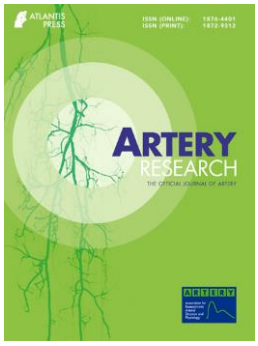

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PO-21: RACIAL DIFFERENCES IN VASCULAR FUNCTION

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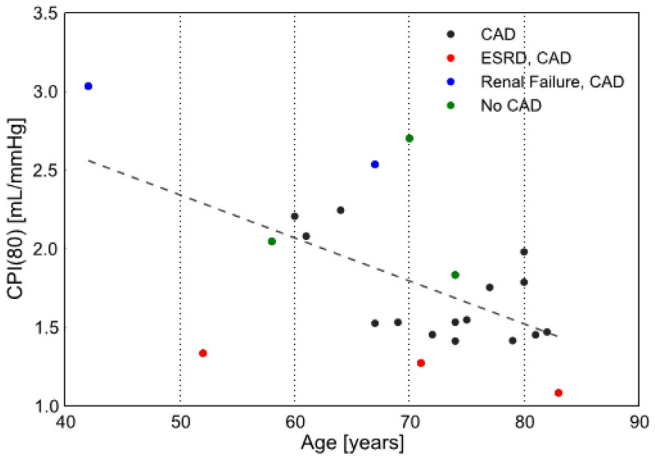

PO-18
ULTRASOUND BIOMICROSCOPIC STUDY OF ARTERIES IN DETECTION OF DOXORUBICIN-INDUCED DISORDERS

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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 cardiotoxity, 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 ($2^{\delta\delta}$CT) 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·cm^2·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

the differences in markers of vascular function between Hispanics (HS), Caucasians (CA), and African Americans (AA). This study sought to assess the differences in vascular function at the endothelial cell level between these racial groups.
Methods: Three human umbilical vein endothelial cell (HUVEC) lines from different donors with HS, CC, and AA backgrounds were used. All cells were grown until confluent before cell medium and cell lysate was harvested. The cell medium was collected for the measurement of Interleukin 6 (IL-6) in an ELISA assay kit. The harvested cell lysate was used for western blotting for the measurement of Endothelial Nitric Oxide Synthase (eNOS), Phosphorylated Endothelial Nitric Oxide Synthase (p-eNOS), and Endothelin Converting Enzyme (ECE).
Results: The expression of eNOS in both the CC and HS cell lines was significantly lower when compared to the AA cell lines ($p \leq 0.001$). p-eNOS expression was significantly higher in the HS cell lines compared to both the AA and the CA cell lines ($p \leq 0.001$). The p-eNOS to eNOS ratio was significantly lower in both the AA ($p \leq 0.03$) and CA ($p \leq 0.001$) cell lines compared to the HS cell lines. ECE expression was significantly higher in the HS cell lines compared to the AA cell lines ($p \leq 0.001$). IL-6 levels were significantly higher in the CA and HS cell lines compared to the AA cell lines ($p \leq 0.001$).
Conclusions: Differences in endothelial cell biology that could affect function were evident among cell lines of different racial origin.

PO-22
HIGHER AORTIC STIFFNESS AND CAROTID SYSTOLIC AND PULSE PRESSURE ARE SELECTIVELY ASSOCIATED WITH LOWER WHITE MATTER INTEGRITY IN THE GENU AND FRONTAL CORTEX IN OLDER HEALTHY ADULTS

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Introduction: Previous studies have demonstrated an association between higher aortic stiffness and central pulse pressure (PP) with lower brain white matter structural integrity (WMI) and neuropsychological functioning in older adults. However, it is unknown if aortic stiffness and central PP are associated with lower WMI in select brain regions or if they relate to cognitive abilities that decline with age such as processing speed.
Objectives: We hypothesized that greater aortic stiffness and carotid PP would be associated with lower regional WMI and slower processing speed.
Methods and results: In younger (n = 12, age 23.2 ± 2.3 yrs) and older (n = 7, 67.7 ± 2.7 yrs) healthy adults, aortic stiffness (carotid-femoral pulse wave velocity, cfPWV) and carotid blood pressure (BP) were determined non-invasively using applanation tonometry and brachial cuff BP (Cardiovascular Engineering, Inc.). Fractional anisotropy (FA) (3T MRI, Siemens) assessed from diffusion imaging measured WMI. The association between vascular variables and FA was determined using voxel-wise and region-of-interest (ROI) analyses. Letter and pattern comparison assessed processing speed.
Results: In the entire cohort, cfPWV (adjusted for age, mean BP) and carotid and brachial PP (adjusted for age) were not correlated with WMI in any brain regions using voxel-wise or ROI. Among older adults using ROI, cfPWV (adjusted for mean BP) was correlated with genu corpus callosum ($r = -0.90$, $p < 0.05$) and frontal ($r = -0.77$, $p < 0.05$) FA values and corroborated in voxel-wise analyses. Carotid, but not brachial systolic BP or PP, was negatively correlated with genu and superior frontal gyrus and medial prefrontal cortex FA values ($p < 0.05$) using voxel-wise analysis. cfPWV, but not FA in the genu or frontal ROIs, was correlated with processing speed ($p < 0.05$) in older adults.
Conclusion: Preliminary results suggest that greater aortic stiffness is selectively associated with lower WMI in the genu and frontal cortex, and slower processing speed in older adults.

PO-23
DEPENDENCY OF ARTERIAL STIFFNESS INDICATORS ON ACUTE BLOOD VOLUME CHANGES

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Increased arterial stiffness is associated with greater risk for cardiovascular disease. It is unknown if indicators of stiffness are dependent on acute changes in cardiovascular conditions (such as altered central blood volume).
Objectives: To examine if arterial stiffness indicators change with acute reductions in stroke volume (SV) within normal physiological variability.
Methods: Seven young healthy volunteers (4M, 3F) were recruited to participate in this study. To acutely alter blood volume, subjects were sealed from their waist down into a lower body negative pressure (LBNP) box and a vacuum was used to create a pressure gradient of 30mmHg. Heart rate (HR) was continuously monitored and SV was obtained with Doppler ultrasound. Aortic and femoral artery velocity profiles were obtained with Doppler ultrasound to determine central pulse wave transit time (cPWTT). cPWTT was calculated by subtracting the time between the peak of the R-wave and the foot of the aortic velocity profile from the time between the peak of the R-wave and the foot of the femoral velocity profile. Common carotid distensibility (cDa) was determined with simultaneous tonometry to determine pulse pressure (PPcar) and ultrasound imaging to determine diastolic and systolic diameters (cDa = systolic area − diastolic area / PPcar − carotid diastolic area).
Results: The increase in HR from baseline to LBNP was not significant while SV was significantly lower at LBNP (45±13mL/beat) compared to baseline (69±11mL/beat; $p = 0.002$). PPcar was lower at LBNP (43±6mmHg) compared to baseline (48±5mmHg; $p = 0.007$). While cDa was significantly decreased (Baseline = $0.00732 \pm 0.00186 mmHg^{-1}$ vs. LBNP = $0.00592 \pm 0.00219 mmHg^{-1}$; $p = 0.033$), cPWTT tended to get faster with LBNP (baseline = 95±17sec vs. LBNP = 87±13sec; $p = 0.089$).
Conclusions: The arterial stiffness indicators, cDa and cPWTT, might be affected by acute changes in central blood volume and cardiac SV within normal physiological variations.

PO-24
SEX DIFFERENCES IN HEMODYNAMIC RESPONSES FOLLOWING ACUTE INFLAMMATION: WAVE SEPARATION ANALYSIS

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Acute inflammation temporarily increases risk of cardiovascular events and alters hemodynamics. However, it is unknown whether acute inflammation differentially affects blood pressure and pulse wave characteristics, including forward or reflected pressure waves, in males versus females.
Objectives: The purpose of this study was to investigate the potential sex differences in the response to acute inflammation in blood pressure and pulse wave characteristics, measured with wave separation analysis.
Methods: 63 adults (29 males, 34 females) participated in the study. Participants received an influenza vaccine to induce acute inflammation. Central blood pressure and pulse waves were measured using tonometry and separated into forward and reflected waves, at baseline, 24hr post, and 48 hr post-vaccination. 2 x 3 repeated measure Analysis of Variance (ANOVA) was performed to investigate sex differences in acute inflammation.

PO-24. Table 1

	Brachial DBP(mmHg)†			Aortic DBP(mmHg)†			Aortic MAP(mmHg)†			Forward wave pressure(mmHg)			Reflected wave pressure(mmHg)		
	Baseline	24 hr Post	48 hr post	Baseline	24 hr Post	48 hr post	Baseline	24 hr Post	48 hr post	Baseline	24 hr Post	48 hr post	Baseline	24 hr Post	48 hr post
Male	69±9	67±9	69±9	70±9	68±9	69±9	87±10	84±9	85±10	29±5	29±5	28±6	19±7	17±7	18±6
Female	66±8*	63±7	64±7	66±8*	64±7	64±7	82±11*	79±8	79±9	27±5	27±5	26±5	17±7	15±5	15±4

∗ Different from other time point, $p < 0.05$.
† Sex difference. Significant at $p < 0.05$.