



Artery Research

ISSN (Online): 1876-4401

ISSN (Print): 1872-9312

Journal Home Page: <https://www.atlantis-press.com/journals/artres>

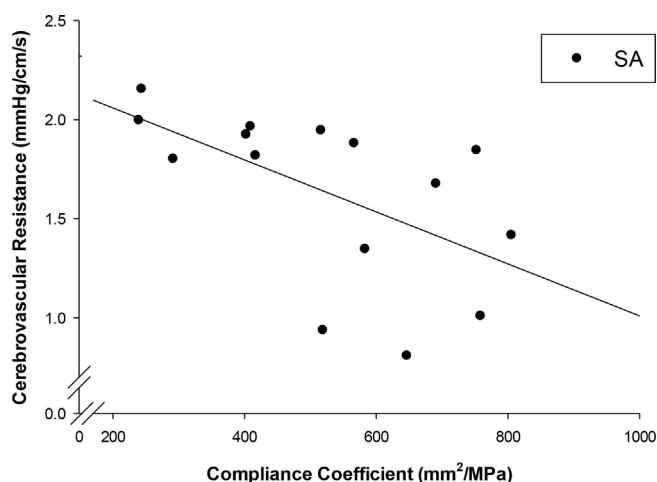
PO-17: A NEW ARTERIAL STIFFNESS INDEX PERMITTING ISOBARIC COMPARISONS

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To cite this article: T.S. Phan, K. Khaw, J.K.-J. Li (2014) PO-17: A NEW ARTERIAL STIFFNESS INDEX PERMITTING ISOBARIC COMPARISONS, Artery Research 8:4, 172–173, DOI: <https://doi.org/10.1016/j.artres.2014.09.023>

To link to this article: <https://doi.org/10.1016/j.artres.2014.09.023>

Published online: 7 December 2019



PO-15

THE TEMPORAL RELATIONSHIP BETWEEN METABOLICALLY HEALTHY OBESITY AND CAROTID ATHEROSCLEROSIS IN MEN

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There is conflicting evidence regarding the relationship between metabolically healthy obesity and the burden of carotid atherosclerosis, but whether metabolically healthy obesity is related to the progression of atherosclerosis remains unclear.

Purpose: We investigated the cross-sectional and follow-up associations between metabolically healthy obesity and carotid atherosclerosis.

Methods: Cardiometabolic risk factors and carotid artery intima-media thickness (CIMT) in 556 men, mean aged 51 yrs (36-76 yrs), were measured at baseline and one year later. All participants were free of hypertension and type 2 diabetes at baseline. Participants were divided into four groups based on cross-classifications of body mass index (BMI) and metabolic health status using the ATP-III criteria: metabolically healthy normal weight (MHNW, less than one metabolic abnormality with BMI <25 kg/m²), metabolically unhealthy normal weight (MUNW, more than one metabolic abnormality with BMI <25 kg/m²), metabolically healthy obesity (MHO, less than one metabolic abnormality with BMI ≥25 kg/m²), metabolically unhealthy obesity (MUO, more than one metabolic abnormality with BMI ≥25 kg/m²). Carotid atherosclerosis was defined as >75 percentiles of CIMT. The changes in CIMT were calculated as the difference between the first and second examinations (median interval 367 days).

Results: At baseline, mean CIMT was not significantly different between the MHNW and the MHO (0.58±0.12mm vs. 0.62±0.13mm, *P*=0.13), but was different between the MHNW and the MUO (0.64±0.13mm, *P*=0.01) after adjusting for age. The prevalence of carotid atherosclerosis tended to be higher in the MHO as compared to the MHNW after adjusting for age, heart rate, CRP, and VO_{2peak}, but this was not statistically significant (Odds Ratio (OR) 1.80 95% Confidence Interval (CI) 0.93-3.52). There was an increase in the OR for carotid atherosclerosis in the MUO (OR 2.08 95% 1.16-3.73). After one year, the progression of mean CIMT was not significantly different between the MHO and the MHNW after adjusting for covariates (Δ 0.03±0.11mm vs. Δ 0.05±0.10mm, *P*=0.52). Furthermore, the MHO at baseline was not significantly associated with the prevalence of carotid atherosclerosis at the second examination (OR 0.85 95% 0.39-1.87) when compared with MHNW.

Conclusions: These results demonstrate that the burden of carotid atherosclerosis was not increased in the MHO when compared with the MHNW in both cross-sectional and longitudinal associations.

PO-16

REDUCED CARDIAC BAROREFLEX SENSITIVITY IS ASSOCIATED WITH GREATER AORTIC STIFFNESS IN MIDDLE-AGED/OLDER HUMANS: BENEFICIAL EFFECT OF HABITUAL AEROBIC EXERCISE

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Introduction: Sedentary aging is characterized by reduced cardiac baroreflex sensitivity (BRS) and increased aortic stiffness, both independent predictors of higher cardiovascular disease (CVD) risk in middle-aged/older (MA/O) adults. However, MA/O adults who perform habitual endurance exercise demonstrate lower CVD risk perhaps in part from reduced aortic stiffness and enhanced cardiac BRS.

Objectives: We hypothesized that reduced BRS (sequence technique derived from intra-brachial artery BP waveforms) is associated with greater aortic stiffness (aortic pulse wave velocity, aPWV) among sedentary and endurance-trained MA/O adults, and that endurance exercise training initiated in previously sedentary MA/O adults enhances BRS and reduces aPWV.

Methods and results: In a cross-sectional study, MA/O sedentary (MA/O-S, n=24, age 62 ± 4 yrs, VO_{2max} 26 ± 1 ml/kg/min) adults demonstrated reduced BRS (11.7 ± 1.5 vs 40.7 ± 8.6 ms/mmHg, *P*<0.05) and greater aortic stiffness (aPWV 9.7 ± 0.8 vs. 6.4 ± 0.8 m/sec, *P*<0.05) compared with young sedentary (YS, n=6, age 22 ± 2 yrs; VO_{2max} 39 ± 2 ml/kg/min) adults. MA/O endurance-trained (MA/O-T, n=15, age 61 ± 2 yrs, VO_{2max} 46 ± 1 ml/kg/min, *P*<0.05) adults had greater BRS (24.3 ± 4.0 ms/mmHg) and smaller aPWV (8.0 ± 0.3 m/sec, *P*<0.05) than MA/O-S. In the entire cohort after adjustment for age and mean blood pressure, aPWV was inversely correlated with BRS (*r*=-0.55, *P*<0.05). In a subset of MA/O-S adults (n=18), 8 weeks of aerobic exercise training (n=12, 6-7 days/week, 40-45 min/day, 60-80% HRmax) improved BRS (11.7 ± 2.1 vs. 16.1 ± 2.7 ms/mmHg, *P*<0.05) but not aPWV (9.8 ± 0.8 vs. 9.2 ± 0.9 m/sec, *P*=0.08), while there was no change in sedentary time-controls (n=6, *P*>0.05).

Conclusions: Habitual aerobic exercise attenuates the age-related reduction in cardiac BRS and greater aortic stiffness in humans. However, short-term aerobic exercise training initiated in MA/O-S adults improves BRS but not aortic stiffness.

PO-17

A NEW ARTERIAL STIFFNESS INDEX PERMITTING ISOBARIC COMPARISONS

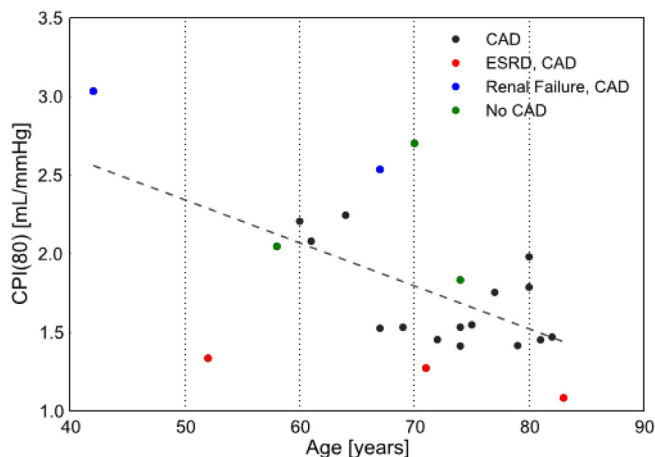
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Objectives: Arterial stiffness is pressure-dependent and comparisons among individuals and between groups should be made under isobaric conditions. Statistical methods are typically employed to adjust stiffness indices for pressure-dependence. In this ongoing study, we employ our new stiffness index, CPI, which allows for explicit evaluation at a reference pressure and stroke volume, to investigate its change with age and disease.

Methods: We studied twenty-three patients (n=23: 9 men and 14 women; mean age 70 years) that underwent diagnostic cardiac catheterization. Aortic pressure waveforms were used to evaluate CPI at a reference pressure of 80 mmHg and stroke volume of 100 mL. A closed-form expression of pressure-dependent compliance index, or CPI, was derived and computed for each subject. Linear regression was used to assess the trend of CPI with age.

Results: CPI values ranged from 1.08 to 3.03 mL/mmHg. A negative correlation was found between CPI and age (*r*=-0.57, *p*<0.01). End-stage renal disease patients had the lowest values within their respective decade of age. Patients without coronary artery disease had the higher values within their decade.

Conclusions: CPI is an index of pressure-dependent arterial compliance. Its decrease with age, further exaggerated by presence of disease, is consistent with studies using other stiffness indices. The allowance for explicit evaluation at a common pressure relieves the need for statistical adjustments for pressure-dependence and permits a more individualized measure of arterial stiffness. Moreover, this allows separation of active and passive changes in arterial stiffness when cardiac properties or blood pressure levels are altered. Continuing studies will provide better sampling of age and disease states.



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