

Hounsfield Units after exclusion of other causes of liver fat (alcohol/hepatitis/medications). Latent mixture modeling was used to identify 25-year trajectories in HOMA-IR over time. Multivariable logistic regression models were used to assess associations between HOMA-IR trajectory groups and prevalent NAFLD with adjustment for baseline or Y25 HOMA-IR. RESULTS/ANTICIPATED RESULTS: Among 3060 participants, we identified 3 distinct trajectory groups for HOMA-IR for individuals free from diabetes in middle adulthood: qualitatively low-stable (46.7% of the cohort), moderate-increasing (42.0%), and high-increasing (11.3%) with a NAFLD prevalence at Y25 of: 8.3%, 33.4%, and 63.5%, respectively (p -trend < 0.0001). After adjustment for confounders (baseline smoking status, alcohol use, body mass index, physical activity score, systolic blood pressure, antihypertensive medication use, and total/HDL cholesterol ratio) and baseline HOMA-IR, increasing HOMA-IR trajectories were associated with greater NAFLD prevalence compared with the low-stable trajectory group [odds ratio (95% CI): 5.8 (4.3–7.9) and 22.3 (14.2–34.9) for moderate and high, respectively]. These associations were attenuated, but remained significant, even after controlling for current Y25 HOMA-IR [OR = 3.6 (2.6–5.0) for moderate and 5.9 (3.4–10.3) for high (referent: low)]. Among participants with NAFLD ($n = 511$), high-increasing HOMA-IR trajectory was associated with greater prevalent [OR = 6.5 (1.6–25.7)] and incident [OR = 8.7 (2.2–34.4)] T2DM at Y25 independent of confounders and Y25 HOMA-IR (referent: low-stable). DISCUSSION/SIGNIFICANCE OF IMPACT: In this community-based sample of individuals free from diabetes at baseline, an increasing HOMA-IR trajectory through young adulthood was associated with greater NAFLD prevalence in midlife. Knowledge of changes in IR throughout adulthood provides new information on the risk of T2DM among persons with NAFLD in midlife independent of current level of IR. These findings highlight early identification of increasing IR as a potential target for primary prevention of T2DM in the setting of NAFLD.

2115

Post-traumatic stress disorder associated with Hurricane Katrina predicts cardiovascular disease events among elderly adults

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OBJECTIVES/SPECIFIC AIMS: Cardiovascular disease (CVD) is the leading cause of death among US adults and its prevalence is increasing, despite efforts to identify, and address risk factors. Post-traumatic stress disorder (PTSD) has been identified as a potential risk factor for CVD, though the results to date have focused on male veterans with combat-related PTSD. To our knowledge, there are no prospective analyses/reports among older community-dwelling adults following Hurricane Katrina. The purpose of this study was to explore the link between PTSD associated with Hurricane Katrina and incident CVD among elderly adults using data from the Cohort Study of Medication Adherence among Older Adults (CoSMO). METHODS/STUDY POPULATION: PTSD associated with Katrina and incident CVD events were assessed among 2075 hypertensive participants age ≥ 65 who were enrolled in a managed care organization in southeastern Louisiana. Baseline surveys were conducted between August 2006 and September 2007. Baseline surveys were conducted between August 2006 and September 2007. PTSD was assessed using the civilian PTSD Checklist (PCL-17) and 2 cut-off points, ≥ 37 and ≥ 44 , for primary and secondary analyses, respectively. Participants were followed through February 2011 for a composite CVD outcome of MI, stroke, CHF, or CVD death. Multivariable logistic regression was performed with 13 covariates identified in bivariate analysis: age, sex, race, marital status, education, hypertension knowledge, comorbidities, number of antihypertensive medication classes, dissatisfaction with healthcare, reduced medications due to cost, number of visits to healthcare provider in last year, depression, and coping. RESULTS/ANTICIPATED RESULTS: Participants were 59.8% female and 30.4% black, with a mean age of 75 years. The prevalence of PTSD using the primary and secondary cut points was 6.1% and 4.2%, respectively. In total, 240 (11.5%) participants had a CVD event during a median 3.8 year follow-up. After multivariable adjustment, the odds ratios and 95% confidence intervals (CI) for CVD event for the primary and secondary analyses were 1.90 (95% CI: 1.17, 3.09) and 3.74 (95% CI: 2.05, 6.81), respectively. DISCUSSION/SIGNIFICANCE OF IMPACT: PTSD was associated with an increased risk of incident CVD events among elderly adults. This finding from a prospective cohort study supports earlier reports suggesting PTSD is an independent risk factor for CVD. To our knowledge, this association has not been previously reported among a cohort of elderly community-dwelling adults. This study included hypertensive, elderly, insured participants living in southeastern Louisiana following Hurricane Katrina and may not be generalizable to all people with PTSD. Strengths of this study include its longitudinal design, the identification of incident CVD, the diversity of the study population with respect to gender, race and CV risk, and

reduced confounding due to access to care and insurance status. Future research is needed to confirm this finding in other populations and to assess if efforts to minimize the impact of PTSD following disasters reduce CVD risk and premature CVD events among older adults.

2122

Factors associated with unintended pregnancy in cancer survivors after cancer

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OBJECTIVES/SPECIFIC AIMS: In the United States, it is estimated that approximately half of all pregnancies are unintended. This study examines the prevalence of unintended pregnancy in a cohort of cancer survivors and identifies factors associated with unintended pregnancy after cancer. METHODS/STUDY POPULATION: The FUCHSIA Women's Study is a population-based study of female cancer survivors at a reproductive age of 22–45 years. Cancer survivors diagnosed between the ages of 20 and 35 years and at least 2 years postdiagnosis were recruited in collaboration with the Georgia Cancer Registry. Participants were interviewed about their reproductive histories. The prediagnosis analysis included all women who completed the interview; the postdiagnosis analysis excluded those who had a hysterectomy, bilateral oophorectomy, or tubal ligation by cancer diagnosis. RESULTS/ANTICIPATED RESULTS: Of the 1282 survivors interviewed, 57.5% reported at least 1 pregnancy before cancer diagnosis; of which, 44.5% were unintended. Of the 1088 survivors included in the postdiagnosis analysis, 36.9% reported a post-cancer pregnancy. Among those who had a pregnancy after cancer diagnosis, 38.6% reported at least 1 pregnancy was unintended. Of the 80 breast cancer survivors who had a pregnancy after diagnosis, 52.5% of them were unintended. Predictors of unintended pregnancy in cancer survivors included being younger than 30 years at diagnosis [odds ratio (OR) 2.1; 95% confidence interval (CI) 1.4, 2.9], identifying as Black (OR 1.6, 95% CI 1.1, 2.3, comparison: White), and having resumption of menses after cancer treatment (OR 8.1, 95% CI 2.0, 33.0). Compared with being <4 years from cancer diagnosis, those who were farther from diagnosis at the time of the interview also had increased odds of unintended pregnancy (4–7 years: OR 1.5, 95% CI 0.9, 2.7; 8–10 years: OR 1.3, 95% CI 0.7, 2.4; >10 years: OR 2.7, 95% CI 1.6, 4.7). DISCUSSION/SIGNIFICANCE OF IMPACT: Despite being at higher risk of infertility, cancer survivors may still be at considerable risk of unintended pregnancy. Women with certain types of cancer that are more likely to be hormone responsive, such as some types of breast cancer, may be hesitant to use hormonal birth control and thus be at higher risk of unintended pregnancy. Counseling for cancer survivors should include a discussion of the risk of unintended pregnancy and contraceptive options.

2156

A confounder assessment of patient frailty in the relationship between antidiabetic medication and heart failure

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OBJECTIVES/SPECIFIC AIMS: This study is part of a parent grant evaluating antidiabetic medications and risk for heart failure in an observational cohort of Veterans with type 2 diabetes (T2DM). Confounding by indication remains a concern in many observational studies of medications because difficult to measure confounders such as frailty may influence prescribing of different medications based on patient characteristics. Frailty is a multidimensional syndrome of loss of reserves (energy, physical ability, cognition, health) that gives rise to vulnerability to adverse outcomes. The objective of this study is to determine if frailty is a potential confounder in Veterans with T2DM, that is, independently associated with exposure to a specific antidiabetic medications and hospitalization for decompensated heart failure. METHODS/STUDY POPULATION: We conducted a cross-sectional study of patients with diabetes who were hospitalized within the Veterans Health Administration (VHA) Tennessee Valley Healthcare System from 2002 to 2012. Inclusion criteria were: age 18 years or older, receive regular VHA care (prescription fill or visit at least once every 180 d), a diagnosis of T2DM. A probability sample of HF and non-HF hospitalizations was collected. HF hospitalizations were selected on the basis of meeting either a primary diagnosis code (ICD-9) and/or disease related group (DRG) code for HF. For each hospitalization using a standardized chart abstraction tool, data was abstracted on: antidiabetic medication(s), patient

frailty status, and reason for hospitalization (HF or non-HF). Antidiabetic medication regimens were categorized as follows: no medication treatment, metformin alone, sulfonylurea alone, insulin alone, insulin and one oral agent, and all other regimens. Patient frailty status was measured using a modified version of the Canadian Health and Aging frailty index (FI), which generates a score (range 0–1) by dividing the number of deficits present by the number of deficits measured. Established categories for FI scores are: non frail ≤ 0.10 , vulnerable 0.10–0.21, frail 0.22–0.45, and very frail > 0.45 . Patient frailty status at the time of hospitalization was used as a surrogate for patient frailty at the time of prescription of antidiabetic medication; this is a limitation of this approach. Hospitalizations were classified as HF hospitalizations if 2 major or 1 major and 2 minor Framingham criteria were present. FI was compared across antidiabetic medication regimen categories and hospitalization type using analysis of variance (ANOVA) and Student *t*-test, respectively. RESULTS/ANTICIPATED RESULTS: Of the 500 hospitalizations reviewed, 430 patients had confirmed diabetes diagnosis, adequate data to calculate FI scores, and were included in this analysis. Patients were on average 66.9 (10.9) years old; 99% male and 75% were White. Overall, 268 patients (62.3%) were categorized as frail or very frail. The mean FI score was 0.23 (SD 0.07). FI scores were highest in patients receiving insulin alone (mean 0.26) compared with patients receiving metformin alone (mean 0.22), sulfonylurea alone (mean 0.23), or no medication (mean 0.22). The lowest mean frailty score was seen in patients taking all other drug combinations, 0.19. The differences across these patient groups were statistically significant with $p < 0.01$. Further, 75% of patients on insulin alone were frail or very frail compared with 68% on sulfonylurea alone, 58% on metformin alone, and 58% on no medication. Framingham criteria for acute HF were present for 318 of 430 patients (74.0%). FI scores were higher in patients hospitalized for HF compared with non-HF hospitalizations (mean 0.24 vs. 0.21, $p < 0.01$). A higher proportion of patients hospitalized for HF were classified as frail or very frail compared with those hospitalized for non-HF diagnosis (66.4% vs. 50.9%, $p < 0.01$). DISCUSSION/SIGNIFICANCE OF IMPACT: This study demonstrates that certain antidiabetic medications are associated with patient frailty. In addition, those patients admitted for HF have higher FI scores than those admitted for non-HF diagnoses. Further investigation is planned to assess the degree to which frailty is captured by traditional covariates used in observational studies.

2187

Investigation of antimicrobial resistance in *Ureaplasma* species and *Mycoplasma hominis* isolates from urine cultures in college-aged females

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OBJECTIVES/SPECIFIC AIMS: Urinary tract infections (UTIs) serve as one of the most common infections affecting women. With rising reports of antibiotic resistance (ABR), which can prolong illness and limit treatment options, the Infectious Disease Society of America recommends using local resistance patterns to shape empirical treatment selection. Although no studies have evaluated ABR in *Ureaplasma* spp. urinary isolates in college-aged women, regional studies in the Southeast United States have found levels of tetracycline resistance in over 30% of *Ureaplasma* spp. clinical isolates. Thus, this study aims to determine the antibiogram for 73 *Ureaplasma* spp. and 10 *Mycoplasma hominis* isolates collected from women with first-time UTI against a panel of 9 antibiotics, and assess resistant isolates for genetic mechanisms associated with resistance. METHODS/STUDY POPULATION: This study used archival samples and data collected from college-aged women with first-time UTI recruited to participate in a prospective cohort study conducted at a student healthcare facility from 2001 to 2006 in Florida. *Ureaplasma* spp. and *M. hominis* isolates cultured from urine samples collected at the initial clinical presentation and for any recurrent UTI were evaluated for susceptibility to a panel of 9 antibiotics (8 for *M. hominis*) using validated microbroth and agar dilution methods, respectively. *Ureaplasma* spp. isolates were tested against azithromycin, chloramphenicol, ciprofloxacin, clindamycin, erythromycin, doxycycline, gentamicin, levofloxacin, and tetracycline. *M. hominis* isolates underwent the same testing, with the addition of linezolid and exclusion of azithromycin and erythromycin, as *M. hominis* is intrinsically resistant to 14 and 15-membered macrolides and azilides. PCR and Sanger sequencing were employed to identify molecular mechanisms associated with resistance. RESULTS/ANTICIPATED RESULTS: Of the 73 *Ureaplasma* spp. isolates, 1 isolate was resistant to levofloxacin (MIC: 4 $\mu\text{g}/\text{mL}$) and 1 to tetracycline (MIC: 8 $\mu\text{g}/\text{mL}$). All *M. hominis* isolates were sensitive. For the *Ureaplasma* spp. isolates, MIC90s were highest against gentamicin (32 $\mu\text{g}/\text{mL}$) and lowest against doxycycline (0.25 $\mu\text{g}/\text{mL}$). PCR amplification identified tetM present in the tetracycline resistant isolate, an established gene associated with tetracycline resistance in *Ureaplasma* spp. A S83W mutation within the quinolone-resistance-determining region (QRDR) of parC was detected in the levofloxacin resistant isolate.

DISCUSSION/SIGNIFICANCE OF IMPACT: Overall, antibiotic resistance in this population of college-aged women with first-time UTI was low. A previous study detected a novel S83W substitution in a perinatal *Ureaplasma* spp. isolate from Japan, and provided in silico evidence that a S83W change would prevent levofloxacin from binding to its target. However, that study was unable to cultivate the isolate. Our study has provided the corresponding phenotypic evidence that a S83W substitution results in quinolone resistance in *Ureaplasma* spp.

2220

Pharmacogenomic determinants in Caribbean Hispanics of clopidogrel failure in acute coronary syndrome

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OBJECTIVES/SPECIFIC AIMS: The objective of this study is to measure the association of CYP2C19 (*1,*8,*17), ABCB1(C3435T; rs1045642), PON1 (p.Q192R; rs662), and B4GALT2 (c.909 C>T and c.366 G>C) gene polymorphisms in the Caribbean Hispanic population with major adverse cardiovascular events (MACE). METHODS/STUDY POPULATION: Patients of Caribbean Hispanic ethnicity from all geographic regions of the Island of Puerto Rico, male and female, aged > 21 will be recruited. Cases will consist of patients receiving a daily clopidogrel dose of 75 mg following acute coronary syndrome (ACS) who experience a MACE within the first year of treatment. Control study patients must have received clopidogrel 75 mg daily for a minimum of 1 year without experiencing MACE. Genomic DNA samples will be genotyped to determine the frequency distribution of major CYP2C19, ABCB1, PON1, and B4GALT2 gene polymorphisms. Observed frequencies will be compared with other reported populations. An association study will be performed between genetic variables and MACE and a multivariable logistic regression model (additive) will be constructed. RESULTS/ANTICIPATED RESULTS: We anticipate finding a significant association between major genetic determinants of clopidogrel response and MACE where cases with MACE will carry higher frequency of CYP2C19, ABCB1, PON1, and B4GALT2. DISCUSSION/SIGNIFICANCE OF IMPACT: As the range of multiloci allelic combinations in admixed Caribbean Hispanics is higher than in other populations due to its unique 500-year history of genomic admixture, a wide spectrum of genetic variances is expected to be present in the study population. Determining the prevalence and effect of CYP2C19, ABCB1, PON1, and B4GALT2 polymorphisms holds the potential to personalize anti-platelet treatment for Caribbean Hispanic patients requiring treatment after ACS.

2232

Acute kidney injury in patients on SGLT-2 inhibitors: A propensity matched analysis

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OBJECTIVES/SPECIFIC AIMS: In June 2016, the FDA cautioned against the use of SGLT-2 inhibitors because of increased risk of acute kidney injury (AKI) after 101 cases of AKI were reported between March 2013 and October 2015. This study seeks to determine risk of AKI associated with SGLT-2 inhibitors in a large cohort of type 2 diabetic patients. METHODS/STUDY POPULATION: Retrospective cohort study including SGLT-2 inhibitor users and nonusers in the Mount Sinai Chronic Kidney Disease Registry between January 2013 and September 2016. SGLT-2 inhibitor users and nonusers were type 2 diabetics with new SGLT-2 inhibitor prescription after January 2013 and an outpatient visit between 2013 and 2015, respectively. Subjects were propensity matched by nearest neighbor method based on demographics, comorbidities, laboratory values, medications, estimated glomerular filtration rate (eGFR), and length of follow-up. The primary end point was AKI (defined by KDIGO laboratory algorithm) occurring during the follow-up period. RESULTS/ANTICIPATED RESULTS: In total, 372 SGLT-2 inhibitor users [mean age 63 years; 205 (55%) men] and 372 [mean age 63; 194 (52%) men] nonusers were included in the primary analysis. Proportions of AKI events defined by KDIGO criteria in users and nonusers were 4.0% and 10.0%, respectively. Adjusted odds ratio for AKI was 1.00 (95% CI, 0.28–2.62). Median peak serum creatinine measurements during AKI events for user and nonuser groups were 1.60 (IQR 1.36–1.78) and 1.88 (IQR 1.55–2.44) ($p = 0.02$), respectively. Sensitivity analyses yielded similar results. DISCUSSION/SIGNIFICANCE OF IMPACT: These findings suggest that there is no evidence of increased odds of AKI in SGLT-2 inhibitor users compared with propensity-matched nonusers with type 2 diabetes.