prostatectomy. Out of 28 evaluable patients, 26 (93%) had detectable prostatic DIM levels, with a mean concentration of 14.2 ng/gm. The mean DIM plasma level on BR-DIM therapy was 9.0 ng/mL; levels were undetectable at baseline and in follow-up samples. AR localization in the prostate was assessed with immunohistochemistry. After BR-DIM therapy, 96% of patients exhibited exclusion of the AR from the cell nucleus. In contrast, in prostate biopsy samples obtained prior to BR-DIM therapy, no patient exhibited AR nuclear exclusion. Declines in PSA were observed in a majority of patients (71%). Compliance was excellent and toxicity was minimal. In summary, BR-DIM treatment resulted in reliable prostatic DIM levels and anti-androgenic biologic effects at well tolerated doses. These results support further investigation of BR-DIM as a chemopreventive and therapeutic agent in prostate cancer.

Pathology

Newman LA, Jiagge E, **Bensenhaver JM**, **Chitale D**, Kleer C, Merajver S, Kyei I, Aitpillah F, Oppong J, Amankwaa-Frempong E, Adjei E, Wicha M, Awuah B, and **Stark A**. Comparative analysis of breast cancer phenotypes in African American, white American, and African patients-correlation between African ancestry and triple negative breast cancer *Cancer Res* 2016; 76(4)PMID: Not assigned. Abstract

L.A. Newman

Introduction: Population-based incidence rates of triple negative breast cancer (TNBC) are higher for African American (AA) compared to White American (WA) women, but it is unclear whether TNBC risk is genetically associated with African ancestry because AA women represent an ancestrally admixed population. Higher frequencies of TNBC have also been observed in sub-Saharan African breast cancer (BC) patients, but comparative analyses of biomarker expression among datasets that include AA, WA, and African women are sparse. We report findings from an international registry that features specimens from a diverse patient population in Detroit, Michigan as well as a hospital in Kumasi, Ghana. Methods: The study dataset included formalin-fixed, paraffin-embedded invasive BC tumors diagnosed between 1998 and 2014 at the Komfo Anokye Teaching Hospital in Ghana and the prospectively-maintained/annotated Henry Ford Health System cohort in Michigan. All Ghanaian tumors underwent pathology confirmation and immunohistochemistry for estrogen receptor (ER), progesterone receptor (PR) and HER2/neu expression at the University of Michigan. Women were classified into five BC phenotypes and dichotomized into two age groups, <50 and ≥50 years. Polychotomous multivariate GLM models were developed to estimate the risk for each BC phenotype. Statistical analyses were performed in SAS v. 9.0 (Carey, NC). This research was approved by the Institutional Review Boards of the participating institutions. Results: A total of 234 Ghanaian cases with mean age 49 years (range 24-92); 271 AA with mean age 60 (range 27-87); and 321 WA with mean age 62 (range 31-91) (P=0.001) contributed to this study. Prevalence of histologic grade 3 was lowest in WA (n=107, 33.7%) which was statistically significant from the observed prevalence in AA (n=135, 50.4%) and Ghanaians (n=84, 53.8%) (P<0.0001). ER-negative and TNBC were more common among Ghanaian and AA compared to WA cases (frequency ER-negativity 67.5%, 37.1%, and 19.8%, respectively, p<0.0001; frequency TNBC 53.2%, 29.8%, and 15.5%, respectively, p<0.0001). In the age group <50 years, 82 women (42.5%) were diagnosed with ER+/PR+/HER2-, 65 (33.7%) with TNBC, 27 (14.0%) with ER+/PR+/HER2+, 14 (7.2%) with ER-/PR-/HER2+ and 5(2.6%) with ER-/PR+/HER2- phenotypes. In this young age group, prevalence of TNBC remained highest among Ghanaian women (50.8%), followed by AA (34.3%) and WA (15.9%); (P=.0006). In contrast, highest prevalence of ER+/PR+/HER2+ and ER+/PR+/HER2- phenotypes was observed in WA, followed by AA and Ghanaians. On multivariate analysis histologic grade 3 and racial heritage remained statistically significantly associated with the TNBC phenotype (OR for AA vs. WA with TNBC 1.87, 95% CI 1.15-3.04; OR for Ghanaian vs. WA with TNBC 10.63, 95% CI 5.32-21.25; OR for Grade 3 vs Grade 1 histology with TNBC 33.3, 95% CI 13.45-82.4). Conclusions: This study confirms an association between the TNBC phenotype and African ancestry; furthermore, extent of African ancestry appears to be associated with an increased likelihood of having a TNBC tumor, since frequency of TNBC among AA patients was intermediate between WA and Ghanaian patients.

Pathology

Worsham MJ, **Chen KM**, **Chitale D**, **Stephen JK**, and **Divine G**. Differentially methylated miRNA methylomes of normal breast tissue from ER negative and ER positive breast cancer mimic their respective tumor phenotypes *Can Res* 2016; 76(4)PMID: Not assigned. Abstract

M.J. Worsham, Henry Ford Health System, Detroit, United States

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Pathology

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Background: Micro RNAs (miRNA) are endogenous, small non-coding RNAs that control gene expression by directing their target mRNAs for degradation and/or posttranscriptional repression. Compared to mRNA signatures, miRNAs have better and stronger biomarker properties with 20 times more power in biomarker studies as compared to mRNAs (when comparing 20,000 mRNAs to ~1,000 miRNAs). Emerging evidence now supports the idea that DNA methylation is crucially involved in the dysregulation of miRNAs in cancer, representing a novel class of potential biomarkers for diagnosis, prediction of treatment, or prognosis. ER-negative breast cancer (BC) is an aggressive histological subtype with limited treatment options and very poor prognosis. Our long term objective is to derive a diagnostic, prognostic, and predictive ER-negative specific miRNA panel for detection of early cancer, recurrence/metastasis, and as potential therapeutic targets for better management of ER-negative BC. Methods: The initial discovery step profiled 39 primary ER negative and 40 ER positive BC cases using the Illumina Infinium HumanMethylation450 BeadChip followed by a subanalysis focusing on 2249 miRNA CpGs assigned to 615 unique miRNAs. T-tests were used to compare the means of the M-values for the ER-positive and ER-negative groups. The t-test p-values were used to generate adaptive FDR (aFDR) levels and aFDRs of 0.05 or lower were considered to be statistically significant (Tier 1). Tier 1 CpGs were subsequently filtered to select only those with a mean beta ratio between ER positive and ER negative of under 0.5 or over 2.0 (Tier 2). The Tier 2 CpGs were further filtered to select only those with a mean beta difference of 0.2 or more (Tier 3). Because miRNAs perform their important functions via their targets, the targets of miRNAs were assessed for functional enrichment analysis in IPA for biologic involvement. Results: Over half of the miRNA CpGs (1224/2249, 54%) were differentially methylated between ER negative and ER positive BC with significant aFDR levels. The 1224 CpGs at Tier 1 were associated with 379 miRNAs; the 24 and 2

CpGs for Tiers 2 and 3 with 22 and 2 miRNAs, respectively. The 22 miRNA genes were assigned to 4621 targets using online databases that predict miRNA targets. The degree of confidence that a target gene is associated with a miRNA is characterized in these databases as either “experimentally observed”, or just as “high” (predicted). Of these 4621 targets, 87 were designated as experimentally observed and were examined in IPA. Top pathways and networks designated by miRNA targets included the cell cycle G1/S checkpoint regulation canonical pathway, and the cell-to-cell interaction/cancer networks among others. MiRNA targets in top pathways and networks were circled back to their respective miRNAs revealing cooperatively mediated pathway dysregulation of ER negative BC. Conclusion: Aberrantly methylated miRNAs showed perturbation of biologically significant pathways and networks, suggesting that miRNAs mediate pathway dysregulation in a coordinated manner, strengthening the case for utility of miRNAs as viable biomarkers in ER negative BC.

Physical Therapy

Arena SK, Simon L, and **Peterson EL**. Aneroid blood pressure manometer calibration rates in physical therapy curricula: A descriptive study *Cardiopulm Phys Ther J* 2016; 27(2):56-61. PMID: Not assigned. Full Text

S.K. Arena, Physical Therapy Program, School of Health Sciences, Oakland University, Rochester, United States

Purpose: The purposes of this study were to (1) describe the calibration rates of aneroid blood pressure (BP) devices used in physical therapist (PT) education programs and (2) determine the validity of having the gauge needle resting within the zero-accuracy indicator as a proof of device calibration. Methods: We conducted a prospective descriptive study using a sample of convenience with an estimated 30-35 aneroid BP sphygmomanometers available for calibration check from each of the 6 PT education programs. Calibration of the measurement device used a certified mercury sphygmomanometer following the recommendations of the European Society of Hypertension. Descriptive statistics reported calibration rates, gauge needle position, device brand, cuff sizes, and whether the device was portable or wall mounted. Additionally, BP device calibration rates measured at universities that had or had not performed equipment calibration checks within the previous 2 years were compared using the Chi-square test with significance set at P ≤.05. Results: Calibration failure was identified in 22.5% of 289 BP gauges, whereas 16.2% of devices with a gauge needle resting in the zero accuracy indicator failed calibration validity measures. Additionally, a significant difference between the calibration rates of equipment from universities that had (n 47) and had not (n 242) regularly performed calibration checks was identified (P .001). Conclusion: This study found that 22.5% of aneroid BP devices used in the participating PT education programs were not in calibration. Additionally, visual confirmation of a gauge needle resting position falling within the zero accuracy indicator did not assure that a device was in calibration. Routine inspection of BP devices is imperative to assure that accurate BP readings are guiding clinical recommendations.

Public Health Sciences

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Public Health Sciences

Azuh O, **Gammon H**, **Burmeister C**, **Frega D**, **Nerenz D**, **DiGiovine B**, and **Siddiqui A**. Benefits of early active mobility in the medical intensive care unit - a pilot study *Am J Med* 2016;PMID: 27107920. Full Text

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BACKGROUND: Pressure ulcer formation continues to be problematic in acute care settings, especially intensive care units (ICUs). Our institution developed a program for early mobility in the ICU using specially-trained nursing aides. The goal was to impact hospital acquired pressure ulcers incidence as well as factors associated with ICU deconditioning by using specially-trained personnel to perform the acute early mobility interventions. METHODS: A five-point mobility scale was developed and used to establish a patients' highest level of activity achievable during evaluation. A Mobility Team was created consisting of skin-care prevention/mobility nurses and a new category of worker called a patient mobility assistant. Each level has a corresponding plan of care (intervention) that was followed and adjusted according to the patient's progress and nursing evaluation. Data collection included the type of interventions at each encounter, mobility and skin assessments, new hospital-acquired pressure ulcer, the current mobility level, Braden score, rate of ventilator associated pneumonia, ICU length of stay and hospital readmission. Staff was also surveyed about their attitudes toward mobilization and perception of mobility barriers, pre-pilot and a post-pilot survey is planned. RESULTS: During the 1-year study interval, 3233 patients were enrolled from the medical intensive care unit (MICU). The 2011 pre-implementation MICU hospital-acquired pressure ulcer rate was 9.2%. After 1 year of employing the mobility team, there was a statistically significant drop in the medical intensive care unit hospital-acquired pressure ulcer rate to 6.1% (p = 0.0405). Hospital readmission of medical intensive care unit patients also significantly decreased from 17.1% to 11.5% (p = .0010). The mean medical intensive care unit length of stay decreased by 1 day. There were no safety issues directly or indirectly associated with these interventions. CONCLUSIONS: Use of this mobility program resulted in a 3% decrease in the most recalcitrant patients in the MICU. This corresponds to a decrease of 1.2 per 1000 patient days. It is definitely both statistically and clinically significant. We believe this lays the groundwork for further work in this area. We have shown that properly trained non-licensed professionals can safely and effective mobilize patients in the ICU setting. This can represent a cost effective way to introduce early mobility in the ICU setting.

Public Health Sciences

Bossick AS, Peters RM, Burmeister C, Kakumanu N, **Shill JE**, and **Cassidy-Bushrow AE**. Antenatal inflammation and gestational diabetes mellitus risk among pregnant African-American women *J Reprod Immunol* 2016; 115:1-5. PMID: 27061480. Full Text

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Although inflammation is associated with risk of gestational diabetes mellitus (GDM), little is known if there is an association between inflammation and GDM in African-American women, a group at higher risk for GDM complications. In the present study, we aimed to determine if selected inflammatory cytokines (i.e. TNF-alpha, hs-CRP, IL-6, IL-10, IL-6/IL-10 ratio, IL-1beta) measured in the 2nd trimester, were associated with GDM risk in 185 pregnant African-American women. GDM was defined as a physician-documented GDM diagnosis, a fasting glucose between 92 and 125mg/dl, or evidence of glucose intolerance (defined using the 3-h glucose tolerance test). A total of 18 women (9.7%) had GDM. After covariate adjustment, C-reactive protein, measured at a mean 21.2+/-3.7 weeks gestation, was statistically significantly associated with GDM development (P=0.025); for every one-unit increase in log-transformed C-reactive protein, the odds of GDM increased by 5.3. Results were similar using a principal component analysis approach. This study provides evidence that higher levels of 2nd trimester C-reactive protein is associated with increased risk of GDM in African-American women. Further research is needed to examine whether C-reactive protein may be a useful early-pregnancy screen for evaluating potential GDM risk in African-American women.

Public Health Sciences

Castillo JJ, Glezerman IG, Boklage SH, **Lamerato LE**, Chiodo JA, Tidwell BA, and Schulman KL. Incidence and prognostic importance of hyponatremia in a cohort of patients with breast cancer *Cancer Res* 2016; 76(4)PMID: Not assigned. Abstract

J.J. Castillo

Background: It has been suggested that hyponatremia (HN) may be a negative prognostic factor in patients with cancer but little research has been conducted specifically in breast cancer (BC). We measured the incidence of hyponatremia (hypervolemic and euvolemic) after BC diagnosis and its prognostic importance for progression free (PFS) and overall survival (OS) Methods: This retrospective cohort analysis utilized data from the Henry Ford Health System electronic medical record, tumor registry, and administrative databases. Study data were collected electronically and via medical record abstraction. Adults diagnosed (2002-2010) with incident invasive BC were selected if they had a known disease stage at the time of tumor registration, were classified as an analytic case, had ≥ 1 administration of chemo/radiation therapy ≤ 6 months from diagnosis, met continuous enrollment thresholds, and did not experience hypovolemic HN post index. Only the first tumor registered from each patient was considered study-eligible. Hypervolemic or euvolemic HN incidence (serum sodium ≤ 135 mEq/L) was measured per 1000 person-years (PY) of observation and classified as mild (131-135 mEq/L), moderate (125-130 mEq/L) or severe (<125 mEq/L) based on the lowest observed value. A Cox proportional hazards model was used to assess the prognostic value of HN as a time-varying covariate on PFS and OS while controlling for age, race, income, morphology code, diagnosis year, cancer stage at diagnosis, performance status at diagnosis, and hormone receptor status Results: 527 patients were eligible (mean [SD] age 56.4±11.3 years, 61% Caucasian). Mean (SD) follow-up was 3.7±2.8 years. Eighty-five percent of patients had infiltrating ductal carcinoma; 72% and 65% had estrogen or progesterone sensitive tumor, respectively; 35% were HER2 positive; and 15% had triple negative disease. Eighty-two percent of patients had early stage (I, II) disease at time of diagnosis. HN episodes (n=377) occurred in 204 patients (39%) at a rate of 193 per 1000 PY (95% CI, 174-213.5), with 89% of the total episodes (337/377) classified as mild, 10% (36/377) as moderate, and 1% (4/377) as severe. Additionally, 7% of all BC patients (37/527) had at least one episode of moderate/severe HN. Median time to first HN episode was 174.5 days and the median HN episode duration was 24.0 days. Five year OS in patients developing HN was 92%, compared to 97% in patients who never developed HN. Hazard ratio (95% CI, p-value) for OS in the HN group was 4.4 (1.5-12.7; p=0.006) after controlling for age, diagnosis year, race, income, morphology, cancer stage, performance status, and hormone receptor status. Fifty patients had progressive disease during follow-up with a mean (SD) time to progression of 763.4 (758.1) days. Hazard ratio (95% CI, p-value) for PFS in the HN group was 1.4 (0.8-2.7; p=0.262) after controlling for age, race, income, morphology, cancer stage, performance status, and hormone receptor status Conclusions: Incidence of hypervolemic or euvolemic HN is high (39%) after a BC diagnosis, and the occurrence is associated with significantly poorer OS. A significant impact on disease progression was not observed.

Public Health Sciences

Demos D, **Divine G**, **Paone G**, **Borgi J**, **Morgan J**, **Allenspach L**, **Stagner L**, and **Nemeh H**. Abo compatibility in lung transplantation *J Heart Lung Transplant* 2016; 35(4):S368. PMID: Not assigned. Abstract

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Purpose: Lung transplantation (LT) remains the only definitive treatment for end-stage lung disease (ESLD) refractory to medical therapy. The necessity for an identical blood-type (ABO) match for optimal outcome is controversial. Recent studies have demonstrated equivalent outcomes between ABO identical and compatible LT, but do not differentiate any individual ABO combinations. The purpose of this study was to evaluate whether certain ABO compatible combinations affect outcomes in LT. Methods: Observational analysis of the United Network for Organ Sharing (UNOS) database for adult Double LT (DLT) recipients from May 2005 to September 2014 was performed. Results: Of 9615 DLT, 8941 (93%) were ABO “identical”, with 2347 (26%) of those having A-subtype differences. 674 (7%) compatible patients included 415 (62%) with donor O and recipient A, 93 (14%) with donor O and recipient B, and 84 (12%) donor B and recipient AB. The remaining 72 (11%) patients included multiple combinations and were placed into a single group due to the small number of patients in each subgroup (ABO Compat Oth). ABO compatibility status was not associated with either bronchiolitis obliterans syndrome (BOS, p= 0.389) or overall mortality (p= 0.333) in multivariate analysis. Recipients in the ABO Compat Oth group had a higher risk of acute rejection (HR 1.44, 95% CI 1.05-1.97, p= 0.023), but showed no increased risk of BOS (p= 1.0) or mortality (p= 0.826). The other groups showed no association with acute rejection, though the AB-B group trended toward significantly less risk for rejection (HR 0.69, 95% CI 0.47-1.03, p= 0.07).Conclusion: Our results agree with recent findings in ABO compatibility and LT, and do not show negative effect on the short or long term outcome when the different subgroups are analyzed. In light of these findings, the lung allocation system could potentially be changed to consider the identical and compatible blood group combinations as the same to give patients with higher LAS a better chance at a shorter wait time.

Public Health Sciences

Frendl D, Epstein M, Fouayzi H, **Krajenta R**, **Rybicki B**, and Sokoloff M. Impact of guidelines on prostate cancer screening in a population-based setting, 2000-2014: Preliminary results from the first AUA data grant *J Urol* 2016; 195(4):e543. PMID: Not assigned. Abstract

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INTRODUCTION AND OBJECTIVES: This study evaluates temporal trends in the use of prostate specific antigen (PSA) tests among men ages 40-80 years at two sites in the NCI-funded Cancer Research Network following the publication of prostate cancer (PCa) screening trial results in 2009 and changes to the US Preventive Services Task Force (USPSTF) guidelines in 2012. METHODS: 142,531 men aged 40-80, without a history of PCa, who sought care at Fallon Health (Meyers Primary Care Institute; Worcester, MA) and 127,238 men who sought care at the Henry Ford Health System (Detroit, MI), between 2000 and 2014, contributed to this analysis. We examined annual trends in PSA testing between 2000-08, 2009-12, and 2013-14, counting one PSA test per person per calendar year. Trends were assessed separately among those ages 55-69, ≥70, and high-risk men (African-American or family history of PCa). Men were censored upon PCa diagnosis, disenrollment, death, or end of follow-up (12/31/2014). RESULTS: Mean age at PSA test was 57 years, which increased over time at both sites. Overall, use of PSA testing rose gradually from 2000-2008 with between 27-32% of men ages 40-80 undergoing a test per year, followed by a decline in mean testing rates to 25% (2009-12) and 23% by 2013-14. On average, the percentage of eligible men receiving a PSA test per year decreased by 26% between 2000-08 and 2013-14. PSA testing declined similarly in both the 55-69 (33%) and ≥70 age groups (31%) over this time period (Figure 1). We also observed a 25% decline in PSA testing among high-risk men; these men were also less likely to be screened across all periods. CONCLUSIONS: This analysis of two population-based electronic health datasets provides evidence of decreasing use of PSA testing over time. Decreases in testing were similar across age groups and were not concentrated among those least likely to benefit from screening (men ages ≥70). High-risk men, who were mostly African-American, also experienced large declines in PSA testing. It is plausible that results of recent trials and changes to the USPSTF guidelines have broadly impacted recent PSA testing practices. (Figure presented)

Public Health Sciences

Fu AZ, Tsai HT, Haque R, Ulcickas Yood M, Van Den Eeden SK, **Cassidy-Bushrow AE**, Zhou Y, Keating NL, Smith MR, Aaronson DS, and Potosky AL. Use of androgen deprivation therapy as salvage treatment after primary therapy for clinically localized prostate cancer *World J Urol* 2016;PMID: 27084777. Full Text

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PURPOSE: The optimal use of androgen deprivation therapy as salvage treatment (sADT) for men after initial prostatectomy or radiotherapy for clinically localized prostate cancer is undefined. We describe patterns of sADT use and investigate clinical and sociodemographic characteristics of insured men who received sADT versus surveillance in managed care settings. METHODS: Using comprehensive electronic health records and cancer registry data from three integrated health plans, we identified all men with newly diagnosed clinically localized prostate cancer between 1995 and 2009 who received either prostatectomy (n = 16,445) or radiotherapy (n = 19,531) as their primary therapy. We defined sADT based on the timing of ADT following primary therapy and stage of cancer. We fit Cox proportional hazard models to identify sociodemographic characteristics and clinical factors associated with sADT. RESULTS: With a median follow-up of 6 years (range 2-15 years), 13 % of men who underwent primary prostatectomy or radiotherapy received sADT. After adjusting for selected covariates, sADT was more likely to be used in men who were older (e.g., HR 1.70, 95 % CI 1.48-1.96 or HR 1.33, 95 % CI 1.17-1.52 for age 70+ relative to age 35-59 for primary prostatectomy or radiotherapy, respectively), were African-American, had a short PSA doubling time, had a higher pre-treatment risk of progression, had more comorbidities, and received adjuvant ADT for initial disease. CONCLUSIONS: In men with localized prostate cancer in community practice initially treated with prostatectomy or radiotherapy, sADT after primary treatment was more frequent for men at greater risk of death from prostate cancer, consistent with practice guidelines.

Public Health Sciences

Greenlee H, Neugut AI, Falci L, Hillyer GC, Buono D, Roh JM, Ergas IJ, Kwan ML, Lee M, Tsai WY, Shi Z, **Lamerato L**, Mandelblatt JS, Kushi LH, and Hershman DL. Complementary and alternative medicine use and breast cancer chemotherapy initiation: The BQUAL study *Cancer Research* 2016; 76(4)PMID: Not assigned. Abstract

H. Greenlee

PURPOSE: Adjuvant therapy is associated with improved survival for women with breast cancer, but not all women who could benefit initiate treatment. Women's belief systems are related to treatment initiation. It has been hypothesized that complementary and alternative (CAM) use is associated with decreased initiation of standard oncology treatments because patients may be exploring alternative treatment approaches. However, there are limited data on the association between CAM use and cancer treatment initiation. We examined the association between CAM use and initiation of adjuvant breast cancer chemotherapy in a prospective cohort of early stage breast cancer patients. PATIENTS AND METHODS: Subjects participated in a multi-center prospective cohort study of women with early stage invasive breast cancer (n=1,156). National Comprehensive Cancer Network guidelines were used to define groups based on whether chemotherapy was indicated. Three subgroups were created: chemotherapy indicated for subjects <70 years, chemotherapy discretionary for subjects <70 years, and chemotherapy discretionary for subjects ≥70 years. CAM use was assessed based upon self-reported use of 5 CAM modalities, including vitamin/mineral supplements, herbal supplements, other over-the-counter natural products, mind-body based approaches, and body/energy-based treatments. Psychosocial factors potentially related to chemotherapy initiation were assessed.
Multivariable logistic regression models evaluated the associations between CAM use and chemotherapy initiation, adjusted for demographic, clinical and psychosocial factors. RESULTS: Current CAM use was reported by 87% of women and 38% reporting current use of ≥3 modalities. The most commonly used CAM modalities were mind body therapies (63%) and other natural products (41%). In bivariate analyses, among women <70 years where chemotherapy was indicated, women who reported current use of vitamins/minerals or current use of all 5 CAM modalities were less likely to initiate chemotherapy compared to non-users (P<.0001), but this was not observed among women for whom chemotherapy was discretionary. Psychosocial factors were also associated with high levels of current CAM use in this group, including higher expectations of adverse effects from chemotherapy, more concerns about the physical effects of chemotherapy, lower beliefs in the benefits of chemotherapy, and lower positive decision balance while making chemotherapy decisions (all P<.05). Among women age <70 years for whom chemotherapy was indicated, 89% initiated treatment, and current use of all 5 CAM modalities was inversely associated with initiation in multivariable analyses adjusted for demographic and clinical factors (OR=0.08, CI: 0.02-0.32). The association remained after separately adjusting for psychosocial factors (all P<.05), except for positive decision balance, which was no longer statistically significant. CONCLUSIONS: High use of CAM was associated with decreased chemotherapy initiation among women with breast cancer for whom chemotherapy was indicated. It is important for oncologists to discuss CAM use with their patients, especially since high CAM use is associated with negative expectations and beliefs about chemotherapy.

Public Health Sciences

Gusev A, Shi H, Kichaev G, Pomerantz M, Li F, Long HW, Ingles SA, Kittles RA, Strom SS, **Rybicki BA**, Nemesure B, Isaacs WB, Zheng W, Pettaway CA, Yeboah ED, Tettey Y, Biritwum RB, Adjei AA, Tay E, Truelove A, Niwa S, Chokkalingam AP, John EM, Murphy AB, Signorello LB, Carpten J, Leske MC, Wu SY, Hennis AJ, **Neslund-Dudas C**, Hsing AW, Chu L, Goodman PJ, Klein EA, Witte JS, Casey G, Kaggwa S, Cook MB, Stram DO, Blot WJ, Eeles RA, Easton D, Kote-Jarai Z, Al Olama AA, Benlloch S, Muir K, Giles GG, Southey MC, Fitzgerald LM, Gronberg H, Wiklund F, Aly M, Henderson BE, Schleutker J, Wahlfors T, Tammela TL, Nordestgaard BG, Key TJ, Travis RC, Neal DE, Donovan JL, Hamdy FC, Pharoah P, Pashayan N, Khaw KT, Stanford JL, Thibodeau SN, McDonnell SK, Schaid DJ, Maier C, Vogel W, Luedeke M, Herkommer K, Kibel AS, Cybulski C, Wokolorczyk D, Kluzniak W, Cannon-Albright L, Teerlink C, Brenner H, Dieffenbach AK, Arndt V, Park JY, Sellers TA, Lin HY, Slavov C, Kaneva R, Mitev V, Batra J, Spurdle A, Clements JA, Teixeira MR, Pandha H, Michael A, Paulo P, Maia S, Kierzek A, Conti DV, Albanes D, Berg C, Berndt SI, Campa D, Crawford ED, Diver WR, Gapstur SM, Gaziano JM, Giovannucci E, Hoover R, Hunter DJ, Johansson M, Kraft P, Le Marchand L, Lindstrom S, Navarro C, Overvad K, Riboli E, Siddiq A, Stevens VL, Trichopoulos D, Vineis P, Yeager M, Trynka G, Raychaudhuri S, Schumacher FR, Price AL, Freedman ML, Haiman CA, and Pasaniuc B. Atlas of prostate cancer heritability in European and African-American men pinpoints tissue-specific regulation *Nat Commun* 2016; 7:10979. PMID: 27052111. Full Text

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Although genome-wide association studies have identified over 100 risk loci that explain approximately 33% of familial risk for prostate cancer (PrCa), their functional effects on risk remain largely unknown. Here we use genotype data from 59,089 men of European and African American ancestries combined with cell-type-specific epigenetic data to build a genomic atlas of single-nucleotide polymorphism (SNP) heritability in PrCa. We find significant differences in heritability between variants in prostate-relevant epigenetic marks defined in normal versus tumour tissue as well as between tissue and cell lines. The majority of SNP heritability lies in regions marked by H3k27 acetylation in prostate adenoc7arcinoma cell line (LNCaP) or by DNaseI hypersensitive sites in cancer cell lines. We find a high degree of similarity between European and African American ancestries suggesting a similar genetic architecture from common variation underlying PrCa risk. Our findings showcase the power of integrating functional annotation with genetic data to understand the genetic basis of PrCa.

Public Health Sciences

Hershman DL, Kushi LH, Hillyer GC, Coromilas E, Buono D, **Lamerato L**, Bovbjerg DH, Mandelblatt JS, Tsai WY, Zhong X, Jacobson JS, Wright JD, and Neugut AI. Psychosocial factors related to non-persistence with adjuvant endocrine therapy among women with breast cancer: the Breast Cancer Quality of Care Study (BQUAL) *Breast Cancer Res Treat* 2016;PMID: 27086286. Full Text

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Non-adherence to adjuvant endocrine therapy (ET) for breast cancer (BC) is common. Our goal was to determine the associations between psychosocial factors and ET non-persistence. We recruited women with BC receiving care in an integrated healthcare system between 2006 and 2010. Using a subset of patients treated with ET, we investigated factors related to ET non-persistence (discontinuation) based on pharmacy records (>/=90 days gap). Serial interviews were conducted at baseline and every 6 months. The Functional Assessment of Cancer Therapy (FACT), Medical Outcomes Survey, Treatment Satisfaction Questionnaire (TSQM), Impact of Events Scale (IES), Interpersonal Processes of Care measure, and Decision-making beliefs and concerns were measured. Multivariate models assessed factors associated with non-persistence. Of the 523 women in our final cohort who initiated ET and had a subsequent evaluation, 94 (18 %) were non-persistent over a 2-year follow-up. The cohort was primarily white (74.4 %), stage 1 (60.6 %), and on an aromatase inhibitor (68.1 %). Women in the highest income category had a lower odds of being non-persistent (OR 0.43, 95 % CI 0.23-0.81). Quality of life and attitudes toward ET at baseline were associated with non-persistence. At follow-up, the FACT, TSQM, and IES were associated with non-persistence ($p < 0.001$). Most women continued ET. Women who reported a better attitude toward ET, better quality of life, and more treatment satisfaction, were less likely to be non-persistent and those who reported intrusive/avoidant thoughts

were more likely to be non-persistent. Interventions to enhance the psychosocial well-being of patients should be evaluated to increase adherence.

Public Health Sciences
Lu M, **Li J**, **Rupp LB**, Holmberg SD, Moorman AC, Spradling PR, Teshale EH, **Zhou Y**, Boscarino JA, Schmidt MA, **Lamerato LE**, Trinacty C, **Trudeau S**, and **Gordon SC**. Hepatitis C treatment failure is associated with increased risk of hepatocellular carcinoma *J Viral Hepat* 2016;PMID: 27028626. Full Text

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Center for Health Research, Kaiser Permanente-Hawai'i, Waipahu, HI, USA.
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Sustained virological response (SVR) to antiviral therapy for hepatitis C (HCV) reduces risk of hepatocellular carcinoma (HCC), but there is little information regarding how treatment failure (TF) compares to lack of treatment. We evaluated the impact of treatment status on risk of HCC using data from the Chronic Hepatitis Cohort Study (CHeCS-an observational study based in four large US health systems, with up to 7 years of follow-up on patients). Multivariable analyses were used to adjust for bias in treatment selection, as well as other covariates, followed by sensitivity analyses. Among 10 091 HCV patients, 3681 (36%) received treatment, 2099 (57%) experienced treatment failure (TF), and 1582 (43%) of these achieved sustained virological response (SVR). TF patients demonstrated almost twice the risk of HCC than untreated patients [adjusted hazard ratio (aHR) = 1.95, 95% confidence interval (CI) 1.50-2.53]; this risk persisted across all stages of fibrosis. Several sensitivity analyses validated these results. Although African Americans were at increased risk of treatment failure, they were at lower risk for HCC and all-cause mortality compared to White patients. SVR patients had lower risk of HCC than TF patients (aHR = 0.48, CI 0.31-0.73), whereas treatment - regardless of outcome - reduced all-cause mortality (aHR = 0.45, CI 0.34-0.60 for SVR patients; aHR = 0.78, CI 0.65-0.93 for TF patients).

Public Health Sciences
Maturu S, **Dayyoub T**, **Schultz L**, **Snyder J**, **Wasade V**, Elsayed M, **Gaddam S**, **Mahmood N**, **Constantinou J**, **Barkley G**, **Spanaki-Varelas M**, and **Zillgitt A**. Outcomes of genetic generalized epilepsy at a comprehensive epilepsy center *Neurology* 2016; 86(16)PMID: Not assigned. Abstract

S. Maturu, Henry Ford Hospital, Detroit, United States

Objective: This study aimed to provide a review of clinical outcomes for patients with genetic generalized epilepsy (GGE) from a diverse population in Metro-Detroit, Michigan. Background: The prognosis of GGE and its electroclinical syndromes remains poorly understood despite comprising approximately 20[percnt] of all epilepsy cases. The available data is comprised of methodological heterogeneity and often population homogeneity. Furthermore, the data is limited in its scope of prognostic factors regarding specific GGE electroclinical syndromes. Methods: A retrospective search of the Henry Ford Health System database was done from 1999 to 2012 on ICD-9 codes 345.10 or 345.11 for patients with a diagnosis of GGE. Inclusion criteria included a diagnosis of GGE or EEG with generalized epileptiform discharges 3 Hz (or both), age > 6 y, and treatment with at least 1 seizure medication. The associations of seizure freedom, initial and current seizure types, seizure freedom at 6 months and 1 year, and EEG findings were assessed using chi-square and two sample t-tests. Results: A total of 137 patients were analyzed. Nearly half were on 2 or more seizure medications at last follow-up, with an average of 3.8 seizure medication trials before arriving at their current seizure medication regimen. The primary outcome was seizure freedom at last follow-up. Of the 137 patients, 60 (44[percnt]) were seizure free at their last follow-up. Comparisons of the seizure types revealed a statistically significant difference in seizure freedom between patients with absence and GTCS and patients with absence, myoclonic, and GTCS. Conclusions: A substantial portion of patients were unable to achieve prolonged seizure freedom despite multiple seizure medication trials. Early seizure control within 1 year is predictive of long-term seizure freedom. In addition patients with a presumed diagnosis of JAE tended to have a more favorable outcome than those with JME.

Public Health Sciences
Muller CC, **McCord J**, **Michaels A**, **Nowak R**, Giannitsis E, Body R, Christ M, Lindahl B, DeFilippi C, Christenson R, Bendig G, **Jacobsen G**, and Mueller C. Symptoms predictive of acute myocardial infarction in the troponin era: Analysis from the TRAPID-AMI study *J Am Coll Cardiol* 2016; 67(13):518. PMID: Not assigned. Abstract

C.C. Muller, Henry Ford Hospital, Detroit, United States

Background: The TRAPID-AMI study was an Emergency Department (ED) multicenter trial evaluating a rapid "rule-out" acute myocardial infarction (AMI) protocol over 1 hour using changes in high-sensitivity cardiac troponin (cTn) T∗ (Roche Diagnostics). We studied which symptoms were predictive of AMI, as part of a sub-study of TRAPID-AMI. Methods: There were 1,282 patients evaluated in EDs for possible AMI from 12 centers in Europe, USA, and Australia from 2011 to 2013. The diagnosis of AMI was centrally adjudicated by 2 independent cardiologists in accordance with the universal definition of AMI, using all available clinical information and serial measurements of cTnI-Ultra (Siemens Healthcare). A total of 26 symptom variables were prospectively obtained. Multivariable logistic regression analysis was done; Odds Ratios (OR) with 95% confidence intervals (CI) were calculated. Results: There were 213/1282 (17%) AMIs. Independent predictors of AMI are shown (Figure). The presence of more predictors increased the risk of an AMI. In the entire group 131 (10%) had radiation to right arm/shoulder, 897 (70%) had chest pressure, 385 (30%) worsened with activity, and 448 (35%) had radiation to left arm/shoulder. Duration of symptoms was not predictive of AMI. There were no symptoms that were independently predictive of not having AMI. Conclusions: In a multicenter trial there were only 4 symptoms that were independently associated with the diagnosis of AMI. ∗510(K) submitted to FDA, but not yet approved in the U.S. (Figure presented).

Public Health Sciences
Takahashi K, **Obeid J**, **Burmeister CS**, **Bruno DA**, **Kazimi MM**, **Yoshida A**, **Abouljoud MS**, and **Schnickel GT**. Intrahepatic cholangiocarcinoma in the liver explant after liver transplantation: Histological differentiation and prognosis *Ann Transplant* 2016; 21:208-215. PMID: 27068242. Article Request Form

Department of Transplant and Hepatobiliary Surgery, Henry Ford Hospital, Detroit, MI, USA.
Department of Public Health Sciences, Henry Ford Hospital, Detroit, MI, USA.

BACKGROUND: The aim of this study was to evaluate the outcome of patients with intrahepatic cholangiocarcinoma (ICCA) incidentally found in the explanted liver after liver transplantation. MATERIAL AND METHODS: We retrospectively reviewed 1188 recipients undergoing liver transplantation from August 2003 to August 2014; 13 patients were found to have ICCA (1.1%). Recurrence-free survival (RFS) rate was compared between ICCA patients and the matched cohort of 39 patients with hepatocellular carcinoma (HCC). We also investigate the relevance of clinical and pathological parameters in recurrence of ICCA. RESULTS: ICCA patients showed significantly higher recurrence rate with lower 1-year and 3-year RFS rates than HCC patients (recurrence rate, 12.8% vs. 54.8%; 1-year and 3-year RFS rates, 94% and 84% vs. 67% and 42%). Of the 13 ICCA patients, 4 were diagnosed with a well-differentiated ICCA and 9 with a moderately-differentiated ICCA. There was no recurrence among those with a well-differentiated ICCA, whereas 78% recurred in the moderately-differentiated group. The median RFS time for the moderately-differentiated group was 13.0 months, yielding RFS rates of 56% at 1 year and 22% at 3 years. CONCLUSIONS: Liver transplantation in patients with a well-differentiated ICCA yielded excellent outcomes as compared to patients with a moderately-differentiated ICCA. This may allow consideration of transplantation in the setting of a well-differentiated ICCA, and obviate the need for adjuvant systemic treatment. Conversely, a moderately-differentiated ICCA carries a poor prognosis with a prohibitively high recurrence rate and poor survival. Liver transplantation should remain a contraindication in this group.

Public Health Sciences
Wegienka G, **Kaur H**, **Sangha R**, and **Cassidy-Bushrow AE**. Maternal-cord blood vitamin d correlations vary by maternal levels *J Pregnancy* 2016; 2016:7474192. PMID: 27066272. Full Text

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Vitamin D levels of pregnant women and their neonates tend to be related; however, it is unknown whether there are any subgroups in which they are not related. 25-Hydroxyvitamin D [25(OH)D] was measured in prenatal maternal and child cord blood samples of participants (n = 241 pairs) in a birth cohort. Spearman correlations were examined within subgroups defined by prenatal and delivery factors. Cord blood as a percentage of prenatal 25(OH)D level was calculated and characteristics compared between those who did and did not have >/=25% and >/=50% of the maternal level and those who did and did not have a detectable 25(OH)D level. The correlation among Black children

was lower than in White children. When the maternal 25(OH)D level was <15 ng/mL, the overall correlation was r = 0.16. Most children had a 25(OH)D cord blood level less than half of their mother's; 15.4% had a level that was <25% of their mother's. Winter birth and maternal level were associated with the level being less than 25%. Children with undetectable levels were more likely to be Black and less likely to be firstborn. These data suggest mothers may reduce their contribution to the fetus's 25(OH)D supply once their own level becomes low.

Public Health Sciences
Woodhouse SJ, **Peterson EL**, Schmitt T, and Aquino S. Intraocular pressure in southern rockhopper (eudyptes chrysocome) and macaroni penguins (eudyptes chrysolophus): Evaluation of influencing factors *J Zoo Wildl Med* 2016; 47(1):223-235. PMID: 27010282. Article Request Form

Ophthalmic examinations were performed on 160 macaroni penguins (Eudyptes chrysolophus) and 90 southern rockhopper penguins (Eudyptes chrysocome) at eight North American zoos and aquaria. Intraocular pressure (IOP) was measured using rebound tonometry while penguins were held in two different body positions. Correlations between IOP and factors including age, body position, eye pathology, and housing parameters were evaluated. Normal macaroni penguins had a mean IOP of 42.0 +/- 9.7 mm Hg. Normal rockhopper penguins had a mean IOP of 32.9 +/- 6.2 mm Hg. Neither species had significantly different IOP between sexes or between left and right eyes of the same penguin. In both species, there was a negative linear correlation between age and IOP. In the macaroni population, IOP was significantly higher when IOP measurement was performed before ophthalmic exam; this was not true in rockhoppers. In both species, IOP measured in a horizontal body position was significantly higher than IOP measured in a vertical body position. In both species, eyes with corneal lesions had significantly lower IOP than normal eyes. In the macaroni penguin, eyes with rubeosis iridis had significantly lower IOP than normal eyes. In macaroni penguins, eyes with cataracts had significantly lower mean IOP than normal eyes; this was not true for rockhoppers.

Public Health Sciences
Worsham MJ, **Chen KM**, **Chitale D**, **Stephen JK**, and **Divine G**. Differentially methylated miRNA methylomes of normal breast tissue from ER negative and ER positive breast cancer mimic their respective tumor phenotypes *Can Res* 2016; 76(4)PMID: Not assigned. Abstract

M.J. Worsham, Henry Ford Health System, Detroit, United States
Background: The unique structure and function of normal tissues is known to be regulated by epigenetic mechanisms. Understanding how normal cells in their respective tumor milieus might affect their susceptibility to become not only malignant but acquire breast cancer (BC) subtype-specific phenotypes, may determine tumor clinical behavior outcomes. The goal was to compare genome wide methylation profiles of non-coding miRNAs of breast cancer tissue and normal breast epithelium, respectively, from ER negative and ER positive tumors, and assess their miRNA methylomes in the context of tumor ER phenotypes as ER negative vs ER positive. Methods: Breast cancer tissue from 79 patients (40 ER-positive and 39 ER-negative) and normal tissue from 39 of these patients (19 ER-negative and 20-ER-positive) were assayed using the Illumina 450K bead array. A sub analysis focused on 2249 miRNA CpGs assigned to 615 unique miRNAs. M-values were computed as a logit function [(log (beta/ (1-beta))] of the methylation beta values. T-tests were used to compare the means of the M-values for the ER-positive and ER-negative groups. The t-test p-values were used to generate adaptive FDR (aFDR) levels and aFDRs of 0.05 or lower were considered to be statistically significant (Tier 1). Tier 1 CpGs were subsequently filtered to select only those with a mean beta ratio between ER-positive and ER-negative of under 0.5 or over 2.0 (Tier 2). The Tier 2 CpGs were further filtered to select only those with a mean beta difference of 0.2 or more (Tier 3). Results: In the tumor cohort, 1224/2249 (54%) CpGs were differentially methylated between ER negative and ER positive BC at Tier 1 (aFDR 0.05 or lower). Of the 1224, 963 (78.7%) were hypermethylated, and 1035 (84.6%) were associated with the promoter region. The 1224, 24 and 2 CpGs were associated with 379, 22 and 2 genes for Tiers 1, 2 and 3, respectively. When the same analysis was performed on normal tissue only (19 ER-negative and 20-ER-positive) 76 of the 2249 CpGs had significant aFDR values and none of those met the Tier 2 or Tier 3 criteria. Seventy-one of the 76 (93.4%) where hypermethylated, and 65 (85.5%) were associated with the promoter region. The 76 significant Tier 1 (aFDR) differentially methylated CpGs were associated with 48 genes of which 43 were common to tumor Tier 1 differentially methylated miRNA genes, 10 were common to tumor Tier 2 genes, and 5 were restricted to normal tissue only. Conclusions Normal epithelial tissues demonstrated similar differential methylation directionality as their respective tumor counterparts (although to a lesser extent), favoring promoter region localization. Accordingly, the recognition of normal breast tissue-specific epigenetic propensities that align with their tumor phenotypes, suggest the possibility of progression markers specific for estrogen receptor status as well as markers not associated with progression. This provides insights into our view of possible links between epigenetic programming, progression continuums, and how hormonal receptor subtypes may be determined.

Public Health Sciences

Worsham MJ, **Chen KM**, **Datta I**, **Stephen JK**, **Chitale D**, and **Divine G**. Epigenetically altered microRNA mediated pathway dysregulation in ER negative breast cancer *Can Res* 2016; 76(4)PMID: Not assigned. Abstract

M.J. Worsham, Henry Ford Health System, Detroit, United States

Background: Micro RNAs (miRNA) are endogenous, small non-coding RNAs that control gene expression by directing their target mRNAs for degradation and/or posttranscriptional repression. Compared to mRNA signatures, miRNAs have better and stronger biomarker properties with 20 times more power in biomarker studies as compared to mRNAs (when comparing 20,000 mRNAs to ~1,000 miRNAs). Emerging evidence now supports the idea that DNA methylation is crucially involved in the dysregulation of miRNAs in cancer, representing a novel class of potential biomarkers for diagnosis, prediction of treatment, or prognosis. ER-negative breast cancer (BC) is an aggressive histological subtype with limited treatment options and very poor prognosis. Our long term objective is to derive a diagnostic, prognostic, and predictive ER-negative specific miRNA panel for detection of early cancer, recurrence/metastasis, and as potential therapeutic targets for better management of ER-negative BC. Methods: The initial discovery step profiled 39 primary ER negative and 40 ER positive BC cases using the Illumina Infinium HumanMethylation450 BeadChip followed by a subanalysis focusing on 2249 miRNA CpGs assigned to 615 unique miRNAs. T-tests were used to compare the means of the M-values for the ER-positive and ER-negative groups. The t-test p-values were used to generate adaptive FDR (aFDR) levels and aFDRs of 0.05 or lower were considered to be statistically significant (Tier 1). Tier 1 CpGs were subsequently filtered to select only those with a mean beta ratio between ER positive and ER negative of under 0.5 or over 2.0 (Tier 2). The Tier 2 CpGs were further filtered to select only those with a mean beta difference of 0.2 or more (Tier 3). Because miRNAs perform their important functions via their targets, the targets of miRNAs were assessed for functional enrichment analysis in IPA for biologic involvement. Results: Over half of the miRNA CpGs (1224/2249, 54%) were differentially methylated between ER negative and ER positive BC with significant aFDR levels. The 1224 CpGs at Tier 1 were associated with 379 miRNAs; the 24 and 2 CpGs for Tiers 2 and 3 with 22 and 2 miRNAs, respectively. The 22 miRNA genes were assigned to 4621 targets using online databases that predict miRNA targets. The degree of confidence that a target gene is associated with a miRNA is characterized in these databases as either “experimentally observed”, or just as “high” (predicted). Of these 4621 targets, 87 were designated as experimentally observed and were examined in IPA. Top pathways and networks designated by miRNA targets included the cell cycle G1/S checkpoint regulation canonical pathway, and the cell-to-cell interaction/cancer networks among others. MiRNA targets in top pathways and networks were circled back to their respective miRNAs revealing cooperatively mediated pathway dysregulation of ER negative BC. Conclusion: Aberrantly methylated miRNAs showed perturbation of biologically significant pathways and networks, suggesting that miRNAs mediate pathway dysregulation in a coordinated manner, strengthening the case for utility of miRNAs as viable biomarkers in ER negative BC.

Public Health Sciences

Yadav P, **Eng M**, **Divine G**, **Wang DD**, **Arjomand-Fard H**, **Wyman J**, **Isley M**, **Borgi J**, **Paone G**, **Greenbaum A**, and **O'Neill W**. Outcomes of impella assisted percutaneous balloon aortic valvuloplasty in very high risk severe aortic stenosis patients *J Am Coll Cardiol* 2016; 67(13):404. PMID: Not assigned. Abstract

P. Yadav, Henry Ford Hospital, Detroit, United States

Background: Limited data available suggests poor outcomes with high risk Percutaneous Balloon Aortic Valvuloplasty (PBAV) in patients with severe aortic stenosis and coexistent severe left ventricular dysfunction, recent decompensated heart failure or severe coronary artery disease. Methods: Retrospective analysis of patients with severe aortic stenosis who underwent high risk PBAV with hemodynamic support with Impella (Abiomed). Time to death was assessed with Kaplan-Meier estimates and by hazard ratios estimated by univariate Cox regression models Results: 28 patients, mean age 79 ± 8.6 years, STS mortality risk 13 ± 12%, average NYHA class 3.7, left ventricular ejection fraction 29% ± 17%, mean creatinine 2.1 ± 1.9 mg/dL, mean GFR 52 ± 28. Successful PBAV performed with rapid pacing in 100% cases. Impella removed in 68% of the patients at the end of the case. Overall, survival was 75% at 30 days and 63% at 1 year. Earlier death associated with: higher STS (HR=1.07, p=0.002), higher mean creatinine (HR=1.33, p=0.020) and lower GFR (HR=0.97, p=0.015). When Impella placed sequentially after PBAV (n=12), 50% of the patients survived to 30 days (4 patients had intraprocedural cardiac arrest). If Impella placed first with simultaneous support during BAV (n=16) 94% patients alive at 30 days with no intraprocedural cardiac arrest. (HR for simultaneous support=0.36, p=0.115) Conclusions: Hemodynamic support with Impella in high risk PBAV patient showed survival higher than reported in the limited literature. (Figure Presented).

Pulmonary

Attaway A, Sroujieh L, Mersfelder TL, Butler C, and **Ouellette D**. "Ping-pong gaze" secondary to monoamine oxidase inhibitor overdose *J Pharmacol Pharmacother* 2016; 7(1):34-37. PMID: 27127395. Full Text

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An infrequent manifestation of monoamine oxidase inhibitor (MAOI) toxicity is "ping-pong gaze" (PPG). We describe the case of a 26-year-old female who was found unresponsive after taking 40 tablets of phenelzine. On presentation to the hospital, her eyes were moving in characteristic "ping pong" fashion. After 6 hours her gaze terminated. The following day her neurologic exam was benign and she had no long-term sequelae. While the etiology of PPG is unknown, it is most often seen with irreversible structural brain damage. However, a detailed literature review revealed that previous cases of MAOI toxicity where the patient survived have all had complete neurologic recovery.

Pulmonary

Azuh O, **Gammon H**, **Burmeister C**, **Frega D**, **Nerenz D**, **DiGiovine B**, and **Siddiqui A**. Benefits of early active mobility in the medical intensive care unit - a pilot study *Am J Med* 2016;PMID: 27107920. Full Text

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BACKGROUND: Pressure ulcer formation continues to be problematic in acute care settings, especially intensive care units (ICUs). Our institution developed a program for early mobility in the ICU using specially-trained nursing aides. The goal was to impact hospital acquired pressure ulcers incidence as well as factors associated with ICU deconditioning by using specially-trained personnel to perform the acute early mobility interventions. METHODS: A five-point mobility scale was developed and used to establish a patients' highest level of activity achievable during evaluation. A Mobility Team was created consisting of skin-care prevention/mobility nurses and a new category of worker called a patient mobility assistant. Each level has a corresponding plan of care (intervention) that was followed and adjusted according to the patient's progress and nursing evaluation. Data collection included the type of interventions at each encounter, mobility and skin assessments, new hospital-acquired pressure ulcer, the current mobility level, Braden score, rate of ventilator associated pneumonia, ICU length of stay and hospital readmission. Staff was also surveyed about their attitudes toward mobilization and perception of mobility barriers, pre-pilot and a post-pilot survey is planned. RESULTS: During the 1-year study interval, 3233 patients were enrolled from the medical intensive care unit (MICU). The 2011 pre-implementation MICU hospital-acquired pressure ulcer rate was 9.2%. After 1 year of employing the mobility team, there was a statistically significant drop in the medical intensive care unit hospital-acquired pressure ulcer rate to 6.1% ($p = 0.0405$). Hospital readmission of medical intensive care unit patients also significantly decreased from 17.1% to 11.5% ($p = .0010$). The mean medical intensive care unit length of stay decreased by 1 day. There were no safety issues directly or indirectly associated with these interventions. CONCLUSIONS: Use of this mobility program resulted in a 3% decrease in the most recalcitrant patients in the MICU. This corresponds to a decrease of 1.2 per 1000 patient days. It is definitely both statistically and clinically significant. We believe this lays the groundwork for further work in this area. We have shown that properly trained non-licensed professionals can safely and effective mobilize patients in the ICU setting. This can represent a cost effective way to introduce early mobility in the ICU setting.

Pulmonary

Demos D, **Divine G**, **Paone G**, **Borgi J**, **Morgan J**, **Allenspach L**, **Stagner L**, and **Nemeh H**. Abo compatibility in lung transplantation *J Heart Lung Transplant* 2016; 35(4):S368. PMID: Not assigned. Abstract

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Purpose: Lung transplantation (LT) remains the only definitive treatment for end-stage lung disease (ESLD) refractory to medical therapy. The necessity for an identical blood-type (ABO) match for optimal outcome is controversial. Recent studies have demonstrated equivalent outcomes between ABO identical and compatible LT, but do not differentiate any individual ABO combinations. The purpose of this study was to evaluate whether certain ABO compatible combinations affect outcomes in LT. Methods: Observational analysis of the United Network for Organ Sharing (UNOS) database for adult Double LT (DLT) recipients from May 2005 to September 2014 was performed. Results: Of 9615 DLT, 8941 (93%) were ABO “identical”, with 2347 (26%) of those having A-subtype differences. 674 (7%) compatible patients included 415 (62%) with donor O and recipient A, 93 (14%) with donor O and recipient B,

and 84 (12%) donor B and recipient AB. The remaining 72 (11%) patients included multiple combinations and were placed into a single group due to the small number of patients in each subgroup (ABO Compat Oth). ABO compatibility status was not associated with either bronchiolitis obliterans syndrome (BOS, p= 0.389) or overall mortality (p= 0.333) in multivariate analysis. Recipients in the ABO Compat Oth group had a higher risk of acute rejection (HR 1.44, 95% CI 1.05-1.97, p= 0.023), but showed no increased risk of BOS (p= 1.0) or mortality (p= 0.826). The other groups showed no association with acute rejection, though the AB-B group trended toward significantly less risk for rejection (HR 0.69, 95% CI 0.47-1.03, p= 0.07).Conclusion: Our results agree with recent findings in ABO compatibility and LT, and do not show negative effect on the short or long term outcome when the different subgroups are analyzed. In light of these findings, the lung allocation system could potentially be changed to consider the identical and compatible blood group combinations as the same to give patients with higher LAS a better chance at a shorter wait time.

Radiation Oncology

Nazem-Zadeh MR, **Bowyer SM**, **Moran JE**, **Davoodi-Bojd E**, **Zillgitt A**, Weiland BJ, **Bagher-Ebadian H**, **Mahmoudi F**, Elisevich K, and **Soltanian-Zadeh H**. MEG Coherence and DTI Connectivity in mTLE *Brain Topogr* 2016;PMID: 27060092. Full Text

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Magnetoencephalography (MEG) is a noninvasive imaging method for localization of focal epileptiform activity in patients with epilepsy. Diffusion tensor imaging (DTI) is a noninvasive imaging method for measuring the diffusion properties of the underlying white matter tracts through which epileptiform activity is propagated. This study investigates the relationship between the cerebral functional abnormalities quantified by MEG coherence and structural abnormalities quantified by DTI in mesial temporal lobe epilepsy (mTLE). Resting state MEG data was analyzed using MEG coherence source imaging (MEG-CSI) method to determine the coherence in 54 anatomical sites in 17 adult mTLE patients with surgical resection and Engel class I outcome, and 17 age- and gender- matched controls. DTI tractography identified the fiber tracts passing through these same anatomical sites of the same subjects. Then, DTI nodal degree and laterality index were calculated and compared with the corresponding MEG coherence and laterality index. MEG coherence laterality, after Bonferroni adjustment, showed significant differences for right versus left mTLE in insular cortex and both lateral orbitofrontal and superior temporal gyri ($p < 0.017$). Likewise, DTI nodal degree laterality, after Bonferroni adjustment, showed significant differences for right versus left mTLE in gyrus rectus, insular cortex, precuneus and superior temporal gyrus ($p < 0.017$). In insular cortex, MEG coherence laterality correlated with DTI nodal degree laterality ([Formula: see text] in the cases of mTLE. None of these anatomical sites showed statistically significant differences in coherence laterality between right and left sides of the controls. Coherence laterality was in agreement with the declared side of epileptogenicity in insular cortex (in 82 % of patients) and both lateral orbitofrontal (88 %) and superior temporal gyri (88 %). Nodal degree laterality was also in agreement with the declared side of epileptogenicity in gyrus rectus (in 88 % of patients), insular cortex (71 %), precuneus (82 %) and superior temporal gyrus (94 %). Combining all significant laterality indices improved the lateralization accuracy to 94 % and 100 % for the coherence and nodal degree laterality indices, respectively. The associated variations in diffusion properties of fiber tracts quantified by DTI and coherence measures quantified by MEG with respect to epileptogenicity possibly reflect the chronic microstructural cerebral changes associated with functional interictal activity. The proposed methodology for using MEG and DTI to investigate diffusion abnormalities related to focal epileptogenicity and propagation may provide a further means of noninvasive lateralization.

Radiation Oncology

Small W, Jr., James JL, Moore TD, Fintel DJ, Lutz ST, **Movsas B**, Suntharalingam M, Garces YI, Ivker R, Moulder J, Pugh S, and Berk LB. Utility of the ace inhibitor captopril in mitigating radiation-associated pulmonary toxicity in lung cancer: Results from nrg oncology rtog 0123 *Am J Clin Oncol* 2016;PMID: 27100959. Full Text

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OBJECTIVES: The primary objective of NRG Oncology Radiation Therapy Oncology Group 0123 was to test the ability of the angiotensin-converting enzyme inhibitor captopril to alter the incidence of pulmonary damage after radiation therapy for lung cancer; secondary objectives included analyzing pulmonary cytokine expression, quality of life, and the long-term effects of captopril. MATERIALS AND METHODS: Eligible patients included stage II-IIIB non-small cell lung cancer, stage I central non-small cell lung cancer, or limited-stage small cell. Patients who met eligibility for randomization at the end of radiotherapy received either captopril or standard care for 1 year. The captopril was to be escalated to 50 mg three times a day. Primary endpoint was incidence of grade 2+ radiation-induced pulmonary toxicity in the first year. RESULTS: Eighty-one patients were accrued between June 2003 and August 2007. Given the low accrual rate, the study was closed early. No significant safety issues were encountered. Eight patients were ineligible for registration or withdrew consent before randomization and 40 patients were not randomized postradiation. Major reasons for nonrandomization included patients' refusal and physician preference. Of the 33 randomized patients, 20 were analyzable (13 observation, 7 captopril). The incidence of grade 2+ pulmonary toxicity attributable to radiation therapy was 23% (3/13) in the observation arm and 14% (1/7) in the captopril arm. CONCLUSIONS: Despite significant resources and multiple amendments, NRG Oncology Radiation Therapy Oncology Group 0123 was unable to test the hypothesis that captopril mitigates radiation-induced pulmonary toxicity. It did show the safety of such an approach and the use of newer angiotensin-converting enzyme inhibitors started during radiotherapy may solve the accrual problems.

Radiology

Patel K, Le M, **Achakzai B**, Paidpally V, Jaber M, Danier S, Shah K, Harvill M, Critchfield J, and Saad W. Normal postablative changes vs. residual/ recurrent tumor: How to tell them apart on imaging? *J Vasc Interv Radiol* 2016; 27(3):S276. PMID: Not assigned. Abstract

K. Patel, Wayne State University, Detroit, United States

Learning Objectives: In this exhibit, we review sequential changes that occur on computed tomography (CT) and magnetic resonance (MR) imaging after percutaneous thermal ablation of renal tumors. We identify postablation findings of residual or recurrent tumor. We discuss appropriate time interval for follow up CT or MR imaging. Background: Kidney cancer is the twelfth most common cancer in the world with 338,000 new cases diagnosed in 2012. Percutaneous thermal ablation has played an important role in management of small renal tumors and has emerged as an effective, minimally invasive nephron-sparing treatment option. Postablation CT and MR imaging play an important part in evaluation of the ablation zone, surveillance of residual or recurrent tumor, and identification of procedure related complications. The appearance of the ablation zone can vary depending on tumor size, location and composition and interventional radiologists who perform this procedure should be able to recognize typical CT and MR imaging findings to prevent confusion with other pathologic processes. Clinical Findings/Procedure Details: We describe CT and MR imaging appearances and sequential changes of renal tumors after successful thermal ablative treatment. We depict CT and MR imaging features of normal postablative vs. residual/recurrent tumor. We highlight appropriate time interval for follow up CT or MR imaging. Conclusions: Percutaneous thermal ablation has emerged as an effective treatment method for eradication of small renal tumors. As more patients undergo renal thermal ablation procedures, accurate assessment of ablated tumors at postprocedural imaging in essential for evaluating the adequacy of treatment and guiding further management. Thorough knowledge of the postablative imaging findings is necessary to provide optimal patient care.

Radiology

Patel K, Le M, Yu H, **Achakzai B**, Paidpally V, Jaber M, Kakos R, Danier S, Shah K, Harvill M, Critchfield J, and Saad W. Do no harm: Advanced protective techniques during image-guided percutaneous thermal ablation of renal tumors *J Vasc Interv Radiol* 2016; 27(3):S243. PMID: Not assigned. Abstract
K. Patel, Wayne State University, Detroit, United States

Learning Objectives: In this exhibit, we discuss the physical properties of different ablative technologies and their associated thermal effects. Specifically, we describe the principles governing radiofrequency/microwave/cryo ablation. We illustrate various protective measures utilized in preventing damage to surrounding tissues when performing an ablation for kidney tumors. Background: Percutaneous thermal ablation is an effective, minimally

invasive nephron-sparing treatment option for small solid renal tumors. Although the procedure is safe, thermally induced damage to structures adjacent to a targeted lesion (nontarget damage) remains a concern. Depending on tumor location, the major complications include injury to nearby organs (stomach, pancreas, bowel), strictures of both the ureter and collecting system, neuromuscular injury (psoas lumbar plexus), and damage to the diaphragm/lung. Interventional radiologists who perform percutaneous kidney ablation should be familiar with these protective techniques in order to achieve a successful outcome with the lowest complication rate. Clinical Findings/Procedure Details: We will describe in depth and illustrate different techniques that can be used to keep surrounding susceptible structures at bay during a kidney ablation. We will list the necessary steps and technical considerations for the following: hydrodissection, gas-insufflation, balloon interposition, electrode torquing, pyeloperfusion, iatrogenic pneumothorax. In addition, we will highlight the advantages and potential drawbacks pertaining to each technique. Conclusions: Percutaneous thermal ablation has emerged as an effective treatment method for eradication of small renal tumors. However, the most common complication of the procedure is iatrogenic thermal damage of surrounding sensitive structures. Thorough knowledge of the available protective techniques is necessary for a safe and successful procedural outcome.

Radiology

Riaz R, **Achakzai B**, and **Getzen T**. Effectiveness of yttrium-90 radioembolization delivery: Comparison of microcatheter flow dynamics and residual activity *J Vasc Interv Radiol* 2016; 27(3):S67. PMID: Not assigned. Abstract

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

Purpose: To compare the flow dynamics of Yttrium-90 within two different brands of microcatheters during radio-embolization of hepatocellular carcinoma. Materials: Between April 2007 and September 2015, a total of 173 radioembolizations of primary hepatocellular carcinoma were performed using Yttrium-90 (Y-90). Initially, these were performed utilizing a 130 cm high-flow microcatheter (Progreat, Terumo). Due to logistics during the therapy administration by the Nuclear Medicine team, a longer microcatheter was desired but initially unavailable. A different high-flow microcatheter (Renegade, Boston Scientific) was acquired in the desired length and was primarily utilized. As part of the routine Nuclear Medicine safety checklist, it was observed that a higher percentage of residual activity was observed using the Progreat microcatheter following Y-90 administration. It was theorized that this could be in part to a small step-off present in the hub of the Progreat microcatheter. The difference in the mean percentage of residual activity was retrospectively analyzed using the Student t-test (unpaired t-test). Results: During the timeframe of this single institution's experience with Y-90 radioembolization, 83 and 90 radioembolizations were performed using the Renegade and Progreat microcatheter respectively. Patients who underwent mapping using MAA without Y-90 Therasphere administration were excluded. The mean residual activity of Y-90 in the microcatheter connection was 0.82% in the Renegade group, and 1.2% in the Progreat group, with a statistically significant difference ($p = 0.044$). Conclusions: There is a statistically significant increased percentage of residual activity found in the Progreat microcatheter when compared to the Renegade microcatheter. While this percentage of residual activity did not alter treatment response or initial therapy dose, this difference needs to be evaluated further with additional studies of microcatheter flow dynamics.

Radiology

Rinker E, **Rodriguez E**, **Vanderhoek M**, **Bevins N**, and **Schwartz S**. Radiation exposure in radial versus femoral artery access in interventional radiology *J Vasc Interv Radiol* 2016; 27(3):S143-S144. PMID: Not assigned. Abstract

E. Rinker, Henry Ford Hospital, Detroit, United States

Purpose: Radial artery access has slowly been gaining popularity due to reduced complication rates and improved patient comfort compared to femoral artery access. However, studies have demonstrated a substantial increase (up to 100% [1]) in operator radiation exposure for radial access. We implemented a unique radial approach using a mobile lead wall placed between the operator and patient. Operator exposure with this shielded radial approach was compared to a standard femoral approach. Materials: Dose data for the principal operator and scrub technologist were measured using the RaySafe i2 staff dosimetry system for 25 interventional radiology cases: 11 radial and 14 femoral artery access. Standard radiation protection including lead aprons, table drapes, and a “floating” acrylic shield were used for all cases. For radial cases, a 1.5 mm lead equivalent mobile wall further protected the operator. For each case, staff doses (in μSv) were normalized by the total fluoroscopy reference point dose (in mGy) in order to account for differences in case complexity. Normalized staff doses were averaged for radial and femoral cases. A t-test was used for statistical significance. Radial and femoral approaches were also simulated by irradiating an anthropomorphic phantom. Dosimeters were placed at typical staff positions both with and without shielding. For each approach, shielding efficacy was determined via the ratio of shielded to unshielded doses. Results: Operator exposure was reduced by 78% for radial access with a mobile lead wall compared to femoral access (0.009 μSv/mGy vs 0.041 μSv/mGy, $p=0.03$). However, there was no significant difference in radiation exposure for the scrub

technologist (0.032 μSv/mGy vs 0.023 μSv/mGy, p=0.42). Phantom data revealed an average dose reduction of 99% for shielded radial cases with the addition of a mobile lead wall, versus 53% for femoral cases utilizing standard shielding. Conclusions: Radial artery access allows the placement of a mobile lead wall between the operator and patient, which can substantially reduce operator exposure compared to femoral access. Interventional radiologists should consider the benefits of radial access to both patients and staff when appropriate.

Research Administration
Afzali M, Ghaffari A, Fatemizadeh E, and **Soltanian-Zadeh H**. Medical image registration using sparse coding of image patches *Comput Biol Med* 2016; 73:56-70. PMID: 27085311. Full Text

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Image registration is a basic task in medical image processing applications like group analysis and atlas construction. Similarity measure is a critical ingredient of image registration. Intensity distortion of medical images is not considered in most previous similarity measures. Therefore, in the presence of bias field distortions, they do not generate an acceptable registration. In this paper, we propose a sparse based similarity measure for mono-modal images that considers non-stationary intensity and spatially-varying distortions. The main idea behind this measure is that the aligned image is constructed by an analysis dictionary trained using the image patches. For this purpose, we use "Analysis K-SVD" to train the dictionary and find the sparse coefficients. We utilize image patches to construct the analysis dictionary and then we employ the proposed sparse similarity measure to find a non-rigid transformation using free form deformation (FFD). Experimental results show that the proposed approach is able to robustly register 2D and 3D images in both simulated and real cases. The proposed method outperforms other state-of-the-art similarity measures and decreases the transformation error compared to the previous methods. Even in the presence of bias field distortion, the proposed method aligns images without any preprocessing.

Research Administration
Iraji A, Calhoun VD, Wiseman N, **Davoodi-Bojd E**, Avanaki MR, Haacke EM, and Kou Z. The connectivity domain: Analyzing resting state fMRI data using feature-based data-driven and model-based methods *Neuroimage* 2016;PMID: 27079528. Full Text

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Spontaneous fluctuations of resting state functional MRI (rsfMRI) have been widely used to understand the macro-connectome of the human brain. However, these fluctuations are not synchronized among subjects, which leads to limitations and makes utilization of first-level model-based methods challenging. Considering this limitation of rsfMRI data in the time domain, we propose to transfer the spatiotemporal information of the rsfMRI data to another domain, the connectivity domain, in which each value represents the same effect across subjects. Using a set of seed networks and a connectivity index to calculate the functional connectivity for each seed network, we transform data into the connectivity domain by generating connectivity weights for each subject. Comparison of the two domains using a data-driven method suggests some advantages in analyzing data using data-driven methods in the

connectivity domain over the time domain. We also demonstrate the feasibility of applying model-based methods in the connectivity domain, which offers a new pathway for the use of first-level model-based methods on rsfMRI data. The connectivity domain, furthermore, demonstrates a unique opportunity to perform first-level feature-based data-driven and model-based analyses. The connectivity domain can be constructed from any technique that identifies sets of features that are similar across subjects and can greatly help researchers in the study of macro-connectome brain function by enabling us to perform a wide range of model-based and data-driven approaches on rsfMRI data, decreasing susceptibility of analysis techniques to parameters that are not related to brain connectivity information, and evaluating both static and dynamic functional connectivity of the brain from a new perspective.

Research Administration

Nazem-Zadeh MR, **Bowyer SM**, **Moran JE**, **Davoodi-Bojd E**, **Zillgitt A**, Weiland BJ, **Bagher-Ebadian H**, **Mahmoudi F**, Elisevich K, and **Soltanian-Zadeh H**. MEG Coherence and DTI Connectivity in mTLE *Brain Topogr* 2016;PMID: 27060092. Full Text

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Magnetoencephalography (MEG) is a noninvasive imaging method for localization of focal epileptiform activity in patients with epilepsy. Diffusion tensor imaging (DTI) is a noninvasive imaging method for measuring the diffusion properties of the underlying white matter tracts through which epileptiform activity is propagated. This study investigates the relationship between the cerebral functional abnormalities quantified by MEG coherence and structural abnormalities quantified by DTI in mesial temporal lobe epilepsy (mTLE). Resting state MEG data was analyzed using MEG coherence source imaging (MEG-CSI) method to determine the coherence in 54 anatomical sites in 17 adult mTLE patients with surgical resection and Engel class I outcome, and 17 age- and gender- matched controls. DTI tractography identified the fiber tracts passing through these same anatomical sites of the same subjects. Then, DTI nodal degree and laterality index were calculated and compared with the corresponding MEG coherence and laterality index. MEG coherence laterality, after Bonferroni adjustment, showed significant differences for right versus left mTLE in insular cortex and both lateral orbitofrontal and superior temporal gyri ($p < 0.017$). Likewise, DTI nodal degree laterality, after Bonferroni adjustment, showed significant differences for right versus left mTLE in gyrus rectus, insular cortex, precuneus and superior temporal gyrus ($p < 0.017$). In insular cortex, MEG coherence laterality correlated with DTI nodal degree laterality ([Formula: see text] in the cases of mTLE. None of these anatomical sites showed statistically significant differences in coherence laterality between right and left sides of the controls. Coherence laterality was in agreement with the declared side of epileptogenicity in insular cortex (in 82 % of patients) and both lateral orbitofrontal (88 %) and superior temporal gyri (88 %). Nodal degree laterality was also in agreement with the declared side of epileptogenicity in gyrus rectus (in 88 % of patients), insular cortex (71 %), precuneus (82 %) and superior temporal gyrus (94 %). Combining all significant laterality indices improved the lateralization accuracy to 94 % and 100 % for the coherence and nodal degree laterality indices, respectively. The associated variations in diffusion properties of fiber tracts quantified by DTI and coherence measures quantified by MEG with respect to epileptogenicity possibly reflect the chronic microstructural cerebral changes associated with functional interictal activity. The proposed methodology for using MEG and DTI to investigate diffusion abnormalities related to focal epileptogenicity and propagation may provide a further means of noninvasive lateralization.

Sleep Medicine

Pillai V, **Cheng P**, Kalmbach DA, **Roehrs T**, **Roth T**, and **Drake CL**. Prevalence and predictors of prescription sleep aid use among individuals with dsm-5 insomnia: The role of hyperarousal *Sleep* 2016; 39(4):825-832. PMID: 26943472.
Full Text

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STUDY OBJECTIVES: Despite mounting evidence for the overuse of prescription sleep aids (PSA), reliable data on PSA use among insomniacs are unavailable. Current studies focus on trends in PSA use at the general population level, and thus do not distinguish between transient sleep disturbance and insomnia disorder. Therefore, we prospectively examined the prevalence and predictors of baseline and chronic PSA use in a well-defined sample of individuals with insomnia. METHODS: We analyzed longitudinal data from an urban, community-based cohort of 649 adults (48.1 +/- 11.6 y; 69.3% female) with Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)-based insomnia disorder. Participants completed standardized measures of sleep disturbance, daytime alertness, depression, and anxiety at baseline and follow-up 1 y later. They also reported whether and with what frequency they used PSA at both time points. RESULTS: Approximately 19% of the sample used PSA at baseline, the majority (69.4%) of whom continued use 1 y later. Anxiety and daytime alertness were the only independent predictors of both acute and chronic PSA use. An increase of 1 standard deviation (SD) in alertness was associated with a 33% increase in the odds of chronic PSA use (chi(2) = 4.98; odds ratio [OR] = 1.33; 95% confidence interval [CI]: 1.04-1.72; P < 0.05), and a 1-SD increase in anxiety was associated with a 41% increase (chi(2) = 6.95; OR = 1.41; 95% CI: 1.09-1.82; P < 0.05). Chronic PSA users did not report any significant improvements in sleep from baseline to follow-up relative to nonusers. CONCLUSIONS: Hyperarousal, as indexed by daytime alertness and anxiety, is a strong determinant of PSA use among individuals with insomnia. These findings are consistent with emerging data showing that insomnia is not just a nocturnal sleep disorder, but one characterized by 24-h arousal. Though current research targets sleep disturbance, this study highlights the role of the arousal system in pharmacological treatment seeking.

Sleep Medicine

Roehrs TA, and **Roth T**. Gender differences in the efficacy and safety of chronic nightly zolpidem *J Clin Sleep Med* 2016; 12(3):319-325. PMID: 26446253. Full Text

Sleep Disorders and Research Center, Henry Ford Health System, Detroit, MI, and Department of Psychiatry and Behavioral Neuroscience, Wayne State University, Detroit, MI.

STUDY OBJECTIVES: Studies have shown pharmacokinetic differences for hypnotics in women compared to men, but few studies have assessed either short-or long-term differences in efficacy and safety. METHODS: To evaluate gender differences in the efficacy and safety of chronic nightly zolpidem (10 mg), we did a post hoc assessment of a large clinical trial. In the trial, participants with primary insomnia (n = 89), ages 23-70, meeting DSM-IV-TR criteria for primary insomnia were randomized, double blind, to nightly zolpidem, 10 mg (n = 47) or placebo (n = 42) 30 minutes before bedtime nightly for 12 months. Polysomnographic sleep on 2 nights in months 1 and 8 and likelihood of next-day sleepiness, rebound insomnia, and dose escalation were evaluated in months 1, 4, and 12. RESULTS: Relative to placebo, zolpidem significantly increased sleep efficiency and reduced sleep latency and wake after sleep onset assessed at months 1 and 8, with no differences in efficacy between women and men and no diminution of efficacy over months. On a next-day multiple sleep latency test (MSLT), no residual sedation was observed for either women or men. No rebound insomnia or dose escalation was seen with no gender differences in either. CONCLUSIONS: In adults with primary insomnia, nightly zolpidem administration showed no gender differences in acute or chronic efficacy or in next-day sleepiness. Zolpidem remained efficacious and safe across 12 months.

Surgery

Azuh O, **Gammon H**, **Burmeister C**, **Frega D**, **Nerenz D**, **DiGiovine B**, and **Siddiqui A**. Benefits of early active mobility in the medical intensive care unit - a pilot study *Am J Med* 2016;PMID: 27107920. Full Text

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BACKGROUND: Pressure ulcer formation continues to be problematic in acute care settings, especially intensive care units (ICUs). Our institution developed a program for early mobility in the ICU using specially-trained nursing aides. The goal was to impact hospital acquired pressure ulcers incidence as well as factors associated with ICU deconditioning by using specially-trained personnel to perform the acute early mobility interventions. METHODS: A five-point mobility scale was developed and used to establish a patients' highest level of activity achievable during evaluation. A Mobility Team was created consisting of skin-care prevention/mobility nurses and a new category of worker called a patient mobility assistant. Each level has a corresponding plan of care (intervention) that was followed and adjusted according to the patient's progress and nursing evaluation. Data collection included the type of interventions at each encounter, mobility and skin assessments, new hospital-acquired pressure ulcer, the current mobility level, Braden score, rate of ventilator associated pneumonia, ICU length of stay and hospital readmission. Staff was also surveyed about their attitudes toward mobilization and perception of mobility barriers, pre-pilot and a post-pilot survey is planned. RESULTS: During the 1-year study interval, 3233 patients were enrolled from the medical intensive care unit (MICU). The 2011 pre-implementation MICU hospital-acquired pressure ulcer rate was

9.2%. After 1 year of employing the mobility team, there was a statistically significant drop in the medical intensive care unit hospital-acquired pressure ulcer rate to 6.1% (p = 0.0405). Hospital readmission of medical intensive care unit patients also significantly decreased from 17.1% to 11.5% (p = .0010). The mean medical intensive care unit length of stay decreased by 1 day. There were no safety issues directly or indirectly associated with these interventions. CONCLUSIONS: Use of this mobility program resulted in a 3% decrease in the most recalcitrant patients in the MICU. This corresponds to a decrease of 1.2 per 1000 patient days. It is definitely both statistically and clinically significant. We believe this lays the groundwork for further work in this area. We have shown that properly trained non-licensed professionals can safely and effective mobilize patients in the ICU setting. This can represent a cost effective way to introduce early mobility in the ICU setting.

Surgery

Bryce K, **Lanfear DE**, **Williams CT**, Lindenfeld J, Allen LA, and McIlvennan C. Risk of death or rehospitalization after LVAD and baseline cognitive status *J Heart Lung Transplant* 2016; 35(4):S126-S127. PMID: Not assigned. Abstract

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

Purpose: Optimal patient selection remains challenging for left ventricular assist devices (LVAD). Cognitive impairment is associated with worse outcomes in other patient populations, but there is little data in the setting of LVAD. Methods: A retrospective review at two centers was performed from 2011-2015. 147 patients received a continuous flow LVAD and were given the Montreal Cognitive Assessment (MoCA) pre-LVAD. The primary endpoint was time to death or rehospitalization. We also examined length of stay (LOS). We dichotomized MoCA at the median and tested for association using regression models adjusted for potential confounders (age, race, gender, indication, etiology, INTERMACS category). Results: Median cohort age was 57 (± 13), 19% were female, 31% were African American, and 66% destination therapy (DT). Mean MoCA score was 23.4(±3.7). MoCA differed only by indication (22.8 vs. 24.4, for DT vs. BTT, p= 0.015). In univariate analysis, low MoCA was associated with higher rates of death or readmission (p= 0.04, Figure). This was driven mostly by readmission rates (p= 0.048) with no significant difference in survival (p= 0.23). In adjusted models there was 50% increased risk of death or re hospitalization in the low MoCA group (HR 1.5, p= 0.035). There was a strong trend toward longer LOS in this group (4 days, p= 0.07). Conclusion: Baseline cognitive impairment is associated with worse outcomes after LVAD. Further study is needed to validate this association and evaluate possible mechanisms. (Figure presented).

Surgery

Bryce K, **Tita C**, **Williams C**, **Morgan J**, **Nemeh H**, **Selektor Y**, **Borgi J**, **Velez M**, and **Lanfear D**. Cognitive functioning is associated with clinical outcomes after LVAD implantation *J Am Coll Cardiol* 2016; 67(13):1273. PMID: Not assigned. Abstract

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

Background: Left ventricular assist devices (LVAD) are accepted therapy for end stage heart failure, but optimal patient selection remains challenging. Cognitive impairment is associated with worse outcomes in other settings, but there is little data on LVAD outcomes. Methods: We performed a retrospective review of 100 consecutive patients who received continuous flow LVADs over a three year period ('11 to '14) and who completed the Montreal Cognitive Assessment (MoCA) at evaluation. Those not surviving to discharge were excluded. The primary endpoints were time to readmission and survival time. We dichotomized MoCA at the median and tested for association with event rates using Cox regression models adjusted for age, race, gender, indication, and INTERMACS category. Results: The average age was 55.6 (± 12.29), 22 patients were female, 42 were non-white race and 69 were destination therapy. Median MoCA was 24 (IQR 22 - 26). MoCA did not differ by race, gender, or INTERMACS, but did differ by indication (22.8 vs. 24.2 for DT vs. BTT, p=0.049). Low MoCA was associated with re-hospitalization in univariate analysis (p = 0.013, Figure). In adjusted models there was double the risk of hospitalization with low MoCA (HR 2.1 p=0.0054) and a trend towards worse survival (HR 2.8, p = 0.059). Conclusions: Lower cognitive function is associated with higher hospital readmission rates post-LVAD and trends towards worse survival. Further study is needed to validate this association and evaluate possible mechanisms. (Figure presented).

Surgery

Carlyle L, **Wang DD**, **Taylor A**, **Swanson B**, **Wyman J**, **Pantelic M**, **Song T**, **Eng M**, **Paone G**, **Greenbaum A**, and **O'Neill W**. No two systoles the same: Personalizing transcatheter heart valve selection for transcatheter aortic valve replacement *J Am Coll Cardiol* 2016; 67(13):327. PMID: Not assigned. Abstract

L. Carlyle, Henry Ford Health System, Detroit, United States

Background: Traditional computed tomographic (CT) definition of systole is at 35% of the cardiac R-R interval. Hence, default sizing of the aortic annulus for transcatheter aortic valve replacement (TAVR) is based upon an automatically
generated reconstruction at this fixed point of the R-R interval. However, given inherent variance in physiology related to each patient's cardiac anatomy and its transduction by the ECG-gating process, this assumption may be incorrect. No study has analyzed whether each patient's maximal systolic annular area truly occurs at exactly 35% interval of the cardiac cycle. Methods: 42 consecutive patients underwent TAVR implantation from 7/2015-10/2015 with the Edwards Sapien 3 valve. Pre-procedural CT scan was acquired and aortic annulus area was measured across the entire cardiac cycle (phases 5 to 95% at 10% intervals). Maximal area obtained from pre-procedural CT measurements dictated recommendations for TAVR sizing. Results: All patients underwent successful TAVR; all CT scans were suitable for analysis. By Chi-squared analysis, recommended valve size differed in 18 of 42 patients ($p<0.0001$) when sizing by smallest measured systolic annular area to that by largest systolic annular area. If sizing strictly by 35% cardiac phase, 5 patients (11.9%, $p<0.0001$) would have received an undersized valve. If purely sized by diastole, 20 patients (47.6%, $p<0.0001$) would have received an undersized valve as compared to maximal systole. In 9% of patients, maximal systolic annular area occurred at the 5% cardiac phase, 16% at 15% phase, 33% at 25% phase, 31% at 35% phase, and 11% at 45% phase. Thus, 69% of patients had maximal annular area on a phase different from 35%. Post procedure, no aortic dissections or major adverse cardiac events occurred. When present, perivalvular leak post TAVR was no more than mild in 97.6% patients. Conclusions: The aortic annulus dynamically changes throughout the cardiac cycle on an individual basis. As such, no automated definition of maximum cardiac systole can be applied to all patients. A more personalized physiological approach to measurement of the aortic annulus may prevent avoidable TAVR valve undersizing and perivalvular leaks.

Surgery

Demos D, **Divine G**, **Paone G**, **Borgi J**, **Morgan J**, **Allenspach L**, **Stagner L**, and **Nemeh H**. Abo compatibility in lung transplantation *J Heart Lung Transplant* 2016; 35(4):S368. PMID: Not assigned. Abstract

D. Demos, Cardiothoracic Surgery, Henry Ford Hospital, Detroit, United States

Purpose: Lung transplantation (LT) remains the only definitive treatment for end-stage lung disease (ESLD) refractory to medical therapy. The necessity for an identical blood-type (ABO) match for optimal outcome is controversial. Recent studies have demonstrated equivalent outcomes between ABO identical and compatible LT, but do not differentiate any individual ABO combinations. The purpose of this study was to evaluate whether certain ABO compatible combinations affect outcomes in LT. Methods: Observational analysis of the United Network for Organ Sharing (UNOS) database for adult Double LT (DLT) recipients from May 2005 to September 2014 was performed. Results: Of 9615 DLT, 8941 (93%) were ABO “identical”, with 2347 (26%) of those having A-subtype differences. 674 (7%) compatible patients included 415 (62%) with donor O and recipient A, 93 (14%) with donor O and recipient B, and 84 (12%) donor B and recipient AB. The remaining 72 (11%) patients included multiple combinations and were placed into a single group due to the small number of patients in each subgroup (ABO Compat Oth). ABO compatibility status was not associated with either bronchiolitis obliterans syndrome (BOS, $p= 0.389$) or overall mortality ($p= 0.333$) in multivariate analysis. Recipients in the ABO Compat Oth group had a higher risk of acute rejection (HR 1.44, 95% CI 1.05-1.97, $p= 0.023$), but showed no increased risk of BOS ($p= 1.0$) or mortality ($p= 0.826$). The other groups showed no association with acute rejection, though the AB-B group trended toward significantly less risk for rejection (HR 0.69, 95% CI 0.47-1.03, $p= 0.07$).Conclusion: Our results agree with recent findings in ABO compatibility and LT, and do not show negative effect on the short or long term outcome when the different subgroups are analyzed. In light of these findings, the lung allocation system could potentially be changed to consider the identical and compatible blood group combinations as the same to give patients with higher LAS a better chance at a shorter wait time.

Surgery

Eng MH, **Greenbaum A**, **Wang DD**, **Wyman J**, **Nemeh H**, **Paone G**, and **O'Neill W**. Transseptal delivery for mitral valve in valve procedures using an apical rail: Technique description and initial results *J Am Coll Cardiol* 2016; 67(13):335. PMID: Not assigned. Abstract

M.H. Eng, Henry Ford Hospital, Detroit, United States
Background: Prior surgical mitral rings or prosthetic valves may degenerate. Re-operation may be prohibitive, thus requiring an alternative such as transcatheter mitral valve replacement (TMVR). Using a transseptal route with an apical access as a rail; we performed TMVR in 11 patients. Methods: From 12/2013 - 8/2015, 11 consecutive patients with degenerated mitral valve repair or valve replacement received TMVR. Patients were assessed for Valve

Academic Research Consortium-2 (VARC-2) complications up to their latest clinical follow up. Results: There was 100% procedural success. 8 of 11 patients utilized an apical rail and all apical rail cases employed a nitinol-based occluder device for hemostasis. There was 1 major bleeding event (Bleeding Academic Research Consortium 3a) and no subsequent bleeding events despite the use of oral anti-coagulants upon discharge. Mean follow-up was 150 days [IQR 40-123 days]. There were 2 late adverse outcomes, a non-cardiac related death (628 days) and a stroke (382 days). The mean mitral gradient decreased from 9.5 +/- 3.4 mmHg to 5.5 +/- 2.6 mmHg (p<0.01). Only 1 patient was found to have ≥moderate regurgitation post-TMVR and none had left ventricular outflow tract obstruction. Conclusions: TMVR with an approach using transseptal access combined with an apical rail is feasibile and prospective studies comparing to the tranaspical route should be considered. (Table Presented).

Surgery

Go PH, and **Alvelo-Rivera M**. An unusual manifestation of diabetic ketoacidosis *Neth J Med* 2016; 74(3):138. PMID: 27020997. Full Text

Department of Surgery, Henry Ford Hospital, Detroit, Michigan, USA.

Surgery

Gupta RC, **Sing-Gupta V**, **Palaniyandi S**, and **Sabbah HN**. Reduced aldehyde dehydrogenase-2 activity and protein level in left ventricular myocardium of dogs with chronic heart failure *J Am Coll Cardiol* 2016; 67(13):1498. PMID: Not assigned. Abstract

R.C. Gupta, Henry Ford Hospital, Detroit, United States

Background: Reactive aldehydes such as 4-hydroxy-2-nonenal (4HNE) are generated in the failing heart and contribute to cardiomyocyte injury and death and to progressive global LV dysfunction. Aldehyde dehydrogenase-2 (ALDH2) plays a pivotal role in detoxifying mitochondrial (MITO) reactive aldehydes. The present study examined the activity, protein level and mRNA expression of ALDH2 in left ventricular (LV) myocardium of dogs with chronic heart failure (HF) (LV ejection fraction ~30%). Methods: Studies were performed in LV tissue from 7 HF dogs produced by intracoronary microembolizations and 7 normal (NL) dogs. Isolated MITO fractions were prepared using a subcellular fractionation kit. ALDH2 activity was measured using a colorimetric ALDH2 assay kit and expressed as nmol NADH formed/min/mg protein. Protein levels of ALDH2 and porin, a MITO protein not altered in HF, were determined by Western blotting coupled to chemiluminescence and band intensities were expressed in densitometric units (du). mRNA expression of ALDH2 and GAPDH, an internal control, was measured in isolated RNA using real-time PCR and expressed as fold change. Results: No changes in protein level of porin was observed between NL and HF dogs (0.24 ± 0.02 vs. 0.22 ± 0.01 du). Compared to NL dogs, ALDH2 activity was significantly decreased (93.3 ± 3.5 vs. 44.5 ± 2.9 nmol NADH/min/mg, p<0.05) as were protein levels (1.01 ± 0.05 vs. 0.53 ± 0.02 du, p<0.05) in LV myocardium of HF dogs. Furthermore, ALDH2 mRNA level normalized to GAPDH was reduced 4 folds in failing hearts compared to NL hearts. Conclusions: Compared to NL dogs, activity and expression of ALDH2 are reduced in LV myocardium of HF dogs. This abnormality may contribute to the observed increase in levels of oxidative stress in the failing heart. ALDH2 represents a potential therapeutic target for attenuating the adverse effects of oxidative stress in HF.

Surgery

Jacobs JP, Shahian DM, Prager RL, Edwards FH, McDonald D, Han JM, D'Agostino RS, Jacobs ML, Kozower BD, Badhwar V, Thourani VH, Gaissert HA, Fernandez FG, Wright C, Fann JI, **Paone G**, Sanchez JA, Cleveland JC, Jr., Brennan JM, Dokholyan RS, O'Brien SM, Peterson ED, Grover FL, and Patterson GA. Introduction to the sts national database series: Outcomes analysis, quality improvement, and patient safety *Ann Thorac Surg* 2015; 100(6):1992-2000. PMID: 26525868. Full Text

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University of Colorado, School of Medicine, Aurora, Colorado.
Duke Clinical Research Institute, Duke University, Durham, North Carolina.
Washington University School of Medicine, St. Louis, Missouri.

The Society of Thoracic Surgeons (STS) National Database is the foundation for most of the Society's quality, research, and patient safety activities. Beginning in January 2016 and repeating each year, The Annals of Thoracic Surgery will publish a monthly Database series of scholarly articles on outcomes analysis, quality improvement, and patient safety. Six articles will be directly derived from the STS National Database and will be published every other month: three articles on outcomes and quality (one each from the STS Adult Cardiac Surgery Database, the STS Congenital Heart Surgery Database, and the STS General Thoracic Surgery Database), and three articles on research (one from each of these three specialty databases). These six articles will alternate with five additional articles on topics related to patient safety. The final article, to be published in December, will provide a summary of the prior 11 manuscripts. This series will allow STS and its Workforces on National Databases, Research Development, and Patient Safety to convey timely information aimed at improving the quality and safety of cardiothoracic surgery.

Surgery
McIlvennan CK, **Bryce K**, Lindenfeld J, Allen LA, and **Lanfear DE**. Assessment of cognitive function prior to and after implantation of left ventricular assist device *J Heart Lung Transplant* 2016; 35(4):S165-S166. PMID: Not assigned
Abstract

C.K. McIlvennan, University of Colorado, Aurora, United States

Purpose: Placement of a left ventricular assist device (LVAD) for end-stage heart failure improves survival and quality of life, but it remains uncertain if cognitive function improves. The Montreal Cognitive Assessment (MoCA) is a simple, validated cognitive evaluation tool. We assessed whether cognitive function changes after LVAD implantation. Methods: Data was collected on 147 consecutive patients undergoing LVAD at two hospitals (2011-2015) where MoCA testing prior to implant was part of evaluation. Patients who had repeat MoCA testing post-LVAD (n= 90) were analyzed. Change in MoCA score (Δ MoCA) was tested using paired t-test. Baseline characteristics (age, race, gender, INTERMACS, etiology, indication, site) were tested for association with Δ MoCA by t-test, chi-square as appropriate. Results: The cohort had a mean age of 57 (±12.9), 66% destination therapy (n= 59), and a mean time to repeat MoCA of 149 days. Mean baseline MoCA was 23.1 (±3.8), and was not associated with any baseline characteristics. MoCA score increased after LVAD implantation; the average change was +1.6 (±3.7) points ($p < 0.0001$) and varied substantially across the cohort (range -11 to +12, Figure). Change in MoCA did not differ by any baseline characteristic (all $p > 0.1$). Conclusion: Cognitive function assessed by MoCA improves statistically after LVAD implant but the small magnitude may not be clinically significant. It seems unlikely to expect major improvements in cognitive function after LVAD for most patients. (Figure Presented).

Surgery
Mohanty S, Rosenthal RA, Russell MM, Neuman MD, Ko CY, and Esnaola NF. Optimal perioperative management of the geriatric patient: A best practices guideline from the american college of surgeons NSQIP and the american geriatrics society *J Am Coll Surg* 2016;PMID: 27049783. Full Text

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Departments of Surgery, Temple University School of Medicine and Fox Chase Cancer Center, Philadelphia, PA.

Surgery
Nash NA, Okoye O, Albuz O, Vogt KN, **Karamanos E**, Inaba K, and Demetriades D. Seat belt use and its effect on abdominal trauma: A national trauma databank study *Am Surg* 2016; 82(2):134-139. PMID: 26874135. Full Text

Department of Surgery, University of Louisville School of Medicine, Louisville, Kentucky, USA.

We sought to use the National Trauma Databank to determine the demographics, injury distribution, associated abdominal injuries, and outcomes of those patients who are restrained versus unrestrained. All victims of motor vehicle collisions (MVCs) were identified from the National Trauma Databank and stratified into subpopulations depending on the use of seat belts. A total of 150,161 MVC victims were included in this study, 72,394 (48%) were belted. Young, male passengers were the least likely to be wearing a seat belt. Restrained victims were less likely to have severe injury as measured by Injury Severity Score and Abbreviated Injury Score. Restrained victims were also less likely to suffer solid organ injuries (9.7% vs 12%, P < 0.001), but more likely to have hollow viscous injuries (1.9% vs 1.3%, P < 0.001). The hospital and intensive care unit length of stay were significantly shorter in belted victims with adjusted mean difference: -1.36 (-1.45, -1.27) and -0.96 (-1.02, -0.90), respectively. Seat belt use was associated with a significantly lower crude mortality than unrestrained victims (1.9% vs 3.3%, P < 0.001), and after adjusting for differences in age, gender, position in vehicle, and deployment of air bags, the protective effect remained (adjusted odds ratio for mortality 0.50, 95% confidence interval 0.47, 0.54). In conclusion, MVC victims wearing seat belts have a significant reduction in the severity of injuries in all body areas, lower mortality, a shorter hospital stay, and decreased length of stay in the intensive care unit. The nature of abdominal injuries, however, was significantly different, with a higher incidence of hollow viscous injury in those wearing seat belts.

Surgery
Newman LA, Jiagge E, **Bensenhaver JM**, **Chitale D**, Kleer C, Merajver S, Kyei I, Aitpillah F, Oppong J, Amankwaa-Frempong E, Adjei E, Wicha M, Awuah B, and **Stark A**. Comparative analysis of breast cancer phenotypes in African American, white American, and African patients-correlation between African ancestry and triple negative breast cancer *Cancer Res* 2016; 76(4)PMID: Not assigned. Abstract

L.A. Newman

Introduction: Population-based incidence rates of triple negative breast cancer (TNBC) are higher for African American (AA) compared to White American (WA) women, but it is unclear whether TNBC risk is genetically associated with African ancestry because AA women represent an ancestrally admixed population. Higher frequencies of TNBC have
also been observed in sub-Saharan African breast cancer (BC) patients, but comparative analyses of biomarker expression among datasets that include AA, WA, and African women are sparse. We report findings from an international registry that features specimens from a diverse patient population in Detroit, Michigan as well as a hospital in Kumasi, Ghana. Methods: The study dataset included formalin-fixed, paraffin-embedded invasive BC tumors diagnosed between 1998 and 2014 at the Komfo Anokye Teaching Hospital in Ghana and the prospectively-maintained/annotated Henry Ford Health System cohort in Michigan. All Ghanaian tumors underwent pathology confirmation and immunohistochemistry for estrogen receptor (ER), progesterone receptor (PR) and HER2/neu expression at the University of Michigan. Women were classified into five BC phenotypes and dichotomized into two age groups, <50 and ≥50 years. Polychotomous multivariate GLM models were developed to estimate the risk for each BC phenotype. Statistical analyses were performed in SAS v. 9.0 (Carey, NC). This research was approved by the Institutional Review Boards of the participating institutions. Results: A total of 234 Ghanaian cases with mean age 49 years (range 24-92); 271 AA with mean age 60 (range 27-87); and 321 WA with mean age 62 (range 31-91) (P=0.001) contributed to this study. Prevalence of histologic grade 3 was lowest in WA (n=107, 33.7%) which was statistically significant from the observed prevalence in AA (n=135, 50.4%) and Ghanaians (n=84, 53.8%) (P<0.0001). ER-negative and TNBC were more common among Ghanaian and AA compared to WA cases (frequency ER-negativity 67.5%, 37.1%, and 19.8%, respectively, p<0.0001; frequency TNBC 53.2%, 29.8%, and 15.5%, respectively, p<0.0001). In the age group <50 years, 82 women (42.5%) were diagnosed with ER+/PR+/HER2-, 65 (33.7%) with TNBC, 27 (14.0%) with ER+/PR+/HER2+, 14 (7.2%) with ER-/PR-/HER2+ and 5(2.6%) with ER-/PR+/HER2- phenotypes. In this young age group, prevalence of TNBC remained highest among Ghanaian women (50.8%), followed by AA (34.3%) and WA (15.9%); (P=.0006). In contrast, highest prevalence of ER+/PR+/HER2+ and ER+/PR+/HER2- phenotypes was observed in WA, followed by AA and Ghanaians. On multivariate analysis histologic grade 3 and racial heritage remained statistically significantly associated with the

TNBC phenotype (OR for AA vs. WA with TNBC 1.87, 95% CI 1.15-3.04; OR for Ghanaian vs. WA with TNBC 10.63, 95% CI 5.32-21.25; OR for Grade 3 vs Grade 1 histology with TNBC 33.3, 95% CI 13.45-82.4). Conclusions: This study confirms an association between the TNBC phenotype and African ancestry; furthermore, extent of African ancestry appears to be associated with an increased likelihood of having a TNBC tumor, since frequency of TNBC among AA patients was intermediate between WA and Ghanaian patients.

Surgery

Onders R, **Carlin A**, Dunkin B, Jossart G, Marohn M, Menegaux F, Morton J, and Smith CD. Multi-center analysis of operative safety of surgery in patients with amyotrophic lateral sclerosis: The diaphragm pacing experience *Surg Endosc* 2016; 30:S317. PMID: Not assigned. Abstract

R. Onders, University Hospitals Case Medical Center, United States

Introduction: With the growing prevalence of patients with amyotrophic lateral sclerosis (ALS) there is a need to describe and analyze the correct perioperative management. ALS is a progressive neurodegenerative disease that has devastating effects to respiratory muscles resulting in respiratory failure death in 80 % of patients. Diaphragm pacing (DP) replaces ventilators in spinal cord injury patients and delays death and tracheostomy in ALS patients. This report outlines the peri-operative outcomes to 90 days for patients in a multicenter pivotal FDA trial of DP in ALS. Methods: The study was conducted under an investigational device exemption (IDE G040142, clinicaltrials.gov NCT00420719) from the U.S. FDA and IRB approval. Patients underwent three pre-operative neurophysiologic assessments to quantify diaphragm function. Inclusion criteria included chronic hypoventilation with intact diaphragm motor units to stimulate. A standardized ALS functional rating scale (ALSFSR-R) was completed serially pre and post-operatively. Patients underwent general anesthesia with no paralytics with laparoscopic implantation of the diaphragm pacing electrodes in each hemi-diaphragm. Post-operative ALSFSR-R results and complications were noted. Data were analyzed with Stata 13.0. Results: At eight worldwide sites, 107 patients went to surgery with 106 patients successfully being implanted with DP. One patient had a reaction to anesthesia requiring cancellation of surgery. Twenty-eight patients received a simultaneous percutaneous gastrostomy tube (PEG). There were 73 males and 36 females with a median age of 57.9 years (range 32-76). The mean lead-in time was 2.7 ± 0.6 months from consent to implant. The mean post-op period was 3.8 ± 1.0 months from implant to data collection. There were no deaths within 30 days post implant. Three in the non-PEG group, died within 90 days. The median ALSFRS-R score at implant was 28 points (on the 48 point scale). The lead-in period rate of decline was compared on a paired, patient-by-patient, basis to the rate of decline for the post-operative treatment period. There was no significant change in the rate of decline of this functional scale (lead-in slope -0.80 vs post-op slope -0.73 with p value = 0.50). There were 4 serious adverse effects: 2 capnothorax, 1 respiratory failure following complications from surgery (dislodgement of gastrostomy); and 1 post-operative chest pain. Conclusion: There was no degradation in function for ALS patients undergoing surgical procedures when no paralytics are used and DP is placed. The diagnosis of ALS should not prevent a patient from being considered for a surgical procedure when necessary and to improve their quality of life.

Surgery

Scally CP, Varban OA, **Carlin AM**, Birkmeyer JD, and Dimick JB. Video ratings of surgical skill and late outcomes of bariatric surgery *JAMA Surg* 2016:e160428. PMID: 27074114. Full Text

Center for Healthcare Outcomes and Policy, Department of Surgery, University of Michigan, Ann Arbor.
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Dartmouth Hitchcock Medical Center, Hanover, New Hampshire.

Importance: Measures of surgeons' skills have been associated with variations in short-term outcomes after laparoscopic gastric bypass. However, the effect of surgical skill on long-term outcomes after bariatric surgery is unknown. Objective: To study the association between surgical skill and long-term outcomes of bariatric surgery. Design, Setting, and Participants: In this retrospective observational study, 20 surgeons performing bariatric surgery submitted videos; surgeons were ranked on their skill level through blinded peer video review and sorted into quartiles of skill. Outcomes of bariatric surgery were then examined at the patient level across skill levels. The patients (N = 3631) undergoing surgery with these surgeons had 1-year postoperative follow-up data available between 2006 and 2012. The study was conducted using the Michigan Bariatric Surgery Collaborative, a prospective clinical registry of 40 hospitals performing bariatric surgery in the state of Michigan. Exposure: Surgeon skill level. Main Outcomes and Measures: Excess body weight loss at 1 year; resolution of medical comorbidities (hypertension, sleep apnea, diabetes, and hyperlipidemia), functional status, and patient satisfaction. Results: Surgeons in the top and bottom quartiles had each been practicing for a mean of 11 years. Peer ratings of surgical skill varied from 2.6 to 4.8 on a 5-point scale. There was no difference between the best (top 25%) and worst (bottom 25%) performance

quartiles when comparing excess body weight loss (67.2% vs 68.5%; P = .86) at 1 year. There were no differences in resolution of sleep apnea (62.6% vs 62.0%; P = .77), hypertension (47.1% vs 45.4%; P = .73), or hyperlipidemia (52.3% vs 63.4%; P = .45). Surgeons with the lowest skill rating had patients with higher rates of diabetes resolution (78.8%) when compared with the high-skill group (72.8%) (P = .01). Conclusions and Relevance: In contrast to its effect on early complications, surgical skill did not affect postoperative weight loss or resolution of medical comorbidities at 1 year after laparoscopic gastric bypass. These findings suggest that long-term outcomes after bariatric surgery may be less dependent on a surgeon's operative skill and instead be driven by other factors. Operative technique was not assessed in this analysis and should be considered in future studies.

Surgery

Shaikh S, Stenz J, McVinnie D, Morrison J, Getzen T, **Carlin A**, and Mir F. Percutaneous gastric remnant gastrostomy following roux-en-Y gastric bypass surgery: A single tertiary center's twelve year experience *J Vasc Interv Radiol* 2016; 27(3):S43. PMID: Not assigned. Abstract

S. Shaikh, Henry Ford Hospital, Dearborn, United States

Purpose: To review the indications, access techniques, and outcomes for percutaneous gastric remnant gastrostomy performed in patients following Roux-en-Y gastric bypass surgery. Materials: The medical records of all Roux-en-Y gastric bypass patients who underwent a percutaneous gastric remnant gastrostomy procedure between April 2003 (first identified patient) and September 2015 were reviewed. Indications, techniques for obtaining access, technical success, complications, and clinical course were reviewed. Complications were recorded per Society of Interventional Radiology practice guidelines. Institutional review board approval was obtained. Results: A total of 31 patients were identified in which 33 procedures were attempted. The mean age was 51 years and 24 patients were female. Access was obtained using fluoroscopy, ultrasound and fluoroscopy, or computed tomography. Technical success rate was 94%. The indications for gastrostomy placement were malnutrition related to gastric bypass in 18 cases (55%), delayed gastric remnant emptying/ biliopancreatic limb obstruction in 8 cases (24%), and malnutrition due to illness unrelated to gastric bypass in 7 cases (21%). The mean duration of gastrostomy access was 117 days with a range of 3 to 698 days. Within the delayed gastric remnant emptying/biliopancreatic limb obstruction group, symptoms resolved in 6 patients while 2 patients underwent subsequent surgery for lysis of adhesions. There were 4 major complications: local cellulitis, leak with peritonitis requiring surgery, delayed gastric bleeding requiring transfusion, and unrelenting pain necessitating tube removal and surgical gastrostomy. There were no procedure related deaths. Conclusions: Percutaneous gastric remnant gastrostomy is a safe procedure with a high technical success rate. This technique allows most patients to avoid a more invasive surgical procedure for establishing enteral nutrition or decompression.

Surgery

Takahashi K, **Obeid J**, **Burmeister CS**, **Bruno DA**, **Kazimi MM**, **Yoshida A**, **Abouljoud MS**, and **Schnickel GT**. Intrahepatic cholangiocarcinoma in the liver explant after liver transplantation: Histological differentiation and prognosis *Ann Transplant* 2016; 21:208-215. PMID: 27068242. Article Request Form

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BACKGROUND: The aim of this study was to evaluate the outcome of patients with intrahepatic cholangiocarcinoma (ICCA) incidentally found in the explanted liver after liver transplantation. MATERIAL AND METHODS: We retrospectively reviewed 1188 recipients undergoing liver transplantation from August 2003 to August 2014; 13 patients were found to have ICCA (1.1%). Recurrence-free survival (RFS) rate was compared between ICCA patients and the matched cohort of 39 patients with hepatocellular carcinoma (HCC). We also investigate the relevance of clinical and pathological parameters in recurrence of ICCA. RESULTS: ICCA patients showed significantly higher recurrence rate with lower 1-year and 3-year RFS rates than HCC patients (recurrence rate, 12.8% vs. 54.8%; 1-year and 3-year RFS rates, 94% and 84% vs. 67% and 42%). Of the 13 ICCA patients, 4 were diagnosed with a well-differentiated ICCA and 9 with a moderately-differentiated ICCA. There was no recurrence among those with a well-differentiated ICCA, whereas 78% recurred in the moderately-differentiated group. The median RFS time for the moderately-differentiated group was 13.0 months, yielding RFS rates of 56% at 1 year and 22% at 3 years. CONCLUSIONS: Liver transplantation in patients with a well-differentiated ICCA yielded excellent outcomes as compared to patients with a moderately-differentiated ICCA. This may allow consideration of transplantation in the setting of a well-differentiated ICCA, and obviate the need for adjuvant systemic treatment. Conversely, a moderately-differentiated ICCA carries a poor prognosis with a prohibitively high recurrence rate and poor survival. Liver transplantation should remain a contraindication in this group.

Surgery

Toursavadkohi S, Kakkos SK, **Rubinfeld I**, and **Shepard A**. Lower extremity microembolism in open vs. Endovascular abdominal aortic aneurysm repair *Front Surg* 2016; 3:18. PMID: 27066488. Full Text

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Although previous studies have documented the occurrence of microembolization during abdominal aortic aneurysm (AAA) repair by both open and endovascular approaches, no study has compared the downstream effects of these two repair techniques on lower extremity hemodynamics. In this prospective cohort study, 20 patients were treated with endovascular aneurysm repair (EVAR) (11 Zenith, 8 Excluder, and 1 Medtronic) and 18 patients with open repair (OR) (16 bifurcated grafts, 2 tube grafts). Pre- and postoperative ankle-brachial indices (ABIs) and toe-brachial indices (TBIs) were measured preoperatively and on postoperative day (POD) 1 and 5. Demographics and preoperative ABIs/TBIs were identical in EVAR (0.97/0.63) and OR (0.96/0.63) patients (p = 0.21). There was a significant decrease in ABIs/TBIs following both EVAR (0.83/0.52, p = 0.01) and OR (0.73/0.39, p = 0.003) on POD #1, although this decrease was greater following OR than EVAR (p = 0.002). This difference largely resolved by POD #5 (p = 0.41). In the OR group, TBIs in the limb in which flow was restored first was significantly reduced compared to the contralateral limb (0.50 vs. 0.61, p = 0.03). In the EVAR group, there was also a difference in TBIs between the main body insertion side and the contralateral side (0.50 vs. 0.59, p = 0.02). Deterioration of lower extremity perfusion pressures occurs commonly after AAA repair regardless of repair technique. Toe perfusion is worse in the limb opened first during OR and on the main body insertion side following EVAR, suggesting that microembolization plays a major role in this deterioration. The derangement following OR is more profound than after EVAR on POD #1, but recovers rapidly. This finding suggests that microembolizarion may be worse with OR or alternatively that other factors associated with OR (e.g., the hemodynamic response to surgery with redistribution of flow to vital organs peri-operatively) may play a role.

Surgery

Varban OA, Cassidy RB, Sheetz KH, Stricklen A, Pesta C, **Genaw J**, **Carlin AM**, and Finks JF. Evaluating the effect of technique and devices on leaks after laparoscopic sleeve gastrectomy *Surg Endosc* 2016; 30:S462. PMID: Not assigned. Abstract

O.A. Varban, University of Michigan Health System, United States

Objective: To assess the effect of technique and surgical devices on staple line leaks after laparoscopic sleeve gastrectomy (LSG). Background: Staple line leaks after LSG are a major source of morbidity and mortality. Variations in technique and devices used to perform LSG exists, however their effect on leaks is poorly understood. Methods: We performed a case-control study comparing patients who sustained a leak after undergoing a primary LSG to those that did not. A total of 45 (0.40 %) patients with leaks were identified between January 2007 and December 2013. The leak group was matched 1:2 to a control group based on procedure type, age, body mass index (BMI), sex and year the procedure was performed. Technique and device specific factors were assessed by reviewing operative notes from all primary bariatric procedures in our study population. Results: Leak rates after LSG have decreased over the past 5 years (0.93 % to 0.20 %) despite variations in technique and device use. The only technique specific factor associated with a lower rate of leaks was oversewing of the staple line (OR 0.218, CI 0.071-0.672, p = 0.008). Surgeons who oversewed routinely were also found to have higher case volume (307 vs 140, p = 0.0216) and less overall complication rate (4.81 % vs 7.95 %, p = 0.0027). Stapler vendor was associated with a higher rate of leaks on univariate analysis but not after controlling for confounding factors. Use of buttressing material, fibrin sealant and drains did not affect leak rates significantly. Conclusions: Despite variations in technique, leak rates have decreased over the past 5 years. Oversewing of the staple line was associated with less leaks after LSG and was performed routinely by more experienced surgeons with less overall complication rates. Vendor, buttressing material, drains and fibrin sealant had no apparent effect. Surgeons should reconsider the use of superfluous and costly devices as a means of reducing leaks after LSG until further evidence justifies their use.

Surgery

Varban OA, Niemann A, Schram J, **Carlin AM**, Poplawski SC, and Dimick JB. Video analysis of surgery: Defining the data set of the future *Surg Endosc* 2016; 30:S482. PMID: Not assigned. Abstract

O.A. Varban, University of Michigan Health System, United States

Background: It has been shown that variations in surgical outcomes can be correlated directly to video based peer-rated evaluation of surgical skill. However, little is known about the use of surgical videos to identify variations in operative technique and how they may affect outcomes. Methods: Representative videos of laparoscopic sleeve gastrectomy were voluntarily submitted by 20 surgeons who participate in the Michigan Bariatric Surgery Collaborative, a statewide consortium that uses a clinical data registry for quality improvement. Each video was devoid of patient identifiers and edited so as to exclude port placement, tissue extraction and camera exchanges. Time to completion of each step was assessed as well as variations in the tasks performed during each step. Results: Twenty-two videos of laparoscopic sleeve gastrectomy were submitted and 11 included concurrent hiatal hernia repair. Data obtained from video identified variation in time to completion of each step of the procedure as well as differences in management of hiatal hernias, stapling technique and management of staple line. Mean time to completion for unedited videos was 47 minutes without hiatal hernia repair (range 28-66 min) and 55 min with hiatal hernia repair
(range 34-80 min). Among cases involving hiatal hernia repair, 55 % performed a posterior cruropexy, 27 % performed an anterior cruropexy and 18 % performed both. Two different vendors and 10 different permutations of staple heights and buttressing material was used during division of the stomach. The median number of staple cartridges used was 6 (range 4-7). Management of the staple line included: use of buttressing (64 %), fibrin sealant (36 %), oversewing (9 %), use of surgical clips (18 %), imbrication of the staple line (36 %) and omentoplasty (55 %). A leak test was performed in 50 % of cases and endoscopy was performed in 17 % of cases. Drains were placed 9 % of the time. Conclusions: Video analysis of laparoscopic sleeve gastrectomy provides a unique dataset that highlights variation in: 1) time to completion of each step of the procedure, 2) variation in hiatal hernia repair, 3) variation in stapling technique and 4) variation in staple line management. Video-based data of technique can be further augmented with peer-reviewed assessment of skill and also combined with a clinical outcomes registry for a robust comparative analysis on the effect of specific techniques, devices and skill on outcomes, cost and quality.

Surgery

Xuereb L, **Kaur B**, **Akrawe S**, **Nemeh HW**, **Borgi J**, **Lanfear DE**, **Williams CT**, **Paone G**, and **Morgan JA**. Does preoperative atrial fibrillation increase the incidence of thromboembolic complications in patients supported with long-term LVADs? *J Heart Lung Transplant* 2016; 35(4):S130-S131. PMID: Not assigned. Abstract

L. Xuereb, Cardiac Surgery, Henry Ford Hospital, Detroit, United States

Purpose: We reviewed our nine year experience of continuous flow left ventricular assist devices (LVADs) to determine the impact of preoperative atrial fibrillation (AF) on stroke, device thrombosis, and survival. Methods: Between March 2006 and May 2015, 231 patients underwent implantation of 240 CF LVADs - 127 (52.9%) as bridge to transplant (BTT) and 113 (47.1%) as destination therapy (DT). Effect of AF on postoperative outcomes was assessed by using Kaplan Meier survival and Cox proportional hazard regression. Results: There were 78 (32.5%) patients with preoperative AF with a mean age of 55.7 + 11.4 years. There was a similar incidence of stroke in patients with and without AF - 12.8% versus 16.0%, respectively (p= 0.803). The incidence of device exchange for thrombosis was also similar in both groups (3.9% vs. 3.7%; p= 0.999). Survival was similar, with 1-month, 6-month, 12-month, and 24-month survivals of 96.2%, 91.7%, 84.5%, and 69.2%, respectively, for AF patients, versus 93.1%, 85.0%, 79.4%, and 74.1%, respectively, for non-AF patients (p= 0.424). Preoperative AF was not a significant independent predictor of survival using Cox proportional hazard regression (HR 1.08, 95% CI 0.66-1.76). Conclusion: Preoperative AF was associated with a similar incidence of postoperative stroke, device thrombosis, and survival. Based on these data, it seems unnecessary to perform a left atrial appendage ligation or alter postoperative anticoagulation in patients with AF undergoing LVAD implantation. (Table presented).

Surgery

Xuereb L, **Kaur B**, **Akrawe S**, **Rashty J**, **Nemeh HW**, **Borgi J**, **Lanfear DE**, **Williams CT**, **Paone G**, and **Morgan JA**. Reoperation for bleeding does not adversely impact long-term outcomes in LVAD recipients *J Heart Lung Transplant* 2016; 35(4):S249. PMID: Not assigned. Abstract

L. Xuereb, Cardiac Surgery, Henry Ford Hospital, Detroit, United States

Purpose: We reviewed our nine year experience with continuous flow LVADs to determine the impact of reoperation for bleeding on outcomes. Methods: Between March 2006 and May 2015, 231 patients underwent implantation of 240 CF LVADs - 127 (52.9%) as bridge to transplant (BTT) and 113 (47.1%) as destination therapy (DT). Effect of reoperation for bleeding on outcomes was assessed. Results: Bleeding requiring reoperation occurred in 33 (13.8%) patients, 42.4% had a prior sternotomy, and 30.3% had previous temporary mechanical support. Survival was 95.2%, 85.7%, 84.5%, and 66.2%, respectively, at 30-days, 6-months, 12-months, and 24-months for patients who required reoperation, versus 92.1%, 88.0%, 80.4%, and 76.1%, respectively, for patients who did not (p= 0.237). The

incidence of postoperative infection, stroke, right ventricular failure, renal failure, and/or device thrombosis was similar (p= NS). Conclusion: Reoperation for bleeding did not adversely impact survival or development of other LVAD-related complications. It therefore may be prudent to re-explore a bleeding patient early to limit transfusions and avoid potential consequences, such as right ventricular failure and prolonged ventilation. (Table Presented).

Surgery

Xuereb L, **Kaur B**, **Akrawe S**, **Rashty J**, **Nemeh HW**, **Borgi J**, **Tita C**, **Selektor Y**, **Velez M**, **Lanfear DE**, **Williams CT**, **Paone G**, and **Morgan JA**. Drive line infections are not associated with an increased incidence of thromboembolic complications in patients on continuous flow LVAD support *J Heart Lung Transplant* 2016; 35(4):S246. PMID: Not assigned. Abstract

L. Xuereb, Cardiac Surgery, Henry Ford Hospital, Detroit, United States

Purpose: We reviewed our single institutional experience of continuous flow left ventricular assist devices (LVADs) to determine the impact of driveline (DL) infections on the incidence of thromboembolic complications. Methods: Between March 2006 and May 2015, 231 patients underwent implantation of 240 LVADs - 127 (52.9%) as bridge to transplant and 113(47.1%) as destination therapy. Effect of DL infections on stroke, pump thrombosis, and survival was assessed. Results: There were 24 (10.0%) patients who developed a DL infection, 6 (25%) were female, and 11 (45.8%) destination therapy patients. Freedom from stroke was similar for patients with and without DL infections - 92.5% vs. 91.0% at 6 months, 77.0% vs. 87.0% at 1 year, and 70.5% vs. 81.0% at 2 years; p= 0.273. The incidence of pump thrombosis was also similar - 4.2% vs. 3.7%%; p= 0.999. Survival was similar between the groups with 1-month, 6-month, 1-year, and 2-year survivals of 100.0%, 100.0%, 94.7%, and 94.7%, respectively, for DL infection patients, versus 93.5%, 85.8%, 79.6%, and 69.8%, respectively, for patients without DL infections (p= 0.259). DL infection was not a significant predictor of survival in Cox proportional hazard regression (HR 1.58, p= 0.277). Conclusion: Drive line infections were not associated with a higher incidence of thromboembolic complications. Based on these data, it does not appear necessary to raise anticoagulation target goals in the setting of a DL infection. (Figure Presented).

Surgery

Yadav P, **Eng M**, **Divine G**, **Wang DD**, **Arjomand-Fard H**, **Wyman J**, **Isley M**, **Borgi J**, **Paone G**, **Greenbaum A**, and **O'Neill W**. Outcomes of impella assisted percutaneous balloon aortic valvuloplasty in very high risk severe aortic stenosis patients *J Am Coll Cardiol* 2016; 67(13):404. PMID: Not assigned. Abstract

P. Yadav, Henry Ford Hospital, Detroit, United States

Background: Limited data available suggests poor outcomes with high risk Percutaneous Balloon Aortic Valvuloplasty (PBAV) in patients with severe aortic stenosis and coexistent severe left ventricular dysfunction, recent decompensated heart failure or severe coronary artery disease. Methods: Retrospective analysis of patients with severe aortic stenosis who underwent high risk PBAV with hemodynamic support with Impella (Abiomed). Time to death was assessed with Kaplan-Meier estimates and by hazard ratios estimated by univariate Cox regression models Results: 28 patients, mean age 79 ± 8.6 years, STS mortality risk 13 ± 12%, average NYHA class 3.7, left ventricular ejection fraction 29% ± 17%, mean creatinine 2.1 ± 1.9 mg/dL, mean GFR 52 ± 28. Successful PBAV performed with rapid pacing in 100% cases. Impella removed in 68% of the patients at the end of the case. Overall, survival was 75% at 30 days and 63% at 1 year. Earlier death associated with: higher STS (HR=1.07, p=0.002), higher mean creatinine (HR=1.33, p=0.020) and lower GFR (HR=0.97, p=0.015). When Impella placed sequentially after PBAV (n=12), 50% of the patients survived to 30 days (4 patients had intraprocedural cardiac arrest). If Impella placed first with simultaneous support during BAV (n=16) 94% patients alive at 30 days with no intraprocedural cardiac arrest. (HR for simultaneous support=0.36, p=0.115) Conclusions: Hemodynamic support with Impella in high risk PBAV patient showed survival higher than reported in the limited literature. (Figure Presented).

Urology

Abdollah F, Ye Z, Miller DC, Linsell SM, Montie JE, **Peabody JO**, and Ghani KR. Understanding the use of prostate biopsy among men with limited life expectancy in a statewide quality improvement collaborative *Eur Urol* 2016;PMID: 27113032. Full Text

Vattikuti Urology Institute and VUI Center for Outcomes Research Analytics and Evaluation, Henry Ford Hospital, Detroit, MI, USA.
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BACKGROUND: The potential harms of a prostate cancer (PCa) diagnosis may outweigh its benefits in elderly men. OBJECTIVE: To assess the use of prostate biopsy in men with limited life expectancy (LE) within the practices comprising the Michigan Urological Surgery Improvement Collaborative (MUSIC). DESIGN, SETTING, AND PARTICIPANTS: MUSIC is a consortium of 42 practices and nearly 85% of the urologists in Michigan. From July 2013 to October 2014, clinical data were collected prospectively for all men undergoing prostate biopsy. OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS: We calculated comorbidity-adjusted LE in men aged >/=66 yr and identified men with <10 yr LE (limited LE) undergoing a first biopsy. Our LE calculator was not designed for men aged <66 yr; thus these men were excluded. Multivariable models estimated the proportion of all biopsies performed for men with limited LE in each MUSIC practice, adjusting for differences in patient characteristics. We also evaluated what treatments, if any, these patients received. RESULTS AND LIMITATIONS: Among 3035 men aged >/=66 yr undergoing initial prostate biopsy, 60% had none of the measured comorbidities. Overall, 547 men (18%) had limited LE. Compared with men with a longer LE, these men had significantly higher prostate-specific antigen levels and abnormal digital rectal examination findings. The adjusted proportion of biopsies performed for men with limited LE ranged from 3.8% to 39% across MUSIC practices ($p < 0.001$). PCa was diagnosed in 69% of men with limited LE; among this group, 74% received any active treatment. Of these men, 46% had high-grade cancer (Gleason score 8-10). CONCLUSIONS: Among a large and diverse group of urology practices, nearly 20% of prostate biopsies are performed in men with limited LE. These data provide useful context for quality improvement efforts aimed at optimizing patient selection for prostate biopsy. PATIENT SUMMARY: In this report, nearly 2 of every 10 men undergoing prostate biopsy had a life expectancy (LE) <10 yr. Implementing LE calculators in clinical practice may help refine patient selection for prostate biopsy.

Urology

Abdollah FFH, **Dalela D**, **Sammon J**, **Sood A**, Fossati N, Gandaglia G, Suardi N, Gaboardi F, Pini G, **Jeong W**, **Rogers C**, **Peabody J**, Montorsi F, Briganti A, **Menon M**, and **Dalela D**. Late recovery of erectile function in men treated with robotic-assisted laparoscopic radical prostatectomy (RALP): A novel nomogram development and validation *European Urology, Supplements* 2016; 15(3):e447. PMID: Not assigned. Abstract

F.F.H. Abdollah, Henry Ford Hospital/Health System, Dept. of Urology, Detroit, United States

INTRODUCTION & OBJECTIVES: It is generally believed that radical prostatectomy patients who did not recover their Erectile Function (EF) within the initial 12 months of surgery are unlikely to recover it subsequently. However, recent data showed that up to 40% of these individuals do recover their EF after 12 months. Unfortunately, the currently available data are largely based on open surgery data, which has been largely replace by RALP as the standard of care in contemporary patients. To address this issue, we set to assess the rate of late EF recovery (EF after 12 months) in patients treated exclusively with RALP. Moreover, we developed the first multivariable model predicting the probability of late EF in those individuals. MATERIAL & METHODS: We evaluated a total of 1986 men who underwent a RALP between 2011 and 2014, in two tertiary care centers. All of these men had an erectile dysfunction during the initial 12 months post surgery, and had an extended follow-up data. Late EF recovery was defined as achieving an International Index of Erectile Function (IIEF)-EF score≥17, in men with erectile dysfunction during the initial 12 months post surgery. Kaplan-Meier curves were used to estimate the rates of late EF recover. Uni- and multi-variable (MVA) cox regression analyses tested the relationship between available covariates and achieving late EF recovery. Independent predictors of late EF recovery at MVA were used to develop a novel nomogram, which was internally validated using 200-bootstraping. All patients were instructed to start PED-5 inhibitors, and/or penile injection to treat erectile dysfunction immediately after surgery. RESULTS: Median (interquartile range [IQR]) age, PSA value, and BMI at surgery were 62.1 yrs (56-66.4), 5.2 ng/ml (4.2-7.1), and 26.6 Kg/m2 (24.5-29.5), respectively. Most patient had a pathological Gleason of 3+4 (39.6%), and pT2c disease (56.9%). Median (IQR) pre-op IIEF-EF was 22 points (16-25). Overall, 81.0% received a bilateral nerve-sparing RALP, 22.9% had positive surgical margins, and 1.3% received any adjuvant treatment. At 24, 36, 48, and 60 months post surgery, the late EF recovery rates were 27.7%, 46.2%, 60.4%, and 64.9%, respectively. At MVA, age (hazard ratio [HR]: 0.95), BMI (HR: 0.96), unilateral nerve sparing (HR: 4.0), bilateral nerve sparing (HR: 4.1), pre-operative IIEF-EF score (HR 1.10), pT3b-4 disease (HR: 0.51), and pathological Gleason 8-10 (HR: 0.39) were independent predictors of late EF recovery (all p≤0.03). A novel nomogram (not shown) was developed based on these variables, which showed favorable discrimination (75%), and calibration characteristics. CONCLUSIONS: Our report represents one of the few reports on late EF recovery in patients treated exclusively with RALP. Our findings can be of great use in counseling patients post-operatively, and in managing their expectations. Up to 65% of patient who had an erectile dysfunction during the initial 12 months post surgery recovered their EF afterward. Our nomogram is the first model that allows identifying these individuals.

Urology

Abdollah FFH, **Dalela D**, **Sood A**, Meyer C, Sun M, Trinh QD, **Menon M**, **Sammon J**, and **Dalela D**. The impact of 2012 United States Preventive Services Task Force (USPSTF) panel update on PSA screening practice: A nationwide, and state-by-state level analyses *European Urology, Supplements* 2016; 15(3):e91+e91a. PMID: Not assigned. Abstract

F.F.H. Abdollah, Henry Ford Hospital / Health System, Dept. of Urology, Detroit, United States

INTRODUCTION & OBJECTIVES: Prostate specific antigen (PSA) screening is a widely debated practice in the US, given the concerns regarding over-diagnosis and over-treatment. In this context, USPSTF 2012 panel update recommended against routine PSA screening. Our aim was to address the impact of this recommendation on PSA screening practice in US at nationwide level, as well as at state-by-state level. Further, it is currently unknown if the USPSTF statement changed physicians' recommendation for PSA screening, or if the USPSTF statement influenced the impact of physician recommendation on the ultimate receipt of PSA screening amongst men.Prostate specific antigen (PSA) screening is a widely debated practice in the United States, given the concerns regarding over-diagnosis and overtreatment. In this context, the draft 2011 (finalized in May 2012) USPSTF panel update recommended against PSA screening. Our aim was to address the impact of this recommendation on PSA screening practice in United States at nationwide level, as well as at state-by-state level. MATERIAL & METHODS: Cohort of 235,503 individuals aged ≥50 years (weighted population size of 50.324 million) that responded to the 2012 or 2014 Behavioral Risk Factor Surveillance System survey (BRFSS). Patients were asked if they underwent PSA screening in the 12 months preceding the survey year, such that the BRFSS 2012 and 2014 reflected screening trends in the preceding year. Complex samples frequencies and logistic regression analyses were used to report outcomes, stratified by individual states within the US. Next, using data from the nationally representative National Health Interview Survey (NHIS) 2010 and 2013, we compared the prevalence of physician recommendation and demographic differences in men receiving recommendation for PSA screening during the two survey years. Multivariate logistic regression models (adjusted for complex survey design) tested the association between survey year and physician recommendation, adjusting for available socio-demographic covariates. In a separate model, predictors of PSA screening were analysed, including the interaction between physician recommendation and survey year. RESULTS: Among individuals aged ≥50, 34.9% (95% CI: 34.4-35.4%) reported a PSA screening in 2012 survey vs. 31.9% (95% CI: 31.4- 32.4%) in 2014 survey. When the same analyses were repeated at a state-by-state level, significant differences were observed between the states (figure). Specifically, Alabama and Alaska had the highest drop in PSA screening (7.5%), Utah and Vermont had virtually no change in PSA screening, while in few states there was a slight increase in PSA screening (0.1-2.5%). In multivariable analysis, year of survey (2014 vs. 2013 OR: 0.84, 95%CI: .80-.87) and State (data not shown) were independent predictors of PSA screening utilization after adjusting to age, race, education, income, health insurance, and marital status. However, within NHIS, the proportion of men who reported receiving physician recommendation did not change significantly between survey years (2137 [48.7%]) vs 2,985 [48.2%]) for NHIS 2010 and 2013 respectively; p=0.2), except for those aged 60-64 (57.8% vs. 49.0%, p<0.001). While physician recommendation continued to be signifcantly associated with receipt of PSA screening overall (odds ratio [OR] 26.8, 95% CI 21.7-33.1) and in age-stratified analyses, the interaction between physician recommendation and survey year was not significant for any age group. CONCLUSIONS: Despite the overall drop in PSA screening practice at a nationwide level after the USPSTF 2012 recommendation, the magnitude of this phenomenon is subject to significant state-by-state heterogeneity. While some states witnessed a significant drop, others showed no change or even a slight increase in PSA screening. Further, we noticed no change in prevalence of physician recommendation for PSA screening despite the 2012 USPSTF statement against PSA screening, suggesting that factors beyond provider influence appear to have precipitated the decline in PSA screening frequency following the 2012 USPSTF recommendations. Future research may shed more light on the underpinnings of the geographical variation in PSA screening, as well as the influence of national guidelines on physicians' attitudes towards widely prevalent screening practices.

Urology

Abdollah FFH, **Dalela D**, **Sood A**, **Sammon J**, **Karabon P**, Meyer C, Sun M, Choueiri T, **Menon M**, Trinh QD, and **Dalela D**. Temporal trends in prostate cancer (PCa) risk group stratification following the 2008 United States preventive services task force recommendations *European Urology, Supplements* 2016; 15(3):e726. PMID: Not assigned. Abstract

F.F.H. Abdollah, Henry Ford Hospital/Health System, Dept. of Urology, Detroit, United States

INTRODUCTION & OBJECTIVES: In 2008, the United States Preventive Services Task Force (USPSTF) recommended against Prostate Specific Antigen (PSA) screening for PCa in men aged ≥75 years. We examined temporal trends in PCa risk profile before and after the 2008 USPSTF recommendations in a nationwide dataset. MATERIAL & METHODS: Men newly diagnosed with PCa within the National Cancer Data Base (NCDB) 2005-07

and 2009-11 were riskstratified according to the National Comprehensive Cancer Network guidelines (low: T1c-T2a, biopsy Gleason ≤6 and PSA20 ng/ml, and metastatic [anyTanyNM1]). A Difference-In-Differences (DID) modeling framework was used to ascertain the independent effect of the 2008 recommendation in older men (aged >75), using younger men (aged <75) that were not subject to the USPSTF statement as a control population to account for baseline secular trends in risk stratification, and adjusting for all available demographic and socio-economic variables. RESULTS: Overall, 195,495 (29.7%) low-risk, 298,386 (45.3%) intermediate-risk, 155,933 (23.7%) high-risk localized PCa, as well as as 8,721 (1.3%) metastatic PCa cases were diagnosed in the NCDB over the study period. Amongst older men, the proportion of high-risk and metastatic PCa increased (from 36.7% to 41.7% and 3.1% to 6.1%, respectively) and low-risk PCa decreased (19.6% to 14.4%) from 2005 to 2011, while the opposite trend was noted in younger men (Cochran-Armitage trend test p10 years were 24% and 20% more likely to be diagnosed with high-risk PCa than men aged 2. CONCLUSIONS: Our study highlights the upward stage migration and increased likelihood of high- risk and metastatic PCa diagnoses in men aged >75 following the USPSTF 2008 recommendations against PSA screening. This was especially true for older men with no comorbidities and good life expectancy. These results might serve as a herald for the changes in risk profile that have taken place in US after the 2011 USPSTF update, which recommended against PSA screening in all patients.

Urology
Cole AP, Leow JJ, Chang SL, Chung BI, Meyer CP, Kibel AS, **Menon M**, Nguyen PL, Choueiri TK, Reznor G, Lipsitz SR, **Sammon JD**, Sun M, and Trinh QD. Surgeon and hospital-level variation in the costs of robot-assisted radical prostatectomy *J Urol* 2016;PMID: 27157376. Full Text

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PURPOSE: To assess surgeon- and hospital-level variation in RARP costs and predictors of high and low-cost surgery. MATERIALS AND METHODS: Population consisted of a weighted sample of 291,015 men who underwent RARP for prostate cancer by 667 surgeons at 197 different United States hospitals from 2003 to 2013. We evaluated 90-day direct hospital costs (2014 USD) in the Premier Hospital Database. High costs per RARP were those above the 90th percentile and low costs were those below the 10th. RESULTS: Mean hospital costs per RARP was $11,878 (95% CI $11,804 - $11,952), Mean cost in the low-cost group was $2,837 (95% CI: $2,805 - $2,869) versus $25,906 (95% CI: $24,702 - $25,490) in the high-cost group. Nearly a third of the variation in RARP cost was attributable to hospital characteristics; over a fifth was attributable to surgeon (R-squared 30.43% and 21.25%, respectively). High-volume surgeons and hospitals (>/=90th percentile) had decreased odds of high-cost surgery (surgeons: OR 0.24, 95% CI 0.11- 0.54; hospitals: OR 0.105 95% CI 0.02-0.46). Performance of RARP at a high-volume hospital was associated with increased odds of low-cost RARP (OR: 839, 95% CI: 122 to >999). CONCLUSIONS: This study provides insight into the role of surgeons and hospitals on RARP costs. Given the substantial variability, identifying and remedying the root cause of outlier costs may yield substantial benefits.

Urology
Dalela D, and **Abdollah F**. The importance of frailty: Know thy patient *BJU Int* 2016; 117(5):716-717. PMID: 27079481. Full Text

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Urology
Dalela D, **Barod R**, Gandaglia G, Abaza R, Adshead J, Ahlawat R, Buffi N, Challacombe B, Dasgupta P, Moon D, Parekh D, Porpiglia F, Rawal S, Novara G, **Bhandari M**, **Rogers C**, and Mottrie A. Outcomes of robot-assisted partial

nephrectomy in patients with complex renal tumours and pre-existing chronic kidney disease in a multi-institutional, multinational database *Eur Urol, Supplements* 2016; 15(3):e412. PMID: Not assigned. Abstract

D. Dalela, Henry Ford Hospital/Health System, Dept. of Urology, Detroit, United States

INTRODUCTION & OBJECTIVES: Partial nephrectomy can help preserve renal function, but may be more challenging in patients with complex tumours. We compare outcomes of robot-assisted partial nephrectomy (RAPN) for complex tumours in patients with and without pre-existing chronic kidney disease (CKD). MATERIAL & METHODS: Using the Vattikuti Collective Quality Initiative (VCQI) database (representing patients and surgeons from 11 centers across 4 continents), we identified 250 patients undergoing RAPN for complex tumours (identified by RENAL or PADUA score of >10). Peri-operative (estimated blood loss [EBL], warm ischemia time [WIT], complications and surgical margins) and functional outcomes (eGFR at 12-month follow-up) were assessed and stratified by preoperative CKD (CKD stage 3 or greater; n=33, 13.2%) vs. no significant CKD (eGFR >60 ml/min/1.73 m2; n=217, 86.8%). RESULTS: Overall, patients had a median body mass index of 25.7 (23.3-28.9) kg/m2and pre-operative eGFR of 83 (70-98) ml/min/1.73 m2 respectively. 48.4% tumors were >4 cm radius and 29.6% entirely endophytic. 95 (38%) tumours were posterior, 118 (47.2%) mid-polar and 67.2% had renal sinus involvement on preoperative imaging. Patients with CKD were older (median age 62 vs. 54; p=0.001), had higher median age-adjusted Charlson comorbidity score (5.5 vs. 2; p<0.001) and significantly larger tumours (median 4.7 vs. 4 cm; p=0.036) than patients without CKD. There were no significant differences in other tumour characteristics. Perioperatively, there were no significant differences in median WIT (24.5 vs. 22.5 min; p=0.5), operative (OR) time (175 vs. 180 min; p=0.2) and EBL (200 vs. 200 ml; p=0.9) between patients with CKD vs. without. Overall, 22 patients (12.1% in CKD group vs. 8.8% in non-CKD group; p=0.6) required intraoperative blood transfusion. A total of 26 patients overall experienced postoperative complications, of which 9 (3 in CKD group and 6 in non-CKD; p=0.09) were Clavien Grade 3 or higher. Positive surgical margin rates were comparable in the two groups (9.1% and 6.0% in CKD and non-CKD group, respectively). Patients with preoperative CKD had a greater percent decrease in eGFR at median 12-month follow up (4.06% vs. 0.3%; p=0.05). CONCLUSIONS: Despite the surgical challenges, RAPN for patients with complex renal tumours is safe and feasible, even for patients with CKD. Perioperative and functional outcomes 1 year after surgery appear acceptable, despite heterogeneity in surgical techniques, experience and patient population across multiple centers.

Urology

East E, Fullen DR, Arps D, Patel RM, **Palanisamy N**, **Carskadon S**, and Harms PW. Morpheaform basal cell carcinomas with areas of predominantly single-cell pattern of infiltration: Diagnostic utility of p63 and cytokeratin *Am J Dermatopathol* 2016;PMID: 27043336. Full Text

Departments of *Pathology and daggerDermatology, University of Michigan Health System, Ann Arbor MI; double daggerMichigan Center for Translational Pathology, University of Michigan Health System, Ann Arbor MI; and section signDepartment of Urology, Vattikutti Urology Institute, Henry Ford Health System, Detroit, MI.

BACKGROUND: Morpheaform basal cell carcinoma (BCC) is a variant of BCC characterized by narrow strands and nests of basaloid cells with dense sclerotic stroma. The histologic extent often exceeds the clinical impression, leading to high recurrence rates after standard excision. The authors encountered a case with single-cell invasion distant from the main tumor. To date a systematic review of single-cell infiltration in morpheaform BCC has yet to be performed. DESIGN: Ten morpheaform BCCs, 10 nonmorpheaform aggressive BCCs, 5 desmoplastic trichoepitheliomas, and 2 microcystic adnexal carcinomas were identified by database search and confirmed on hematoxylin and eosin. Cases were evaluated by hematoxylin and eosin, immunohistochemical staining for p63, and (in a subset) broad-spectrum cytokeratin. Single-cell pattern was defined as individual cells, 2-cell clusters, or single-file invasion. RESULTS: Three types of single-cell pattern were identified: intratumoral (single cells within the main tumor mass), peripheral, and distant. Single cells were typically a minor component relative to larger tumor nodules and strands. Eight of the 10 cases of morpheaform BCC demonstrated areas of single-cell pattern: 3 intratumoral, 3 peripheral, and 2 with distant spread (0.75 and 1.0 mm from the main tumor). Eight of the 10 aggressive BCC demonstrated a peripheral single-cell pattern. Rare intratumoral single cells were identified in 3/5 desmoplastic trichoepitheliomas and 1/2 microcystic adnexal carcinomas. CONCLUSION: Single-cell pattern is frequently a component of morpheaform BCC. Tumor cells at a significant distance from the main component were unique to morpheaform BCC. Thus, when evaluating margins for morpheaform BCC, increased caution is recommended, and immunohistochemical stains for p63 or cytokeratins may be helpful.

Urology

Eleswarapu S, **Sood A**, **Abdollah F**, **Sammon J**, **Jeong W**, **Dalela D**, **Klett D**, **Peabody J**, Eswara J, **Menon M**, Trinh QD, and **Dabaja A**. Complications following male re-constructive urologic surgery *Eur Urol, Supplements* 2016; 15(3):e326. PMID: Not assigned. Abstract

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INTRODUCTION & OBJECTIVES: To evaluate 30-day morbidity rates following urethroplasty, Inflatable Penile Prosthesis (IPP) placement, Artificial Urinary Sphincter (AUS) placement, and male sling placement; further, to identify procedure-specific predictors of complications. MATERIAL & METHODS: Using the ACS-NSQIP (2005-2012) database, patients undergoing urethroplasty, IPP, AUS, and male sling were identified. Rates for wound, UTI, renal, septic, DVT/PE, pulmonary, cardiac, and neurological complications were recorded. Procedurespecific Multi-Variable logistic regression Analyses (MVA) evaluated the independent effect of age, BMI, race, smoking, alcohol use, preoperative creatinine and hematocrit, comorbidities, and ASA score on complications. RESULTS: Overall, 1,832 patients were identified [urethroplasty (n=472), IPP (n=52), AUS (n=689), and male sling (n=619)]. The overall complication rates for IPP, urethroplasty , AUS, and male sling were 9.6%, 6.4%, 5.5%, and 2.6%, respectively (Fig. 1). Wound and cardiopulmonary complications were the most prevalent complications following IPP, while UTI was the leading complication following urethroplasty and AUS placement. Procedure-specific MVA for predictors of overall complications revealed increasing age (OR=1.05, p<0.001) and hypertension (OR=1.54, p=0.027) to be predictors after AUS; DM (OR=3.05, p<0.001), cardiopulmonary comorbidities (OR=5.46, p=0.013), and ASA score ≥4 (OR=3.98, p=0.013) after urethroplasty; and elevated creatinine (OR=3.27, p=0.044) and cardiopulmonary comorbidities (OR=2.30, p=0.003) after male sling. Small patient number in the IPP cohort precluded performance of MVA. CONCLUSIONS: Among male re-constructive urologic procedures, IPP placement had the highest rate of complications. Identifying predictors of complications may be useful in guiding urologists in risk stratifying patients for elective reconstruction and may facilitate improved physician-patient communication.

Urology

Elgin R, Pacha T, Di Loreto R, and **George V**. Office based photovaporization of the prostate for benign prostatic hyperplasia: Outcomes and patient satisfaction *Urology Practice* 2016; 3(1):70-75. PMID: Not assigned. Abstract

V. George, St. Clair Shores, United States

Introduction: We determined the efficacy, safety and tolerability of photovaporization of the prostate in the office setting for benign prostatic hyperplasia. Methods: Between 2009 and 2011, 139 men with moderate to severe benign prostatic hyperplasia based on I-PSS (International Prostate Symptom Score) underwent photovaporization of the prostate using a 980 nm diode laser under local anesthesia. We compared preoperative and postoperative post-void residual urine volume, maximum urine flow and I-PSS/quality of life questionnaire responses. We also evaluated postoperative complications and patient satisfaction survey responses. Results: An average ± SD of 782.5 ± 811.1 seconds of laser exposure at maximum power (180 W) resulted in a significant change in median post-void residual urine volume (-126 ml or -81.3%), maximum urine flow (4 ml per second or 40.0%) and I-PSS (-19 or -79.2%, each p <0.001). In men with a prostate greater than 70 ml the median change in post-void residual volume was considerably more pronounced at -232.5 ml (-97.9%, p <0.001) while changes in maximum urine flow (3.0 ml per second or 25%, p = 0.027) and I-PSS (-16.5 or -71.7%, p = 0.003) were also significant. The most common complications were vesicular neck contracture in 7% of cases and urinary retention in 6.4%. Conclusions: Office based photovaporization of the prostate can be a safe, effective and well tolerated approach to benign prostatic hyperplasia in office settings using local anesthesia. We believe that it can become an attractive low cost treatment option for the rapidly expanding population at risk for benign prostatic hyperplasia.

Urology

Gandaglia G, Zazzara M, Abaza R, Adshead J, Ahlawat R, Buffi NM, Challacombe B, Dasgupta P, Moon DA, Parekh DJ, Porpiglia F, Rawal S, Novara G, **Rogers C**, **Bhandari M**, and Mottrie A. Preoperative predictors of renal failure after robot-assisted partial nephrectomy: Analysis of the Vattikuti Global Quality Initiative in Robotic Urologic Surgery (GQI-RUS) database *Eur Urol, Supplements* 2016; 15(3):e409. PMID: Not assigned. Abstract

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INTRODUCTION & OBJECTIVES: Previous studies assessed predictors of kidney failure after partial nephrectomy. However, evidence is scarce regarding the impact of preoperative patient characteristics on the risk of renal failure after Robot-Assisted Partial Nephrectomy (RAPN) in patients with Renal Cell Carcinoma (RCC) and normal preoperative renal function. MATERIAL & METHODS: We evaluated 243 patients treated with RAPN for RCC at 10 worldwide centers between 2008 and 2013 included in the Vattikuti Global Quality Initiative in Robotic Urologic Surgery (GQI-RUS) database. All patients included in the study had normal preoperative kidney function, as defined by an estimated GFR (eGFR) ≥90 mL/min/1.73m2. Renal failure after RAPN was defined as a decrease in the eGFR ≥25%. Uni- and multi variable logistic regression analyses assessed the impact of preoperative patient and disease characteristics on the risk of renal failure after surgery. In particular, covariates consisted of age at surgery,

preoperative eGFR, PADUA score, Charlson co morbidity index, and gender. RESULTS: Median age at surgery was 51 years. Median preoperative eGFR and BMI were 103 mL/min/1.73m2 and 29, respectively. Median PADUA score and clinical tumour size were 8 and 34.0 mm, respectively. Overall, 153 (63.0%) vs. 90 (37.0%) patients were male vs. female, respectively. Overall, 99 (40.7%) patients experienced kidney failure immediately after RAPN. In uni variable analyses, age at surgery, PADUA-score and baseline eGFR were significantly associated with the risk of postoperative kidney failure (all P<0.01). In multi variable analyses, older age (Odds Ratio [OR]: 1.05; 95% confidence interval [CI]: 1.01-1.11; P=0.04) and higher PADUA-score (OR: 1.34; 95% CI: 1.02-1.78; P=0.04) represented independent predictors of kidney failure after RAPN. CONCLUSIONS: Age and PADUA-score represent independent preoperative predictors of kidney failure after RAPN in patients with RCC and normal kidney function. These parameters should be considered when planning the surgical approach and counselling patients with regards to the risk of renal surgery.

Urology

Ghani KR, Aly A, **Peabody J**, Lane B, Sarle R, Abaza R, Montgomery J, Hu J, Eun D, Fumo M, Comstock B, Linsell S, Miller DC, and Guru K. Assessment of surgical competency for robot-assisted radical prostatectomy: Development and validation of prostatectomy assessment and competency evaluation (PACE) *Eur Urol, Supplements* 2016; 15(3):e364. PMID: Not assigned. Abstract

K.R. Ghani, University of Michigan, Dept. of Urology, Ann Arbor, United States

INTRODUCTION & OBJECTIVES: With the widespread adoption of robot-assisted surgery, it is vital to ensure skill acquisition and maintenance of competency aligns with best surgical outcomes and patient safety. We aimed to develop and validate a scoring tool for robot-assisted radical prostatectomy (RARP) - Prostatectomy Assessment and Competence Evaluation (PACE) - that objectively measures surgical performance during RARP in qualified surgeons. MATERIAL & METHODS: A multi-institutional study was conducted in two phases using surgeons from the Michigan Urological Surgery Improvement Collaborative (MUSIC), which is a consortium of 42 diverse urology practices in the state of Michigan. The first phase was development and content validation of PACE by a panel of 10 experienced robotic surgeons who deconstructed the critical steps of RARP into 7 key domains utilizing the Delphi methodology. Anchor description for poor and ideal level of performance was assigned Likert scores 1 and 5, respectively. Content validation index (CVI) was used to validate the scoring system and report consensus in phase 1. The second phase assessed reliability through assessment of de-identified RARP videos from 10 attending surgeons within MUSIC. Video clips of the seven key steps for each procedure were placed on a web-based system and rated in a blinded manner by 23 robotic surgeons. Each surgical step was reviewed by at least 4 expert reviewers using a fully crossed design. A weighted average was used to compare scores between surgeons. Inter-rater reliability was established by determining the intra-class correlation (ICC). RESULTS: CVI: The expert panel reached consensus after 3 rounds on all aspects, which included language, relevance of skills assessed, and concordance between the language used and the skill assessed. CVI >0.75 was achieved in 56 statements in the first round, 31 statements in the second, and consensus on the 3 remaining statements after the third. PACE: The seven domains of PACE are bladder drop, preparation of the prostate, bladder neck dissection, dissection of the seminal vesicles and posterior plane, preparation of the neurovascular bundle, apical dissection, and anastomosis. Mean evaluation scores for the ten surgeons ranged from 3.34 to 4.39. Reliability: In this cohort without trainee surgeon performances, ICC values were stable. ICC was strongest (>0.3) for dissection of the bladder neck, dissection of the seminal vesicles, and anastomosis, followed by bladder drop, and neurovascular bundle preparation (0.2 to 0.3). CONCLUSIONS: We describe the first procedure-specific scoring system for RARP validated using video performances from qualified robotic surgeons. PACE allows for evaluation of surgical competency of RARP in qualified surgeons, and may have a role in the assessment of surgical performance. Further work is needed to determine if surgeon scores on specific domains predicts patient outcomes.

Urology

Hanna N, Zavaski M, Gelpi-Hammerchmidt F, Meyer C, **Sammon J**, Kibel A, **Menon M**, Leow J, Sun M, **Abdollah F**, and Trinh QD. Informed decision-making for prostate-specific antigen screening *Eur Urol, Supplements* 2016; 15(3):e94. PMID: Not assigned. Abstract

N. Hanna, Brigham and Women's Hospital, Division of Urologic Surgery, Center for Surgery and Public Health, Boston, United States

INTRODUCTION & OBJECTIVES: Prostate-Specific Antigen (PSA)-based Prostate Cancer (PCa) screening remains a controversial practice. Several guidelines and health care organizations, such as the American Urological Association, advocate counselling and shareddecision making for patients considering PSA screening. We sought to identify patient characteristics associated with physician counselling. MATERIAL & METHODS: Using the latest 2014

Behavioral Risk Factor Surveillance System (BRFSS) dataset, men aged 40 and above without a history of PCa who responded to questions regarding PSA screening were extracted. Age, race, education level, marital status, health insurance, health status, residence location and annual income were included as covariates. The BRFSS PCa screening questionnaire includes two different items regarding informed decision-making of patients, specifically patients were asked whether they have had a discussion regarding the advantages or disadvantages of PSA screening. Complex samples multi-variable logistic regression models were computed to predict the odds of receiving counselling regarding the advantages, disadvantages or either. RESULTS: In 2014, 130,592 men older than 40 years old without a history of PCa responded to both questions regarding PSA counselling (weighted estimate 62.2 million). Of those, 58%, 28% and 60% of patients stated having been counselled of the advantages, disadvantages or either regarding PSA-based PCa screening, respectively. In multi-variable logistic regression analyses predicting the receipt of any informed decision-making, black vs. white (Odds ratio [OR] = 1.87), older men (OR=1.32 for men aged >70 vs. 55-70), insurance status (OR=2.16), higher income (OR=1.34 and 1.59 for 25-50,000$/year and >50,000$/year, respectively) and education level (OR=1.54 and 2.40 for high school and college graduate, respectively) were identified as independent predictors ($p<0.001$). Patients from other race (defined as other than non-Hispanic White and Black) (OR=0.81), men aged 40-55 years (OR=0.27), and unmarried patients (OR=0.75) were less likely to receive counselling. CONCLUSIONS: Disadvantages of PSA screening are less often discussed relative to its benefits. Important sociodemographic characteristics are associated with PSA-based PCa screening informed decision-making. Further research is needed to understand these differences.

Urology

Hwang C, Sethi S, Heilbrun LK, **Gupta NS**, **Chitale DA**, Sakr WA, **Menon M**, **Peabody JO**, Smith DW, Sarkar FH, and Heath EI. Anti-androgenic activity of absorption-enhanced 3, 3'-diindolylmethane in prostatectomy patients *Am J Transl Res* 2016; 8(1):166-176. PMID: 27069550. Full Text

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Consumption of cruciferous vegetables is associated with a decreased risk of developing prostate cancer. Antineoplastic effects of cruciferous vegetables are attributable to bioactive indoles, most prominently, 3, 3'-diindolylmethane (DIM). In addition to effects on proliferation and apoptosis, DIM acts as an antiandrogen in prostate cancer cell lines. This study characterized the effects of prostatic DIM on the androgen receptor (AR) in patients with prostate cancer. Men with localized prostate cancer were treated with a specially formulated DIM capsule designed for enhanced bioavailability (BR-DIM) at a dose of 225 mg orally twice daily for a minimum of 14 days. DIM levels and AR activity were assessed at the time of prostatectomy. Out of 28 evaluable patients, 26 (93%) had detectable prostatic DIM levels, with a mean concentration of 14.2 ng/gm. The mean DIM plasma level on BR-DIM therapy was 9.0 ng/mL; levels were undetectable at baseline and in follow-up samples. AR localization in the prostate was assessed with immunohistochemistry. After BR-DIM therapy, 96% of patients exhibited exclusion of the AR from the cell nucleus. In contrast, in prostate biopsy samples obtained prior to BR-DIM therapy, no patient exhibited AR nuclear exclusion. Declines in PSA were observed in a majority of patients (71%). Compliance was excellent and toxicity was minimal. In summary, BR-DIM treatment resulted in reliable prostatic DIM levels and anti-androgenic biologic effects at well tolerated doses. These results support further investigation of BR-DIM as a chemopreventive and therapeutic agent in prostate cancer.

Urology

Leavitt DA, Motamedinia P, Moran S, Siev M, Zhao PT, Theckumparampil N, Fakhoury M, Elsamra S, Hoenig D, Smith A, and Okeke Z. Can activities of daily living predict complications following percutaneous nephrolithotomy? *J Urol* 2016; 195(6):1805-1809. PMID: 26721225. Full Text

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PURPOSE: Activities of daily living provide information about the functional status of an individual and can predict postoperative complications after general and oncological surgery. However, they have rarely been applied to urology. We evaluated whether deficits in activities of daily living could predict complications after percutaneous nephrolithotomy and how this compares with the Charlson comorbidity index and the ASA((R)) (American Society of Anesthesiologists((R))) classification. MATERIALS AND METHODS: We retrospectively reviewed the records of all patients who underwent percutaneous nephrolithotomy between March 2013 and March 2014. Those with complete assessment of activities of daily living were included in analysis. Perioperative outcomes, complications and hospital length of stay were examined according to the degree of deficits in daily living activities. RESULTS: Overall 176 patients underwent a total of 192 percutaneous nephrolithotomies. Deficits in activities of daily living were seen in 16% of patients, including minor in 9% and major in 7%. Complications developed more frequently in those with vs without deficits in daily living activities (53% vs 31%, p = 0.029) and length of stay was longer (2.0 vs 4.5 days, p = 0.005). On multivariate logistic regression activities of daily living were an independent predictor of complications (OR 1.11, p = 0.01) but ASA classification and Charlson comorbidity index were not. CONCLUSIONS: Activities of daily living are easily evaluated prior to surgery. They independently predict complications following percutaneous nephrolithotomy better than the Charlson comorbidity index or the ASA classification. Preoperative assessment of daily living activities can help risk stratify patients and may inform treatment decisions.

Urology

Löppenberg B, Meyer C, Hanna N, Cole A, Vetterlein M, **Menon M**, **Sammon J**, Leow J, Kibel A, and Trinh QD. Sling procedures for female stress incontinence: Does surgical specialty matter? *Eur Urol, Supplements* 2016; 15(3):e7. PMID: Not assigned. Abstract

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INTRODUCTION & OBJECTIVES: Surgery for stress urinary incontinence (SUI) is one of the most commonly performed procedures in women. These procedures are performed by both gynecologists (GYN), and urologists (URO). Against a backdrop of mass litigation regarding complications following sling procedures (SLING), little is known about outcomes and complications in the immediate postoperative period. We sought to to compare 30-day complications of SLING for SUI between GYN and URO and evaluate differences in patient characteristics using the American College of Surgeons National Surgical Quality Improvement Program database (NSQIP). MATERIAL & METHODS: Relying on the NSQIP Participant User files (2005-2013), patients with procedure code for a SLING in the context of female SUI were extracted. Cases with additional procedures except for minor interventions were excluded. Descriptive and logistic regression analyses were performed to assess the impact of surgical specialty (GYN vs. URO) on patient characteristics, intra-, and postoperative outcomes including 30-day overall complications. Prolonged operative time (pOT) was defined as operative time >75th percentile. RESULTS: A total of 10,508 SLING for female SUI were included with 43.2% (4538/10508) and 56.8% (5970/10508) performed by URO and GYN, respectively. Patients operated by URO were significantly older, had higher comorbidity rates, and more often an American Society of Anesthesiologists Score (ASA) score≥3 (p<0.05, respectively). Of all patients, 17.1% (1802/10508) hat at least one other procedure, with GYN performing significantly more additional procedures compared to URO (22.2% vs. 10.5%, p<0.0001). Overall, 3.5% (376/10508) of the patients experienced a complication, the majority (84.3% [317/376]) being urinary tract infections (UTI). Postoperative outcomes did not differ with respect to 30-day cardiovascular, pulmonary, thrombotic, septic, renal, wound, and bleeding complications. Patients performed by GYN had more UTIs (3.6% vs. 2.3%, odds ratio [OR] 1.55, 95% confidence interval [CI] 1.23-1.97, p<0.0001) and more overall complications (4.1% vs. 2.9%, OR 1.42, 95% CI 1.15-1.76, p=0.001). Reoperation and readmission rates did not differ between specialties. Independent predictors of overall complications were an ASA score≥3 (OR 1.6 95%CI 1.2-2.0; p=0.001), pOT (OR 1.9 95% CI 1.5-2.3; p<0.0001) and the procedure being performed by GYN (OR 1.5 95% CI 1.2-1.9 ;p<0.0001), respectively. CONCLUSIONS: Using a large prospectively collected dataset, GYN had higher complication rates for sling procedures in women. However, the observed difference was small and the majority of complications were UTIs.

Urology

Lovegrove CE, Novara G, Guru K, Mottrie A, Challacombe B, Raza J, Van Der Poel H, **Peabody J**, Popert R, Dasgupta P, and Ahmed K. Learning curve in robot-assisted radical prostatectomy: Practice makes perfect, but what practice? *Eur Urol, Supplements* 2016; 15(3):e363. PMID: Not assigned. Abstract

C.E. Lovegrove, King's College London, Dept. of Urology, London, United Kingdom

INTRODUCTION & OBJECTIVES: Reduced training hours and novel technology require that surgical training be adapted accordingly. Effective use of observation, simulation and clinical practice can enhance progression along the learning curve and promote patient safety. This study sought to examine the effect of prior experience in dry-lab simulation, robotic simulation and clinical experience on the learning curve for technical skills in robot-assisted radical prostatectomy (RARP). MATERIAL & METHODS: A multi-institutional, prospective, observational, longitudinal study was conducted using a validated training tool with a scoring scale to measure technical competence in RARP procedural stages. 15 urology trainees and their mentors from Europe and Australia were recruited to examine their learning curves for the procedure. Their previous experiences were noted to assess what effect this had on the technical competence attained. RESULTS: Over eight months, 15 surgeons were assessed by their mentors in 425 RARP cases (range 7-79). Seven surgeons (46.67%) had prior console experience (range 2-8 months). This was associated with a significant difference in scores attained in six of the 17 procedural stages ($p<0.05$), particularly more challenging steps such as “posterior bladder neck transection” ($p=0.017$), “seminal vesicle dissection” ($p=0.029$) and “apical dissection of the prostate” ($p<0.001$). 11/15 surgeons had experience of robotic simulation (73.34%). This related to significantly higher scores in four stages, notably “apical dissection of the prostate” ($p=0.026$) and “lymph node dissection” ($p=0.034$). 9/15 (60%) surgeons had utilised dry-lab simulation. This was significantly associated to greater technical skill in five stages of RARP. Again, more challenging steps such as “dissection of prostate pedicle and neurovascular bundle +/- nerve preservation” ($p=0.028$) and “vesicourethral anastomosis” ($p=0.006$). Of steps where there was a difference related to prior experience, 10/15 (66.67%) were difficulty level III or IV. CONCLUSIONS: Prior experience in robotic or dry-lab simulation and console experience was associated with significantly greater technical skill in numerous stages of RARP. More difficult steps were frequently associated with a difference in the learning curve attained. Results should be used to design modular curricula to optimise surgical training experiences.

Urology

Meyer C, Feldman A, Sanchez A, Reznor G, Hanske J, Hanna N, Kibel A, **Sammon J**, Cole A, Leow J, Sun M, and Trinh QD. Morbidity, mortality and costs of treatment for locally advanced prostate cancer: A populationbased analysis comparing radical prostatectomy and external beam radiation *Eur Urol, Supplements* 2016; 15(3):e71. PMID: Not assigned. Abstract

C. Meyer, Brigham and Women's Hospital, Division of Urologic Surgery, Center for Surgery and Public Health, Boston, United States

INTRODUCTION & OBJECTIVES: To compare the effect of primary External Beam Radiation Therapy (EBRT) or Radical Prostatectomy (RP) on urinary, sexual and Aastrointestinal (GI) toxicities, Androgen Deprivation Therapy (ADT) use, morbidity, mortality and costs in patients with locally advanced (cT3) Prostate Cancer (PCa). MATERIAL & METHODS: Relying on the Surveillance, Epidemiology, and End Results (SEER)-Medicare insurance program linked database, 3387 patients were found to be eligible. Cox proportional hazard and Cox regression models were fitted to predict toxicities, ADT, all-cause and cancer-specific mortality. Quantile regression analyses were employed to assess the total and cancer specific incremental therapy costs after 1-, 2-, and 5 years. RESULTS: In our cohort, 1613 (47.6%) men received RP with a mean follow-up of 11.3 (SD: 6.1) years and 1774 (52.4%) received EBRT with a mean follow-up of 7.3 (SD: 4.1) years ($p<0.001$). Patients with RP had significantly higher odds of urinary toxicities (HR 2.74, 95% CI 2.1-3.57) and sexual toxicities (HR 6.43, 95% CI 3.47-11.9), whereas RP men were less susceptible to GI toxicities (HR: 0.68, 95% CI: 0.51-091). EBRT was associated with a higher risk of ADT at 5 years (HR 1.5, 95% CI 1.2-1.9) ($p<0.001$). The EBRT group had significantly higher overall (HR: 1.65, 95% CI: 1.47-1.84) and PCa-specific (HR: 2.29, 95% CI: 1.8-2.9) mortality. RP treatment was associated with lower PCa-specific expenditures after 5 years [-$2275 (95% CI -$1542 to -$3008)], but no different with regard to total incremental costs [-$1700 (95% CI +$627 to -$4028)]. Overall, the EBRT group had significantly higher (HR: 1.65, 95% CI: 1.47-1.84) and PCa-specific (HR: 2.29, 95% CI: 1.8-2.9) mortality. CONCLUSIONS: We demonstrate significant differences in toxicity and mortality profiles of RP and EBRT for treatment of locally advanced PCa. While RP was significantly associated with worse urinary and sexual outcomes, EBRT patients were more likely to receive ADT and incur higher treatment costs.

Urology

Meyer C, Friedlander D, Choi K, Cole A, **Abdollah F**, Hanske J, Zavaski M, **Sammon J**, Leow J, **Menon M**, Sun M, Kibel A, and Trinh QD. A nationwide survey of prostate specific antigen based screening and counseling for prostate cancer *Eur Urol, Supplements* 2016; 15(3):e93. PMID: Not assigned. Abstract

C. Meyer, Brigham and Women's Hospital, Dept. of Urologic Surgery, Center for Surgery and Public Health, Boston, United States

INTRODUCTION & OBJECTIVES: Prostate cancer represents a significant socioeconomic burden on the US health care system. Significant controversy surrounds the routine use of PSA-based screening for prostate cancer following the 2012 USPSTF's recommendation against screening, regardless of age. While there is significant literature demonstrating decreased PSA utilization since 2012, there is limited evidence evaluating the impact of the USPSTF recommendation on provider PSA counseling and patient perceptions of the PSA test following the 2012 guideline release. We sought to explore the association of prostate cancer screening counseling with patient sociodemographic factors in a nationally representative sample. MATERIAL & METHODS: Using data from the 2013 Health Information National Trends Survey, we identified 768 men (unweighted) between the ages of 40 and 75 without a prior prostate cancer diagnosis who responded to survey data pertaining to PSA counseling. Using logistical regression models, we assessed overall population trends in prostate cancer screening, counseling and PSA utilization. RESULTS: Over half (54.1%) of respondents reported ever having a PSA test performed. Men undergoing PSA testing were more likely to have had a prior cancer diagnosis other than prostate cancer (OR 3.58, 95% CI 1.09-11.72), older (65-75 years of age) (OR 10.17, 95% CI 3.97-26.03), and to have at least some college education (OR 10.58, 95% CI 3.10-36.12). In terms of PSA counseling, prior cancer history (OR 2.47, 95% CI 1.15-5.31) and older age (OR 4.82, 95% CI 1.49-15.59) were associated with greater odds of being counseled on the potential adverse side effects associated with prostate cancer treatment. Similarly, older men were more likely to discuss the PSA test with a health care professional (OR 5.32, 95% CI 2.15-13.16), more likely to be informed by a health care professional that there is controversy among experts regarding the use of PSA screening (OR 3.44, 95% CI 1.03-11.51) and that certain forms of prostate cancer are slow growing (OR 6.76, 95% CI 2.26-20.23). CONCLUSIONS: We show that certain subgroups of men receive substantially different counseling regarding PSA screening. While some of these observations may represent appropriate counseling in the setting of the recent USPSTF guidelines, health care providers should be aware of these potential biases and their impact on shared patient-provider decision making prior to counseling patients on PSA testing.

Urology

Meyer C, **Sood A**, **Abdollah F**, **Sammon J**, Vetterlein M, Löppenberg B, Hanske J, Leow J, Cole A, Sun M, **Menon M**, and Trinh QD. Minimally invasive vs open radical prostatectomy: An analysis of 30-day postoperative complications, unplanned readmissions, and mortality *Eur Urol, Supplements* 2016; 15(3):e443. PMID: Not assigned. Abstract

C. Meyer, Brigham and Women's Hospital, Division of Urologic Surgery, Center for Surgery and Public Health, Boston, United States

INTRODUCTION & OBJECTIVES: In the current state of increasing medical expenditures, a critical appraisal of the benefits of minimally invasive surgery (MIS) in radical prostatectomy is needed, but lacking. Established benefits of MIS remain limited to reduced pain, lower blood loss, shorter hospital stay, better cosmesis and decreased surgical site infections. We sought to compare MIS vs. open RP with regard to 30-day postoperative outcomes including Clavien-Dindo graded complications, hospital stay, unplanned readmission and mortality. MATERIAL & METHODS: The American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database provides a unique opportunity to evaluate 30-day outcomes following surgery. Relying on the ACS-NSQIP database (2005-2013), patients undergoing RP were identified. Non-parsimonious propensity score methods were used to construct procedure-specific matched-pair cohorts that reduced baseline differences between patients who underwent MIS RP as opposed to those that did not. Logistic regression models evaluated the association between surgical approaches for RP and outcomes. Bonferroni correction for multiple comparisons was applied and a $p<0.006$ was considered significant. Primary endpoints were Clavien-Dindo graded complications (I-V) and unplanned readmission within 30 days of surgery. RESULTS: After propensity score matching, 5,401 patients underwent open or MIS RP, resulting in an overall sample of n=10,802. Within the procedure-specific matched-pairs, open RP was associated with significantly higher odds for Clavien-Dindo grade I-II, III and IV complications (OR=1.87, 95%CI=1.57-2.24; OR=1.93, 95%CI=1.33-2.81; OR=1.69, 95%CI=1.18-2.42 and OR=3.97, 95%CI=1.07- 14.79,respectively), and unplanned readmissions (OR=1.08, 95% CI =0.98-1.18). CONCLUSIONS: Open RP was associated with increased 30-day postoperative complications and unplanned readmissions. These findings have important implications on patient safety and health care costs. The utilization of MIS represents a modifiable factor of surgical outcomes, and its use should be strongly considered in suitable patients.

Urology

Meyer C, Trinh QD, Vetterlein M, Löppenberg B, Hanske J, Leow J, **Sammon J**, **Abdollah F**, **Menon M**, Kibel A, Chang S, Choueiri T, and Sun M. Trends of metastasectomy for metastatic renal cell carcinoma and their impact on overall survival *Eur Urol, Supplements* 2016; 15(3):e755. PMID: Not assigned. Abstract

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INTRODUCTION & OBJECTIVES: The treatment of metastatic renal cell carcinoma (mRCC) has profoundly changed over the last decade. There is little comprehensive evidence evaluating the role of metastasectomy (MSx) in in this context. We assessed trends and predictors of MSx and their impact on overall survival in a large national cohort. MATERIAL & METHODS: The National Cancer Data Base from 1998-2012 was queried to identify 25455 mRCC patients with 5315 undergoing MSx. Covariates included the application of targeted chemotherapy (CTX) and immunotherapy (ITX). Baseline descriptive and multivariable logistic regression analyses for prediction of MSx were conducted. Trends for chemo- (CTX) and immunotherapy (ITX) as well as MSx were assessed using the annual percent change linear regression technique (EAPC). Kaplan-Meier curves and adjusted Coxproportional hazard models assessed the impact of MSx on overall survival. RESULTS: Compared to controls, MSx patients were significantly younger (p<0.001), had a lower CCI (p=0.03), more often private insurance (p=0.04) and a higher income (p<0.001). They were more often treated at an academic center (p<0.001), but less often received ITX/CTX (both p<0.001). The rates of MSx increased significantly over the years (9.9-24.5%, EAPC 4.52, p<0.001) while CTX (EAPC 3.08, p<0.001) increased and ITX decreased (EAPC -12.9, p<0.001). Diagnosis after 2006 (OR 1.21, 95%CI 1.02-1.23) and private insurance (OR 1.43, 95% CI 1.14-1.79) were positive predictors of MSx, whereas increasing age (OR 0.98, 95%CI 0.98-0.99), black race (OR 0.73, 95%CI 0.63-0.84), ITX (OR 0.8, 95%CI 0.68-0.94) and CTX (OR 0.75, 95% 0.69-0.82) were negatively associated with MSx. The combined treatment with MSx conferred a survival benefit compared to no MSx (HR 0.75, 95%CI 0.72-0.78) and CTX alone (HR 0.82, 95%CI 0.74- 0.90). CONCLUSIONS: The addition of MSx to CTX conferred a survival benefit in our study despite lower usage of MSx after CTX. This suggests a potential underutilization, which might be a consequence of underlying health care access disparities as implied by lower odds of receiving MSx in blacks and higher odds in privately insured patients.

Urology

Meyer C, Zavaski M, Hanske J, Friedlander D, Cheng P, **Menon M**, Kibel A, Cole A, Leow J, **Abdollah F**, Sun M, **Sammon J**, and Trinh QD. Differences in prostate specific antigen testing among urologists and primary care providers in the United States following the 2011 USPSTF recommendations *Eur Urol, Supplements* 2016; 15(3):e90. PMID: Not assigned. Abstract

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INTRODUCTION & OBJECTIVES: Following the 2011 recommendations by the United States Preventive Services Task Force (USPSTF) to discontinue Prostate Cancer Screening with PSA testing, data suggest the use of PSA screening is broadly decreasing in the United States (US). To further understand the heterogeneity in screening practices, we examine the use of PSA testing among urologists versus Primary Care Providers (PCPs) before and after the latest USPSTF recommendations. MATERIAL & METHODS: We used the National Ambulatory Medical Care Survey (NAMCS) to examine the use of PSA testing in 2010 and 2012. The NAMCS is an annual, nationally representative, survey of ambulatory care in the United States, and collects information about outpatient practices of physicians, as well as visit-level patient demographics, reasons for consultation, diagnoses and medication. We included all outpatient visits for men aged 50-74 (n=1222) who presented to a urologist (9.2%, n=113) or a PCP (80.8%, n=1109) (including general and family practice, internal medicine) for a 'preventive care' visit. Men with previous prostate-related diagnoses were excluded. This resulted in a weighted sample of 27 million (unweighted n=1164) eligible visits in 2010 and 2012. We examined the frequency of PSA testing according to provider speciality and year to evaluate whether the 2011 USPSTF recommendations were associated with a decrease in PSA testing in men 50-74. Results were weighted to reflect the US population based on the complex survey design and a 2-sided level of significance was set at p <0.05. RESULTS: The use of PSA testing among 50-74 year old men decreased from 36.5 to 16.4% among PCP visits, whereas it decreased from 38.7 to 34.5% among urology visits. The decrease in PSA testing was significant among primary care physicians (p=0.009), but not among urologists (p=0.089) (Figure 1). CONCLUSIONS: Our findings elucidate a differential effect of the 2011 USPSTF recommendations on PSA testing among PCPs and urologists. This likely reflects opposing provider perceptions on the benefit of PSA screening, conflicting guidelines and perhaps differences in patient demographics or expectations. This study suggests further need for a dialogue between PCPs and urologists to achieve a consensus statement on prostate cancer screening.

Urology

Ross A, Den R, Yousefi K, Trock B, Davicioni E, Tosoian J, Thompson D, Choeurng V, Haddad Z, Tran P, Trabulsi E, Gomella L, Lallas C, **Abdollah F**, Feng F, Dicker A, Freedland S, Karnes J, and Schaeffer E. Efficacy of early and

delayed radiation in a prostatectomy cohort adjusted for genomic and clinical risk *Eur Urol, Supplements* 2016; 15(3):e435. PMID: Abstract

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INTRODUCTION & OBJECTIVES: In 3 published randomized clinical trials, adjuvant radiation therapy (ART) for prostate cancer (PCa) resulted in improved progression free survival. However, the impact on metastases and overall survival is unclear. To date, there have been no published prospective trials examining the impact of Salvage Radiation Therapy (SRT) in this disease state. Hence, we conducted a retrospective, non-randomized comparative study of adjuvant, salvage, or no radiation following radical prostatectomy (RP) for men with pT3 disease or positive margins (Adverse Pathologic Features, APF). MATERIAL & METHODS: 422 PCa patients treated at four institutions with RP and having APF were analyzed with a primary end point of clinical metastasis. Men undergoing ART (n=111), early SRT (n=70) and delayed SRT (n=83) were defined by having prostate specific antigen (PSA) levels of <0.2, 0.2 to 0.5, and ≥0.5 ng/mL, respectively, prior to initiation of Radiation Therapy (RT). Remaining 157 patients who did not receive additional therapy (RT or hormonal) prior to metastatic onset formed the no RT group. Clinical-genomic risk was assessed by CAPRA-S and Decipher. Cox univariable (UVA) and multivariable (MVA) proportional hazards models were used to evaluate the impact of treatment on outcome. RESULTS: During study follow-up, 37 patients developed metastasis with a median follow-up of 8 years. Both CAPRA-S and Decipher had independent predictive value on MVA for metastatic outcome (both p<0.05). On MVA adjusting for clinical and genomic risk, delayed SRT and no RT had a hazard ratio (HR) of 4.31 (95% confidence interval [CI], 1.20-15.47) and 5.42 (95% CI, 1.59-18.44) for metastasis compared to ART as the reference group. No significance difference was observed between early SRT and ART groups (p=0.28). Men with low to intermediate CAPRA-S scores and low Decipher risk have a low rate of metastatic events regardless of treatment selection. In contrast, men with high CAPRA-S and Decipher scores benefit from ART, however the cumulative incidence of metastasis remains high. CONCLUSIONS: The decision as to the timing and need for additional local therapy following RP is nuanced and requires providers and patients to balance risks of morbidity with improved oncologic outcomes. This analysis provides the most robust and accurate quantification of risk for these patients. Post-RP treatment can be safely avoided for men who are low risk by clinical-genomic risk, whereas those at high risk should strongly favor enrollment in clinical trials.

Urology

Schmid M, Krishna N, Ravi P, Meyer CP, Becker A, **Dalela D**, **Sood A**, Chun FK, Kibel AS, **Menon M**, Fisch M, Trinh QD, and Sun M. Trends of acute kidney injury after radical or partial nephrectomy for renal cell carcinoma *Urol Oncol* 2016;PMID: 27033047. Full Text

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OBJECTIVES: To investigate the prevalence, temporal trends, and predictors of postoperative acute kidney injury (AKI) in a large cohort of patients with renal cell carcinoma treated with radical or partial nephrectomy. METHODS: Between January 1998 and December 2010, patients who underwent radical or partial tumor nephrectomy were identified within the Nationwide Inpatient Sample. First, prevalence and temporal trends of AKI were analyzed. Second, predictors of AKI were identified using multivariable regression analyses. Third, associations between AKI and in-hospital complications, length of stay, hospital costs, and in-hospital mortality were evaluated using logistic regression models adjusted for clustering. RESULTS: Of total 253,046 patients, 5.5% (14,303 in radical and 3,525 in partial nephrectomy) experienced AKI. Rates of AKI significantly increased from 2.0% in 1998 to 10.4% in 2010 (P<0.001). Predictors of AKI included male sex, radical nephrectomy, more contemporary years (2004-2010), older age, black race, higher comorbidities, higher preoperative chronic kidney disease stage, Medicare insurance status, and nephrectomy at urban hospitals (all P<0.01). Postoperative AKI during hospitalization was associated with an increased rate of in-hospital mortality, any complications, transfusion, prolonged length of stay, and higher hospital costs (all P<0.001). CONCLUSIONS: Rising rates of in-hospital AKI after radical and partial nephrectomy were observed. Increasing awareness of AKI, identification of patients at risk before surgery, early postoperative AKI

diagnosis, collaboration with nephrologists, implementation of renoprotective strategies, long-term renal functional follow-up, and a well-designed prospective study, may be warranted.

Urology
Sood A, Ghosh P, **Jeong W**, **Bhandari M**, Ahlawat R, and **Menon M**. Robotic kidney transplantation with regional hypothermia: Results from a prospective two-arm non-randomized controlled trial (Ideal phase 2b) *Eur Urol, Supplements* 2016; 15(3):e715. PMID: Not assigned. Abstract

A. Sood, Henry Ford Hospital/Health System, Dept. of Urology, Detroit, United States

INTRODUCTION & OBJECTIVES: Minimally invasive approaches to kidney transplantation are up-coming. We recently developed and described a novel technique of robotic KT (RKT) using intra corporeal graft cooling. Here, we assess the comparative effectiveness of RKT and open KT (OKT) by evaluating peri- and postoperative outcomes. MATERIAL & METHODS: From January-December 2013, a total of 247 patients with end stage renal disease underwent KT at a tertiary referral center of which 225 patients who met the selection criteria (live donor, first transplant, single organ transplant and low-intermediate immunologic risk) were enrolled into this prospective two-arm non-randomized controlled trial (IDEAL Phase-2b). Primary outcome was post transplant graft function. Secondary outcomes included surgical and immunologic complications, and perioperative parameters. All patients had a minimum follow up of 6 months. RESULTS: Fifty and 175 patients underwent RKT and OKT, respectively. The baseline characteristics of the two groups were comparable. Mean serum creatinine at discharge was 1.2 and 1.3 mg/dl in RKT and OKT patients respectively (p=0.71). Post-operative pain and analgesic requirements were significantly less in patients undergoing RKT (p=0.01). None of the RKT patients developed any wound complications and none had delayed graft function. Eleven patients in the RKT group required a biopsy and 7 developed acute rejection. One RKT patient and 4 (2.2%) of OKT needed post-transplant dialysis. No lymphocele was detected on protocol non-contrast CT done at 3 months in the RKT group (0% vs. 23.8% in OKT; p=0.05). One graft was lost in the OKT group. One patient death in RKT (1.5 months post transplant, cardiac failure) and 2 in OKT group were noted, respectively. CONCLUSIONS: RKT with regional hypothermia is safe and easily reproducible. Early outcomes are equivalent to OKT; with trends towards lower complications, quicker graft function recovery and shorter patient convalescence.

Urology
Sood A, **Sammon J**, **Abdollah F**, **Klett D**, **Dalela D**, Kibel A, **Pucheril D**, Schmid M, **Jeong W**, **Dabaja A**, **Rogers C**, **Peabody J**, **Menon M**, Trinh Q, and **Abdollah F**. Complications after adrenalectomy-does the speciality matter? *Eur Urol, Supplements* 2016; 15(3):e485. PMID: Not assigned. Abstract

A. Sood, Henry Ford Hospital/Health System, Dept. of Urology, Detroit, United States

INTRODUCTION & OBJECTIVES: To evaluate the rates of 30-day complications post adrenalectomy and stratify them into pre- vs. postdischarge; further, to investigate the impact of speciality (general surgery vs. urology) on these outcomes using a large multi-institutional database. MATERIAL & METHODS: Relying on the American College of Surgeons National Surgical Quality Improvement Program (2005-2011) database, patients undergoing adrenalectomy were identified. Complication rates were evaluated in relation to discharge. Multi-variable logistic regression models assessed the association between speciality and the risk of 30-day morbidity (complications, prolonged length of stay, re-intervention and readmission) and mortality. RESULTS: Overall, 4844 patients underwent adrenalectomy (95.7% general surgery, n=4636). Patients presenting to urology were older (median age 57 vs. 54, p=0.004), of male gender (51.4% vs. 39.6%, p=0.001) and were likely to undergo adrenalectomy for cancer (10.1% vs. 5.8%, p=0.010). The overall rate of complications was 7.5% (Fig 1), with the majority of major complications including renal, septic, DVT/PE, pulmonary, cardiac and neurological occurring prior to discharge (70.1%) while the majority of minor complications including wound and UTI occurring post-discharge (57.2%). In both uni-variable and multi-variable analyses, the speciality did not seem to have any effect on the outcomes (Fig 1). CONCLUSIONS: Urology service performs adrenalectomy for older males with cancer in comparison to general surgery service. 1 in 13 patients will have a complication post-adrenalectomy with the serious complications occurring primarily pre-discharge (70%). Speciality did not seem to affect the outcomes in the NSQIP participant hospitals.

Urology
Vetterlein M, Meyer C, Löppenberg B, **Sammon J**, Hanske J, **Menon M**, Preston M, Chun F, Kibel A, Fisch M, and Trinh QD. Radical cystectomy for bladder cancer vs non-malignant indications: Preoperative predictors of perioperative outcomes in a sample of 3269 patients *Eur Urol, Supplements* 2016; 15(3):e632. PMID: Not assigned. Abstract

M. Vetterlein, Brigham and Women's Hospital, Dept. of Urologic Surgery and Center, Surgery and Public Health, Boston, United States

INTRODUCTION & OBJECTIVES: Radical cystectomy is a standard first-line treatment for muscle-invasive Bladder Cancer [BCA], but also an option for select refractory benign bladder conditions. Although both groups usually differ in their baseline characteristics, postoperative treatment standards are commonly identical. Little is known about the difference in peri- and postoperative outcomes between these cohorts. This study aims to evaluate postoperative complications and their predictors to optimize risk-adapted postoperative care. MATERIAL & METHODS: Relying on the American College of Surgeons National Surgical Quality Improvement Program database (2006- 2013) all cases with current procedural terminology codes for cystectomy were abstracted and stratified into malignant vs. benign. Descriptive and multi-variable binominal logistic regression analyses were performed to identify independent predictors of short-term 30-day outcomes including complications, prolonged [>75th percentile] Length Of Stay [pLOS] and prolonged [>75th percentile] Operative Time [pOT]. RESULTS: A total of 3269 cases were included, of which 92.8% (n=3033) and 7.2% (236) were for malignant and benign indications, respectively. In unadjusted analyses, non-cancer patients had significantly higher proportions of postoperative sepsis (16.9 vs. 12.3%, p=0.04), pLOS (38.1 vs. 26.6%, p <0.001), and postoperative Urinary Tract Infections [UTI], while cancer patients had higher proportions of pOT (34.2 vs. 25.0%, p=0.004) and continent urinary diversions (19% vs. 11.4%, p=0.004). In adjusted analyses, patients in the benign group had a 1.7-fold higher likelihood of pLOS (95% confidence interval [CI] 1.29-2.44, p<0.001) and lower odds of pOT (OR 0.56, 95% CI 0.40-0.79, p<0.001) compared to BCA patients. Preoperative systemic sepsis (odds ratio [OR] 5.05, [CI] 2.55-10.01, p<0.001), para- or quadriplegia (OR 5.35, [CI] 2.07-13.88, p<0.001) and partially dependent Functional Health Status [FHS] (OR 1.96, [CI] 1.13-3.40, p=0.017) were independent predictors of pLOS. Furthermore, continent diversion was significantly associated with overall (OR 1.39, [CI] 1.14-1.70, p=0.001) and septic complications (OR 1.42, [CI] 1.09-1.86, p=0.009). CONCLUSIONS: Patients undergoing radical cystectomy for benign, treatment-refractory conditions are associated with increased septic complications and pLOS possibly due to impaired FHS, preoperative UTI and preoperative septic events. Our findings warrant a stringent and individual preoperative assessment in these patients to circumvent potentially fatal outcomes.