imaging, and medication variables; disease diagnosis, procedure, and billing codes) and qualitative data extracted from an integrated health system electronic health record. The heart failure subphenotypes we identify from the integrated health system electronic health record will be replicated in other heart failure population datasets using unsupervised learning approaches. We will explore the potential to establish associations between identified subphenotypes and clinical outcomes (e.g. all-cause mortality, cardiovascular mortality). RESULTS/ANTICIPATED RESULTS: We expect to identify < 10 mutually exclusive phenogroups of patients with heart failure that have differential risk profiles and clinical trajectories. DISCUSSION/SIGNIFICANCE OF FINDINGS: We will attempt to derive and validate a data-driven unbiased approach to the categorization of novel phenogroups in heart failure. This has the potential to improve our knowledge of heart failure pathophysiology, identify novel biomarkers of disease, and guide the development of targeted therapeutics for heart failure.

44499

Heterogeneity of treatment effect among patients with type 2 diabetes and body mass index >=27kg/m^2 in the Jump Start Study

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ABSTRACT IMPACT: This is the first study to use QUINT analyses to examine heterogeneity of treatment effect for group medical visits among individuals with type 2 diabetes. QUINT is a data driven method that assumes no a priori assumptions regarding effect moderators - an important step in the path towards personalized medicine. OBJECTIVES/GOALS: To examine heterogeneity of treatment effect (HTE) in Jump Start, a trial that compared the effectiveness of group medical visits (GMVs) focused on medication management only versus the addition of intensive weight management (WM) on glycemic control for patients with type 2 diabetes and body mass index >=27kg/m^2. METHODS/STUDY POPULATION: Jump Start patients (n=263) were randomized to a GMV-based medication management plus low carbohydrate diet-focused WM program (WM/GMV; n = 127) or GMV-based medication management only (GMV; n = 136) for diabetes control. We used QUalitative INteraction Trees (QUINT), a tree-based clustering method, to determine if there were subgroups of patients who derived greater benefit from either WM/GMV or GMV. Subgroup predictors included 32 baseline demographic, clinical, and psychosocial factors. Outcome was hemoglobin A1c (HbA1c). We conducted internal validation via bootstrap resampling to estimate bias in the range of mean outcome differences among arms. RESULTS/ANTICIPATED RESULTS: QUINT analyses indicated that for patients who had not previously attempted weight loss, WM/GMV resulted in better glycemic control than GMV alone (mean difference in HbA1c improvement = 1.48%). For patients who had previously attempted weight loss and had lower cholesterol and blood urea nitrogen levels, GMV alone was better than WM/GMV (mean difference in HbA1c improvement = 1.51%). Internal validation resulted in moderate corrections in the mean HbA1c differences between arms; however, differences remained in the clinically significant range. DISCUSSION/SIGNIFICANCE OF FINDINGS: Among patients with diabetes and BMI>=27kg/m^2, a low-carbohydrate, weight loss focus may better improve HbA1c in those who have never attempted weight loss. A medication management focus may be better in those who have attempted weight loss and have lower cholesterol and blood urea nitrogen.

89976

ASSESSING PROTEIN BIOMARKERS ROLE IN CVD RISK PREDICTION IN PERSONS LIVING WITH HIV (PWH)

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ABSTRACT IMPACT: Our findings could potentially identify CVD at-risk persons living with HIV who might benefit from aggressive risk-reduction. OBJECTIVES/GOALS: PWH have higher rates of CVD than the general population yet CVD risk prediction models rely on traditional risk factors and fail to capture the heterogeneity of CVD risk in PWH. Here we identify protein biomarkers that are able to discriminate between CVD cases and controls in PWH, and we assess their added benefit beyond traditional risk factors. METHODS/STUDY POPULATION: We analyzed 459 baseline protein expression levels from five OLINK panels in a matched CVD (MI, coronary revascularization, stroke, CVD death) case-control study with 390 PWH from INSIGHT trials (131 cases, 259 controls). We formed 200 datasets via bootstrap. For each bootstrap set, a two-component partial least squares discriminant model (PLSDA) was fit. The importance of each variable in the discrimination of cases and controls in the PLSDA projection was assessed by the variable importance in projection (VIP) score. Proteins with average VIP scores > 1 were used in penalized logistic regression models with elastic net penalty, and proteins were ranked based on the number of times the protein had a nonzero coefficient. Proteins in the top 25th percentile were considered to have high discrimination. RESULTS/ANTICIPATED RESULTS: Participants had mean age 47 years, 13% were females, 4.9% had CVD at baseline and 69% were on ART at baseline. Eight proteins including the hepatocyte growth factor and interleukin-6 were identified as able to distinguish between CVD cases and controls within PWH. A protein score (PS) of the top-ranked proteins was developed using the bootstrap (for weights) and the entire data. The PS was found to be predictive of CVD independent of established CVD and HIV factors (Odds ratio: 2.17 CI: 1.58-2.99). A model with the PS and traditional risk factors had a 5.9% improvement in AUC over the baseline model (AUC=0.731 vs 0.69), which is an increase in model predictive power of 18%. Individuals with a PS above the median score were 3.1 (CI: 1.83- 5.41) times more likely to develop

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