with the development of MetS and identifiable endothelial dysfunction in a cohort of Hispanic pre-pubertal children. To do so we propose the following aims: (1) To measure expression of adiponectin and leptin levels in a Hispanic pre-pubertal cohort and determine their correlation with features of the MetS. (2) To perform proteomic analysis in a Hispanic pre-pubertal cohort. (3) Evaluate early onset of endothelial dysfunction and its correlation with expression of adiponectin and leptin levels in a Hispanic pre-pubertal cohort. METHODS/STUDY POPULATION: A cross-sectional pilot study will obtain a random representative sampling of children aged 6–12 years from all geographical areas of Puerto Rico. Children will be assessed regarding pre-pubertal status through Tanner staging and later divided into pre-MetS Versus MetS groups as well as controls. MetS will include children meeting 3 or more of the current International Diabetes Federation (IDF) criteria. Pre-MetS will include children with at least 1 criterion for MetS. Anthropometric data, blood pressure readings, ultrasound-based noninvasive testing for endothelial dysfunction, and laboratory assays will be performed to the study population and data analyzed for correlation. Total adiponectin and leptin levels will be measured using a commercially available quantitative sandwich enzyme-linked immunoassay test. The study will be submitted to the University of Puerto Rico Medical Sciences Campus' Institutional Review Board (IRB) for approval. Written consent and assent will be obtained from parents and children respectively to ensure patient anonymity. RESULTS/ANTICIPATED RESULTS: We hypothesize that low levels of adiponectin and high levels of leptin will correlate with features of the MetS as defined by the IDF consensus statement, as well as with clinical features of MetS in undiagnosed Hispanic pre-pubertal youth. We also hypothesize that non-invasive testing of endothelial function will correlate both with clinical features of the MetS and with low levels of adinopectin and high levels of leptin. DISCUSSION/SIGNIFICANCE OF IMPACT: The correlation of findings suggestive of endothelial dysfunction and biomarker expression (mainly adiponectin and leptin levels) in a pre-pubertal cohort has yet to be established and could also provide information regarding early atherogenesis in otherwise unidentified youth at risk. Therefore, by using a proteomic approach, this study aims to measure associations between clinical features of the MetS and expression of proteins associated with an adverse cardiometabolic profile in a Hispanic pre-pubertal population. We will concurrently measure the degree of endothelial dysfunction and evaluate whether a correlation exists between previously mentioned protein expression and early onset of dysfunction.

2121

Quantitative structural knee measurements improve classification of accelerated knee osteoarthritis: Data from the osteoarthritis initiative

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OBJECTIVES/SPECIFIC AIMS: The aim of this study is to determine whether quantitative measures of knee structures including effusion, bone marrow lesions, cartilage, and meniscal damage can improve upon an existing model of demographic and clinical characteristics to classify accelerated knee osteoarthritis (AKOA). METHODS/STUDY POPULATION: We conducted a case-control study using data from baseline and four annual follow-up visits from the osteoarthritis initiative. Participants had no radiographic knee osteoarthritis (KOA) at baseline. AKOA is defined as progressing from no KOA to advance-stage KOA in at least 1 knee within 48 months. AKOA knees were matched 1:1 based on sex to (1) participants who did not develop KOA within 48 months and (2) participants who developed KOA but not AKOA. Analyses were person based. Classification and regression tree analysis was used to determine the important variables and percent of variance explained. RESULTS/ANTICIPATED RESULTS: A previous classification and regression tree analysis found that age, BMI, serum glucose, and femorotibial angle explained 31% of the variability between those who did and did not develop AKOA. Including structural measurements as candidate variables yielded a model that included effusion, BMI, serum glucose, cruciate ligament degeneration and coronal slope and explained 39% of the variability. DISCUSSION/SIGNIFICANCE OF IMPACT: Knee structural measurements improve classification of participants who developed AKOA Versus those who did not. Further research is needed to better classify patients at risk for AKOA.

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Radiofrequency renal denervation attenuates kidney fibrosis in spontaneously hypertensive rats

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OBJECTIVES/SPECIFIC AIMS: The goal of this study was to investigate whether RF-RDN attenuates renal fibrosis and inflammation in SHR with established hypertension. METHODS/STUDY POPULATION: Twenty-two-week-old SHR received bilateral RF-RDN or Sham-RDN (Biosense Webster Stockert 70 generator and RF-probe). Four weeks later, SHR were sacrificed and paraffin sections of kidneys were stained for fibrosis by Masson's trichrome staining. Kidney tissue were homogenized for measurement of cytokines levels by ELISA. RESULTS/ANTICIPATED RESULTS: The results showed that Sham-RDN treated SHR had extensive fibrosis as demonstrated by moderate thickening of Bowman's capsule, collagen deposition in glomerulus, extensive tubulointerstitial fibrosis, and segmental glomerulosclerosis. In contrast, RF-RDN significantly reduced each of these pathological components of fibrosis in kidney cortex and medulla as compared with Sham-RDN treated kidneys. In other studies, RF-RDN decreased B cells, CD4 + T cells, and CD8 + T cells in the kidney of SHR as measured by flow cytometry. Meanwhile, kidney tissue levels of IL-17, INF-γ, MIP-3a, TNF-α, and TGF-β were decreased as compared with respective levels in Sham-RDN. DISCUSSION/SIGNIFICANCE OF IMPACT: Together, these findings demonstrate that removal of the influence of heightened renal sympathetic activity by RF-RDN decreases kidney inflammatory markers and attenuates renal fibrosis in hypertensive SHR.

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Regulation of retinal protein O-GlcNAcylation by angiotensin-(1-7) and cAMP

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OBJECTIVES/SPECIFIC AIMS: Increased retinal protein O-GlcNAcylation occurs in response to hyperglycemia and contributes to diabetic retinopathy. Renin-angiotensin system (RAS) blockers reduce the incidence of diabetic retinopathy. Beneficial effects of RAS blockers are often attributed to production of angiotensin-(1-7) (Ang1-7). The objective here is to determine the impact of Ang1-7 on retinal protein O-GlcNAcylation. METHODS/STUDY POPULATION: C57/BL6 mice were fed a high-fat diet for 8 weeks and then treated for 3 weeks with either a vehicle control, the RAS blocker captopril, or captopril and the Ang1-7 receptor antagonist A779. R28 cells were used to assess levels of O-GlcNAcylated proteins in response to Ang1-7, and the role of cAMP was investigated with addition of forskolin, 6-Bnz-cAMP-AM, and 8-pCPT-2-O-Me-cAMP-AM to cell culture medium. RESULTS/ANTICIPATED RESULTS: Captopril attenuated retinal protein O-GlcNAcylation in mice fed a high-fat diet. This effect was reversed by A779. Ang1-7 attenuated protein O-GlcNAcylation and increased cAMP levels. Forskolin and the EPAC selective cAMP analog 8-pCPT-2-O-Me-cAMP-AM, but not the PKA selective cAMP analog 6-Bnz-cAMP-AM, attenuated O-GlcNAcylation. Inhibiting EPAC blocked the effect of forskolin, whereas inhibiting PKA did not. DISCUSSION/SIGNIFICANCE OF IMPACT: This study demonstrates a novel role for Ang1-7 in the retina and identifies a potential EPAC-dependent mechanism that regulates protein O-GlcNAcylation. Thus, future therapeutics targeted at an Ang1-7/EPAC axis in retina may be used to address DR.

2023

Relationship power imbalance and history of male partner HIV testing among pregnant women in central Uganda

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