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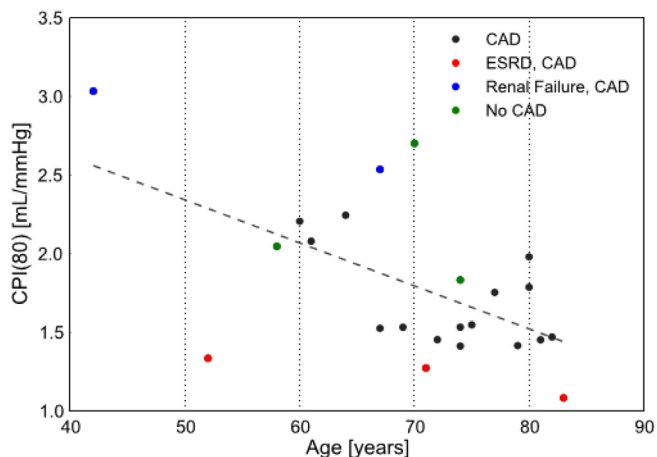
PO-19: SIGNIFICANT BASAL AND STIMULATED VARIATIONS IN INFLAMMATORY GENE EXPRESSION PROFILES IN AFRICAN AMERICAN AND CAUCASIAN HUVECS

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PO-18

ULTRASOUND BIOMICROSCOPIC STUDY OF ARTERIES IN DETECTION OF DOXORUBICIN-INDUCED DISORDERS

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Ultrasound biomicroscopy (UBM) has been a valuable, non-invasive technique in monitoring cardiac function such as echocardiography. However, UBM is not commonly used in vascular research, especially in small animals. In addition, the use of doxorubicin (DOX), an anti-cancer drug, in treatment for malignancies is limited because of its cardiotoxicity. Whether DOX causes vascular disorders is unknown.

Objectives: This study aimed to use UBM to monitor function of major arteries in response to DOX treatment.

Methods: Mice were injected intrapleurally with a single dose of DOX (20 mg/kg body weight) or an equivalent volume of saline. The kinetics of blood flow through ascending aorta (AAo), pulmonary artery trunk (PAT), and left coronary artery (LCA) were monitored with Doppler UBM before and after DOX treatment using Vevo@2100 and VisualSonics® software.

Results: While abnormal cardiac function was usually observed 3 days after DOX treatment, mean velocity and mean pressure gradient of time-integral AAo blood flow were reduced by 30% and 49%, respectively (n=6). The blood flow of LCA was reduced about 40% (n=5) accompanied by an increased resistive index. The reduction in peak velocity of LCA blood flow during systole was greater than that during diastole. In contrast, the peak velocity of blood flow in PAT was reduced by 10% (n=7), which worsened by 22% with a 40% decrease of mean pressure gradient at 7 days after DOX treatment. Meanwhile, no significant change in these arteries was observed in control group. The reduction in AAo blood flow could result from DOX-induced cardiotoxicity, while reduction of LCA blood flow could cause cardiac dysfunction. The change in PAT could be due to the effect of increased oxidative stress by DOX.

Conclusion: UBM could effectively detect hemodynamic changes in major arteries induced by DOX, and thus enhance its application in preclinical research and drug discovery.

PO-19

SIGNIFICANT BASAL AND STIMULATED VARIATIONS IN INFLAMMATORY GENE EXPRESSION PROFILES IN AFRICAN AMERICAN AND CAUCASIAN HUVECS

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Biomarkers related to hypertensive disease onset and progression are differentially implicated in African Americans (AA) and Caucasians (Cau)

and investigation of these biomarkers is needed to elucidate their significance. Racial disparity studies are carried out solely in vivo making it difficult to focus on the cause(s) of endothelial dysfunction (EnDy) leading to vascular complications. Therefore, building on data from our laboratory that reveals a mechanism of EnDy in AA human umbilical vascular endothelial cells (HUVECs) (increased ROS), we report basal differences and effects of activating HUVECs on relative gene expression (2ΔΔCT) of important immune mediators (IL-1β, VCAM-1, ICAM-1, eNOS, and MMP-2).

In an n=2-4 (both AA & Cau) cell lines in passage 6, we show that in control and after 4 hr stimulation with TNF-α (50ng/ml) that basal MMP-2 gene expression, a strong predictor of severe cardiovascular events in AA, is different in AA ECs compared to Cau. IL-1β basal expression is higher in AA and significantly increases (F_{1,12}=10.76;p=.007) after stimulation, being higher in AA. Both AA and Cau ECs show reductions in eNOS expression after TNF-α and there is a trend in AA ECs for eNOS to be lower after stimulation (p=0.06). Further, basal expression of cell adhesion molecules (ICAM-1 & VCAM-1) are significantly greater (p<.05) in AA ECs while after stimulation VCAM-1 was significantly exaggerated in AA (race x treatment interaction: F_{1,12}=6.05;p=.030).

Increases in IL-1β and CAMs in AA ECs indicate they are operating at a higher basal immunological active status. As ROS is known to be indirectly involved with expression of inflammatory genes, it is probable the effect exaggerated ROS has on MMP-2 activation, and its detrimental downstream effects, may play a role in activating immune pathways. Experiments are being performed to assess MMP-2 intracellular activities on cytosolic peptides.

PO-20

AORTIC HEMODYNAMICS FOLLOWING DISCONTINUATION OF MENOPAUSAL HORMONE THERAPY IN POSTMENOPAUSAL WOMEN

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Background and Objective: Arterial stiffness and aortic hemodynamics are important determinants of cardiovascular disease risk. Menopausal hormone therapy (MHT) reduces progression of cardiovascular disease in postmenopausal women due to its effects on the endothelium and smooth muscle of the central and peripheral vasculature. However, it remains unclear whether these effects are sustained after MHT cessation. We hypothesized that MHT administered early during the menopausal transition (less than three years from menopause) would not produce a sustained protective effect on aortic hemodynamics in women following discontinuation of MHT.

Methods: We studied fifty-seven women, as part of the Mayo Clinic Specialized Center of Research on Sex Differences, who were randomized into either oral conjugated equine estrogen (oCEE, n=15), transdermal 17β estradiol (tE2, n=20), or placebo (n=22) for four years. After a three year washout period, aortic hemodynamics were measured using radial arterial applanation tonometry.

Results: Age, body mass index and mean arterial pressure were similar among the women. Augmentation index (AIx) was similar among groups (32.6±2.3%, 33.9±1.9%, 31.5±1.9%; oCEE vs. tE2 vs. placebo, respectively, p>0.05) and did not change when normalized for heart rate at 75 bpm (27.6±2.3%, 28.2±1.6%, 25.7±1.8%; oCEE vs. tE2 vs. placebo, respectively, p>0.05). There were no differences in augmented pressure (12.6±1.6, 13.6±1.2, 12.0±0.9 mmHg; oCEE vs. tE2 vs. placebo, respectively, p>0.05) or left ventricular wasted energy (2843±170, 3208±360, 2559±205 dyne·cm²·sec; oCEE vs. tE2 vs. placebo, respectively, p>0.05) among the three groups.

Conclusion: These data suggest that any changes in aortic hemodynamics during MHT use are not sustained following MHT discontinuation.

PO-21

RACIAL DIFFERENCES IN VASCULAR FUNCTION

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Objective: Racial disparities are evident in regards to cardiovascular health and prevalence. Currently, there have not yet been any studies investigating