

factors have been associated with the presence of HTPR in patients with CAD and PAD, including CYP2C19 loss of function polymorphism, drug-drug interactions, and medical comorbidities. Gender differences are another factor that might influence the levels of platelet inhibition while on Clopidogrel and hence, HTPR. Differences by Gender exist in platelet biology, count, and activation. The evidence for the influence of Gender in HTPR is limited, but a possible association has been described. In this study, we described the association of Gender with HTPR and Major Adverse Cardiovascular Events (MACEs) occurrence. The data is from a sample of Hispano-Caribbean patients on Clopidogrel therapy alone or in combination with Aspirin that were retrospectively evaluated from an ongoing trial in Puerto Rico. The result of this study provided evidence of the influence that Gender has on antiplatelet therapy function and MACEs occurrence. METHODS/STUDY POPULATION: The population in the study consisted of Hispano-Caribbean patients using Clopidogrel alone or in combination with Aspirin for coronary artery disease, peripheral arterial disease, or cerebrovascular disease. The sample was obtained from multiple hospital institutions with cardiovascular services in Puerto Rico during the years 2016-2019. Patients were part of the ongoing trial, "Adopting a precision medicine paradigm in Puerto Rico: leveraging ancestral diversity to identify predictors of Clopidogrel response in Caribbean Hispanics." The sample size consisted of 150 patients. Participants were recruited during routine medical care, pre-admission evaluation for elective cardiac procedures, or during hospitalization in the participating institutions. Platelet reactivity testing was performed with the system Verify Now<sup>®</sup> to determine PRU values, and High on-treatment platelet reactivity was defined as PRU  $\geq$ 208. One year after recruitment, the patients were re-evaluated for the occurrence of MACEs. The association of the variables HTPR, occurrence of MACEs, and Gender were assessed using logistic regression in addition to the role of HTPR and Gender for predicting MACE occurrence. The analysis was done using the statistic software Intellectus ©. RESULTS/ANTICIPATED RESULTS: The sample consisted of 67 females and 83 males with and Mean age of 67.87 years and 61.11 years, respectively. The prevalence of HTPR in the sample was 32.67 % (n = 49) with 36% (n = 24) for females, and 30%(n = 25) for males. The mean PRU values were 179.54 for females and 170.81 for males. The percentage of MACEs one year after recruitment was 29.33 % (n = 44) with 43% on females (n = 19), and 57% on males (n = 25). Logistic regression for Gender predicting HTPR was non-significant with a  $\chi^2(2) = 0.55$ ,  $p = .758$ , and McFadden  $R^2 = 0.00$ . Also, logistic regression for the effects of Gender and HTPR on the Odds of MACEs occurrence was not significant based on a model with an alpha of 0.05,  $\chi^2(2) = 1.99$ ,  $p = .370$ , and McFadden  $R^2 = 0.01$ . DISCUSSION/SIGNIFICANCE OF IMPACT: The sample consisted of 67 females and 83 males with and Mean age of 67.87 years and 61.11 years, respectively. The prevalence of HTPR in the sample was 32.67 % (n = 49) with 36% (n = 24) for females, and 30%(n = 25) for males. The mean PRU values were 179.54 ( $\pm$ 70.42) for females and 170.81( $\pm$ 64.89) for males. The percentage of MACEs one year after recruitment was 29.33 % (n = 44) with 43% on females (n = 19), and 57% on males (n = 25). Logistic regression for Gender predicting HTPR was non-significant with a  $\chi^2(2) = 0.55$ ,  $p = .758$ , and McFadden  $R^2 = 0.00$ . Also, logistic regression for the effects of Gender and HTPR on the odds of MACEs occurrence was not significant based on a model with an alpha of 0.05,  $\chi^2(2) = 1.99$ ,  $p = .370$ , and McFadden  $R^2 = 0.01$ .

4518

### Metabolomic Identifiers Predictive of Adverse Events due to Acetaminophen Administration

Brandon Joseph Sonn, PhD Candidate<sup>1</sup>, Kennon Heard<sup>1</sup>, and Andrew Monte<sup>1</sup>

<sup>1</sup>University of Colorado at Denver

OBJECTIVES/GOALS: Acetaminophen (Tylenol, APAP) toxicity has been well documented and well explored over the last 50 years. However, there has been no investigation into identification of specific metabolites that can *predict* which patients will have adverse reactions to therapeutic doses of APAP. METHODS/STUDY POPULATION: 205 subjects recruited from the Denver, CO community received the highest recommended daily dosing of APAP, 4 grams, for 16 days. Subjects were grouped by 1) alanine aminotransferase (ALT) at any monitored time point above 60units/L (n = 20) vs 2) no increase in ALT at any time point (n = 185). Blood was collected at days 0, 4, 7, 16, and 31. Samples were run on ultra-high performance liquid chromatography mass spectrometry with 27 heavy-labeled standards for metabolites documented to be associated with APAP metabolism. Data will be analyzed to look for significant changes in metabolite and demographic variable expressions using t-tests, chi square and logistic regression, as appropriate. RESULTS/ANTICIPATED RESULTS: It is expected that there will be greater elevations of conjugated non-toxic APAP metabolites (APAP-glucuronide, APAP-sulfate) in subjects whose ALT did not elevate because of successful hepatoprotection. Conjugated APAP metabolites are expected to only be present in samples taken after APAP therapy initiation confirming exposure as compared to being predictive of toxic response. Increases in lactate and cysteine in pre-exposure samples would allow for prediction of APAP toxicity as they are expected to have increased expression in subjects whose ALT became elevated which is indicative of increased hepatic damage due to oxidative damage. DISCUSSION/SIGNIFICANCE OF IMPACT: Identification of metabolites and/or demographic factors associated with toxic response to APAP prior to administration could advise APAP recommendations. Quantification of post-APAP administration metabolites would identify extent of successful hepatoprotective mechanisms.

4267

### Noninvasive hybrid ultrasound and photoacoustic imaging for the assessment of liver fibrosis

Laith Riyadh Sultan<sup>1</sup>, Mrigendra Karmacharya<sup>1</sup>, Julia D'Souza<sup>1</sup>, Brooke Kirkham<sup>1</sup>, Angela K Brice<sup>1</sup>, Andrew KW Wood<sup>1</sup>, Stephen Hunt<sup>1</sup>, and Chandra Sehgal<sup>1</sup>

<sup>1</sup>University of Pennsylvania School of Medicine

OBJECTIVES/GOALS: The detection of liver fibrotic changes at an early and reversible stage is essential to prevent its progression to end-stage cirrhosis and hepatocellular carcinoma. Liver biopsy, which is the current gold standard for fibrosis assessment, is accompanied by several complications due to its invasive nature in addition to sampling errors and reader variability. In this study, we evaluate the use of quantitative parameters extracted from hybrid ultrasound and photoacoustic imaging to detect and monitor fibrotic changes in