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Resolution of right atrial congestion before LVAD implantation is associated with improved outcomes

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OBJECTIVES/SPECIFIC AIMS: Increased right atrial pressure is known to be a predictor of poor outcomes after LVAD implantation. Whether resolution of right heart congestion prior to LVAD implantation is associated with more favorable outcomes is not well understood. METHODS/STUDY POPULATION: We analyzed LVAD recipients from our institution from 1/1/2015 to 2/28/2018. We excluded patients bridged to LVAD with ECMO support. Patients with admission right atrial pressure (RAPadmit) and implant RAP (RAPimplant) ≥ 14 mmHg were defined as having persistent congestion, while patients with RAPadmit ≥ 14 mmHg and RAPimplant < 14 mmHg were defined as having resolved congestion. Baseline characteristics between groups were compared using the Chi-square and unpaired t-tests. Time to death or RVAD was compared between groups using Cox proportional hazards models. RESULTS/ANTICIPATED RESULTS: Of 57 LVAD recipients with RAPadmit ≥ 14 mmHg, 14 (25%) had persistent congestion at the time of LVAD implantation. While there were no statistically significant differences between groups, patients with persistent congestion were more likely to be INTERMACS profile 1 (21.4% vs 9.5%), less likely to have a destination therapy device strategy (28.6% vs 34.9%), less likely to have moderate or severe right ventricular (RV) dysfunction (64.3% vs 83.7%), and had similar RAPadmit (20.4 mmHg vs 18.9 mmHg) compared to patients with resolved congestion. Median follow up was 307 days. Patients with persistent congestion had a higher frequency of death or RVAD implantation compared to those with resolved congestion (50% vs 14%, HR 3.75, 95% CI 1.25–11.25, p=0.02). DISCUSSION/SIGNIFICANCE OF IMPACT: Among patients with elevated RAP at admission, patients with persistently elevated RAP at the time of LVAD implantation had worse outcomes than patients who were able to be decongested prior to surgery. These data support optimization of RV filling pressures prior to LVAD surgery.

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Risk of substance abuse onset in adults diagnosed with epilepsy or migraine

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OBJECTIVES/SPECIFIC AIMS: The study investigated whether adults diagnosed with epilepsy or migraine (a neurological disorder with common features to epilepsy) are at increased risk for developing substance abuse disorders following diagnosis compared to (presumably healthy) adults with lower extremity fracture (LEF). METHODS/STUDY POPULATION: A retrospective cohort analysis was conducted using a subset of surveillance data of hospital admissions, emergency department visits and outpatient visits in South Carolina, USA from January 1, 2000 through December 31, 2011. Individuals aged 18 years or older were identified using the International Classification of Disease, 9th Revision Clinical modification (ICD-9) with a diagnosis of epilepsy (epilepsy-cohort 1; n = 78,547; 52.7% female, mean age [SD] 51.3 years [19.2]), migraine (migraine-cohort 2; n = 121,155; 81.5% female, mean age [SD] 40.0 years [14.5]), or LEF (control cohort; n = 73,911; 55.4% female, mean age [SD] 48.7 years [18.7]). Individuals with substance abuse or dependence diagnosis following epilepsy, migraine, or LEF were identified with ICD-9 codes. Cox proportional hazard regression analyses modelled the time to substance abuse diagnosis comparing epilepsy to LEF and comparing migraine to LEF. RESULTS/ANTICIPATED RESULTS: Adjusting for insurance payer, age and sex, adults with epilepsy are diagnosed with substance abuse disorders at 2.5 times the rate of those with LEF [HR 2.54 (2.43, 2.67)] and adults with migraine are diagnosed with substance abuse disorders at 1.10 times the rate of those with LEF [HR 1.10 (1.04, 1.16)]. An interaction between exposure and insurance payer was found with hazard ratios comparing epilepsy to LEF of 4.56, 3.60, and 1.94 within the commercial payer, uninsured and Medicaid strata, respectively. DISCUSSION/SIGNIFICANCE OF IMPACT: Compared to adults with LEF, adults with epilepsy had a substantially higher hazard of subsequent substance abuse, while adults with migraine showed a small, but still significant, increased hazard of subsequent substance abuse.

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Serum Metabolites from the Trimethylamine Pathway Associate with Left Ventricular Diastolic Function: The Bogalusa Heart Study

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OBJECTIVES/SPECIFIC AIMS: This population-based study aims to assess the individual and collective relationship between TMA-associated metabolites and echocardiographic parameters of left ventricular diastolic function. METHODS/STUDY POPULATION: The study cohort consisted of 1,039 adult participants of the Bogalusa Heart Study (35.13% black, 57.94% female, aged 33.60 to 57.47 years). Left ventricular diastolic function was assessed via two dimensional and tissue Doppler echocardiography. Echocardiographic parameters of diastolic function included peak early (E, cm/s) and late transmitral flow velocities (A, cm/s), septal mitral annular velocity (e', cm/s), left ventricular isovolumic relaxation time (IVRT, ms), and peak early diastolic transmitral flow velocity deceleration time (DT, ms). Metabolomic analysis of fasting serum samples was conducted via ultrahigh performance liquid chromatography-tandem mass spectroscopy. Six metabolites in the TMA pathway, carnitine, choline, TMAO, betaine, ergothioneine, dimethylglycine, and two composite variables, the betaine/choline ratio as well as the weighted sum of the six TMA-associated metabolites (TMA score), were selected a priori and tested for association with echocardiographic parameters of diastolic function. Raw metabolite values were divided by their respective standard deviation to create an exposure variable for each individual metabolite. The betaine/choline ratio was calculated utilizing the raw value of each metabolite. The z-score method was used to transform the six metabolites to the same scale and these values were used to calculate the TMA score. Multivariable-adjusted linear regression models were employed to assess the relationship of TMA-associated metabolites with echocardiographic measures of diastolic function. Covariates adjusted for included sex, age, race, education, alcohol drinking, cigarette smoking, heart rate, systolic blood pressure, glomerular filtrate rate, body mass index, low density lipoprotein cholesterol, high density lipoprotein cholesterol, hemoglobin A1c, serum triglycerides, as

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well as blood pressure-, lipid-, and glucose-lowering medications. RESULTS/ANTICIPATED RESULTS: After stringent Bonferroni correction for multiple testing, four TMA-associated metabolites as well the TMA score were significantly associated with diastolic function. TMAO was inversely associated with IVRT (ß = −0.002 (0.00); p-value = 2.00E-03). Betaine (ß = 0.40 (0.08); p-value = 2.10E-07), carnitine (ß = 0.30 (0.07); p-value = 7.80E-05), dimethylglycine (ß = 0.27 (0.07); p-value = 3.00E-04), and the TMA score (ß = 0.10 (0.02); p-value = 3.40E-05), were positively associated with the septal E/e' ratio. No significant associations were observed between metabolites or metabolite composite scores from the TMA pathway and the E/A ratio or DT. DISCUSSION/SIGNIFICANCE OF IMPACT: This is the first population-based study to assess the role of TMA-associated metabolites in left ventricular diastolic function. Betaine, carnitine, dimethylglycine, and a metabolite score combining serum metabolites from the TMA pathway were positively associated with the septal E/e' ratio, suggesting that a higher concentration of TMA-associated metabolites correlates with impaired diastolic function. These results suggest that both individual and grouped metabolites from the TMA pathway may serve as early biomarkers for pre-clinical diastolic dysfunction, an important causal factor for HFpEF. Future longitudinal, multi-omic studies incorporating microbiome, metabolomic and dietary analyses are needed to characterize the risk of ventricular diastolic function and HFpEF in the setting of exposure to TMA-associated metabolites.

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Sex Differences in Vitamin D and Urinary Stone Disease

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OBJECTIVES/SPECIFIC AIMS: More men than women develop urinary stones and their prevalence alters in women with menopause suggesting a steroidal influence. In men the incidence of stones is highest during July and August suggesting that environmental factors such as Vitamin D (VitD), a steroid, may affect stone formation. Previous studies have found differences in the development of stones between men and women; however, the reasons for sex differences in stone formation and type remain unclear. METHODS/STUDY POPULATION: We examined VitD levels in men and women (n = 18,753) that had no diseases based on a lack of an ICD-9 or ICD-10 code in their electronic medical record. We found that normal, healthy women had significantly higher levels of sera VitD compared to men (p = 6x10-6). We then examined whether sex differences existed for key endpoints/data from the Mayo Clinic Urinary Stone Disease (USD) Registry, which has around 1,600 urinary stone patients that are well-phenotyped according to sex, age and stone type. RESULTS/ANTICIPATED RESULTS: Control women were found to have higher sera VitD levels than men, but the sex difference no longer exists in kidney stone disease patients. When we further separated by race, we found that differences in VitD levels reappeared; this suggests that race also plays a role in sera VitD variances. DISCUSSION/SIGNIFICANCE OF IMPACT: We are developing a disease severity score, which we will use to correlate to sera VitD levels in patients according to sex, age and race. Future analyses will take into account whether subjects had VitD and calcium supplementation. This project begins to explore the mechanism behind the sex differences known to exist in urinary stone disease, which is critically needed to provide improved diagnosis and therapy for this debilitating disease.

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Temporal Trends and Outcomes of Opioid Abuse among Adolescents & Young Adult Sickle Cell Disease Patients

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OBJECTIVES/SPECIFIC AIMS: In this study, we aim to describe temporal trends in opioid abuse among adolescents and 11-21years and young adults 22-35years with Sickle cell disease hospitalized for sickle cell crisis. We also aim to evaluate clinical and healthcare utilization outcomes of opioid abuse in the same population. In addition, we hope to assess for difference in effect by age category. METHODS/STUDY POPULATION: Our study is a cross-sectional study of data secondarily sourced from the 2007-2014 National Inpatient Sample(NIS), a component of the Healthcare Utilization Project (HCUP). Variables were identified using ICD-9-CM codes. We selected inpatient stays for patients aged 11-35 years admitted for sickle cell crisis. Opioid abuse was the primary outcome of interest. Secondary outcomes were inpatient mortality, total charge, length of stay and select clinical outcomes. We analyzed our data for trends and outcomes. We performed trend analysis of prevalence rates between 2007-2014 by age categories. Propensity-Matched Score regression models were deployed to assess for associations between opioid abuse and outcomes while adjusting for relevant covariates. Sub-group analysis of opioid abuse by age was assessed for outcomes of interest. Trend analysis was performed on Joinpoint Software v4.6.0, (National Cancer Institute, NIH, Bethesda, MD). Outcome analysis was performed on SAS v9.4 (SAS Institute, Cary, NC). Statistical significance was set at 95% and p-value of 0.05, two-tailed. RESULTS/ANTICIPATED RESULTS: Of 86,827 inpatients admitted for sickle cell crisis, 2,363 (2.73%) had a diagnosis of opioid abuse while 84,464 (97.27%)did not abuse opioids. 27,004 (31.01%) of admitted patients were 11-21 years while 59,823 (68.99%) were 21-35 years. We found statistically significant APCs (Annual Percentage Change) showing increasing trends in both age categories for years under review, (18.47% [95% CI 15.39-21.63]; p-value <0.001 in young adults vs. 10.31% [95% CI 3.58-17.49]; p-value 0.009 in adolescents). The difference in APCs between both age categories were also significant (−8.16% [95% CI [−14.26-2.05]; p-value 0.009). There were no parallelism or coincidence in the trend lines. Opioid abuse was found to be associated with significantly longer length of stay (7.74 vs 6.05 days), higher total charge ($40,797 vs $32,164), (aOR 1.44; 95% CI [1.19-1.75]) seizures, sepsis (aOR 1.62; 95% CI [1.35-1.94]) and pulmonary hypertension (aOR 1.36; 95% CI [1.12-1.66]). No significant association was found for inpatient mortality, transfusion, cardiac dysrhythmias, pulmonary embolism and acute kidney injury. Significant interaction existed between opioid abuse and age for total charge (for $41,869 vs $29,371 among adolescents & $40,632 vs $32,550 among young adults; interaction p-value 0.03). DISCUSSION/SIGNIFICANCE OF IMPACT: Trends show a significant increase in the prevalence of opioid abuse among adolescents and an increasingly higher prevalence when adolescents transition to young adults. Opioid abuse among sickle cell patients is associated with significant poor healthcare resource utilization and clinical outcomes. Public health

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