



Artery Research

ISSN (Online): 1876-4401

ISSN (Print): 1872-9312

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

P4.7: RELATIONSHIP OF DIFFERENT CARDIOVASCULAR TISSUE BIOMARKERS WITH ESTABLISHED RISK FACTORS AND FRAMINGHAM RISK SCORE IN MIDDLE-AGE SUBJECTS WITHOUT CARDIOVASCULAR EVENTS

C. Palombo, C. Morizzo, D. Guarino, M. Kozakova

To cite this article: C. Palombo, C. Morizzo, D. Guarino, M. Kozakova (2014) P4.7: RELATIONSHIP OF DIFFERENT CARDIOVASCULAR TISSUE BIOMARKERS WITH ESTABLISHED RISK FACTORS AND FRAMINGHAM RISK SCORE IN MIDDLE-AGE SUBJECTS WITHOUT CARDIOVASCULAR EVENTS, Artery Research 8:4, 140–141, DOI: <https://doi.org/10.1016/j.artres.2014.09.130>

To link to this article: <https://doi.org/10.1016/j.artres.2014.09.130>

Published online: 7 December 2019

Aortic stiffness is an independent predictor of adverse CV outcomes and elevated in COPD². However, the influence of gender on aortic stiffness in COPD has not been established. We hypothesized that males with COPD would have greater aortic stiffness than females.

Methods: As part of the ARCADE study, we assessed 500 patients with COPD confirmed by spirometry and 150 comparators. Aortic pulse wave velocity (PWV) was evaluated using the sphygmoCor device. Other assessments included body composition, blood pressure, heart rate, number of exacerbations, smoking history and C-reactive protein and fibrinogen.

Results: Patients and comparators were similar in age, BMI and gender. Males with COPD (255) had greater aortic PWV mean (SD)10.2 (2.7) than females, 9.5 (2.4), $p=0.003$. However, they were similar in age, FEV₁%, BMI, peripheral and central blood pressure indices, heart rate, number of exacerbations, smoking history and inflammatory biomarkers, $p>0.05$. The difference remained after controlling for age and peripheral mean arterial pressure (Adjusted R²=26%, F=6.15, $p=0.014$). The gender difference was not evident in the comparator group.

Conclusion: Males with COPD had greater aortic stiffness compared to the females, independent of traditional cardiovascular risk factors. The increased aortic stiffness may explain the high incidence of fatal and non-fatal cardiac events in the male patients, which may offer a therapeutic target.

1) Agusti et al. 2010. *Respir Res.* 11:122.

2) Vlachopoulos et al. 2010. *J Am Coll Cardiol.* 55(13):1318-1327.

P4.4

DOPPLER INDEXES OF LEFT VENTRICULAR SYSTOLIC AND DIASTOLIC FLOWS AND CENTRAL PULSE PRESSURE IN RELATION TO RENAL RESISTIVE INDEX IN A GENERAL POPULATION

N. Cauwenberghs^a, J. Knez^a, L. Thijs^a, Y.-P. Liu^a, Y.-M. Gu^a, J. Staessen^{a,b}, T. Kuznetsova^a

^aKU Leuven, Leuven, Belgium

^bUniversity of Maastricht, Maastricht, The Netherlands

Background: The cardio-renal interaction occurs via hemodynamic and humoral factors. Non-invasive assessment of renal hemodynamics is currently possible by assessment of renal resistive index (RRI) derived from intrarenal Doppler arterial waveforms. So far, only limited information is available regarding the relationship between RRI and cardiac hemodynamics in the general population. We investigated these associations in randomly recruited subjects from a Flemish population.

Methods: In 171 participants (48.5% women; mean age, 52.2 years), using conventional pulsed wave Doppler, we measured RRI (mean, 0.60) and left ventricular outflow tract (LVOT) and transmitral (E and A) blood flow peak velocities and its velocity time integrals (VTI). Using carotid applanation tonometry, we measured central pulse pressure (cPP) and arterial stiffness indexes such as augmentation pressure and carotid-femoral pulse wave velocity.

Result: In stepwise regression analysis, RRI independently and significantly increased with female sex, age, body weight, brachial pulse pressure and use of β -blockers, whereas it decreased with body height and mean arterial pressure. In multivariable-adjusted models with cPP and arterial stiffness indexes as the explanatory variables, we observed a significant and positive correlation of RRI only with cPP ($P<0.0001$). Among the Doppler indexes of left ventricular blood flow, RRI was significantly and positively associated with LVOT and E peak velocities ($P\leq 0.012$) and VTIs ($P\leq 0.010$).

Conclusions: We demonstrated that in unselected subjects RRI was significantly associated with cPP and left ventricular systolic and diastolic Doppler blood flow indexes. Our findings imply that in addition to the anthropometric characteristics, cardiac hemodynamic factors influence the intrarenal arterial Doppler waveform patterns.

P4.5

CHARACTERISTICS AND DETERMINANTS OF THE SUBLINGUAL MICROCIRCULATION IN A FLEMISH POPULATION

Y. M. Gu^a, L. Thijs^a, Y.-P. Liu^a, T. Petit^a, Z. Zhang^a, H. Vink^b, T. Kuznetsova^a, P. Verhamme^a, J. Staessen^{a,b}

¹University of Leuven, Leuven, Belgium

²Maastricht University, Maastricht, The Netherlands

Background: Endothelial glycocalyx (EG) acts as a protective barrier. Decrease of sublingual perfused boundary region (SPBR) reflects EG loss. We aimed to assess reproducibility of SPBR and to determine its determinants in a general population.

Methods: In 281 subjects randomly recruited in a Flemish population, we measured SPBR using by GlycoCheck software. SPBR is the distance between the median red blood cell column width and the estimated outer edge of the red blood cell perfused lumen. We standardized SPBR to medians of haematocrit and density of perfused capillaries. In 42 participants, we computed repeatability coefficients (RC) expressing bias as percentage of maximal biological variation. We searched for significant ($p<0.05$) correlates of SPBR using stepwise regression.

Results: In 281 subjects (mean age, 51.2y; 53.0% women), SPBR averaged 1.80 μ m. RCs for intra- and inter-observer variability were $\geq 53.4\%$. Of 14 potential covariables, only age and mean arterial pressure (MAP) and use of diuretics correlated with SBPR ($p\leq 0.049$). Changes in SPBR associated with a 1-SD increments in age (+16.6y) and MAP (+11.3mmHg) were -58.2nm and -35.5nm, while SPBR was 97.7nm wider in diuretic users. Disregarding 140 patients with albuminuria, hypertension, diabetes, and cardiovascular disease, the 5th and 95th percentiles of SPBR across age (<30y to ≥ 50 y) ranged from 1.54 μ m to 1.43 μ m and from 2.52 μ m to 2.28 μ m, respectively.

Conclusion: SPBR variability is high probably because of physiological factors, because imaging is software controlled. The inverse association of SPBR with age and MAP might reflect a defense mechanism in the presence of these cardiovascular risk factors.

P4.6

PULSATILE AND STEADY BLOOD PRESSURE COMPONENTS IN RELATION TO ENVIRONMENTAL LEAD EXPOSURE IN THE NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY 2003-2010

A. Hara^a, L. Thijs^a, K. Asayama^b, Y.-M. Gu^a, L. Jacobs^a, Z.-Y. Zhang^a, Y.-P. Liu^a, T. Nawrot^c, J. Staessen^{a,d}

^aUniversity of Leuven, Leuven, Belgium

^bTeikyo University School of Medicine, Tokyo, Japan

^cUniversity of Hasselt, Hasselt, Belgium

^dMaastricht University, Maastricht, The Netherlands

In view of the declining environmental lead exposure in the US, we analyzed the National Health and Nutrition Examination Survey (2003-2010) for association of pulsatile and steady BP components and hypertension (HT) with blood lead (BPb). The 12,725 participants included 21.2% Blacks, 20.5% Hispanics, 58.4% Whites, and 48.7% women. Blacks compared with non-Blacks had higher SBP, DBP, and mean arterial pressure (MAP) (126.5 vs. 123.9; 71.9 vs. 69.6; and 90.1 vs. 87.7mmHg, respectively) and higher HT prevalence (44.7 vs. 36.8%). SBP, DBP and MAP (123.3 vs. 125.5; 68.9 vs. 71.2; and 87.1 vs. 89.3mmHg) were lower in women than men with no significant sex difference in PP and HT prevalence ($P\geq 0.11$). BPb was lower in Whites than non-Whites (1.46 vs. 1.57 μ g/dL) and in women than men (1.25 vs. 1.80 μ g/dL). In multivariable analyses of all participants, BPb doubling was associated with higher ($P\leq 0.0007$) SBP, DBP and MAP (0.76 [CI, 0.38-1.13]; 0.43 [0.18-0.68]; and 0.54 [0.29-0.79]mmHg, respectively) with no change in PP ($P=0.063$) or the odds of HT ($P=0.11$). Associations with BPb were nonsignificant ($P\geq 0.09$) for SBP in women and for DBP and MAP in non-Whites. Among men, SBP increased with BPb ($P\leq 0.060$) with effect sizes associated with BPb doubling ranging from +0.65mmHg in Whites to +1.61mmHg in Blacks. For SBP and PP, interactions of ethnicity and sex with BPb were all significant ($P\leq 0.027$). In conclusion, small and inconsistent effect sizes in the associations of BP with BPb likely exclude current environmental lead exposure as a major HT cause in the US.

P4.7

RELATIONSHIP OF DIFFERENT CARDIOVASCULAR TISSUE BIOMARKERS WITH ESTABLISHED RISK FACTORS AND FRAMINGHAM RISK SCORE IN MIDDLE-AGE SUBJECTS WITHOUT CARDIOVASCULAR EVENTS

C. Palombo^a, C. Morizzo^a, D. Guarino^a, M. Kozakova^b

^aDepartment of Surgical, Medical, Molecular & Critical Area Pathology, University of Pisa, Pisa, Italy

^bDepartment of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy

The relations between emerging biomarkers of preclinical CV disease and established risk algorithms are not well defined.

Aim: this study evaluated the relationships of various tissue CV biomarkers with Framingham risk score (FRS) and its individual determinants.

Methods: in 435 subjects without previous cardiovascular events (287 males, mean age 58 \pm 11, 56% diabetics (DM), 48% treated for hypertension (HBP), 51% with dyslipidemic treatment, 27% smokers), we measured radio-frequency based (QIMT® and QAS®, Esaote) carotid intima-media thickness (IMT), wave speed (WS) and local pulse pressure (cPP), carotid-femoral pulse wave velocity (PWV; Complior), LV mass index (LVMI) and relative wall thickness (RWT).

Results: the correlation ($p < 0.05$) between FRS and CV biomarkers was the highest for WS, cPP, and PWV ($r = 0.50, 0.49, 0.51$), lower for LVMI, IMT and RWT ($r = 0.41, 0.41, 0.21$). Age was main independent determinant of WS, PWV and cPP; WS and PWV were also independently related to systolic BP and DM, and cPP to HBP therapy. Main determinant of IMT was DM, followed by age and HBP therapy, and independent determinants of LVMI and RWT were SBP and HBP therapy, respectively. Lipids and smoking were not independently related to any tissue biomarker.

Conclusions: our data indicate that arterial stiffness and local carotid PP reflect mainly the ageing process, and are more tightly related to FRS than structural carotid and LV indices. Carotid IMT or LV mass and geometry are predominantly influenced by the presence of DM or HBP, respectively. Different tissue biomarkers may contribute to a personalized estimate of CV risk.

P4.8

ARTERIAL STIFFNESS IS ASSOCIATED WITH DEPRESSIVE SYMPTOMS AND THIS ASSOCIATION IS PARTLY MEDIATED BY CEREBRAL SMALL VESSEL DISEASE: THE AGES-REYKJAVIK STUDY

T. Van Sloten^a, G. Mitchell^b, S. Sigurdsson^c, M. Van Buchem^d, P. Jonsson^{e,f}, M. Garcia^g, T. Harris^g, R. Henry^a, A. Levey^h, C. Stehouwer^a, V. Gudnason^{b,f}, L. Launer^g

^aMaastricht University Medical Centre, Maastricht, The Netherlands

^bCardiovascular Engineering Inc, Norwood, USA

^cIcelandic Heart Association, Kopavogur, Iceland

^dLeiden University Medical Center, Leiden, The Netherlands

^eLandsþítali University Hospital, Reykjavik, Iceland

^fUniversity of Iceland, Reykjavik, Iceland

^gNational Institute on Aging, Bethesda, MD, USA

^hTufts Medical Center, Boston, MA, USA

Background: Arterial stiffness may contribute to depression via cerebral microvascular damage, but evidence for this is scarce. We therefore investigated the association between arterial stiffness and depressive symptoms and the potential mediating role of cerebral small vessel disease therein.

Methods: This cross-sectional study included 2,058 participants (mean age 79.6 years; 59.0% women) of the AGES-Reykjavik study. Arterial stiffness (carotid-femoral pulse wave velocity, CFPWV), depressive symptoms (15-item geriatric depression scale, GDS-15) and cerebral small vessel disease (magnetic resonance imaging) were determined. Manifestations of cerebral small vessel disease included higher white matter hyperintensity volume, subcortical infarcts, cerebral microbleeds, Virchow-Robin spaces and lower total brain parenchyma volume.

Results: Higher CFPWV was associated with a higher GDS-15 score, after adjustment for age, sex, education level, smoking, digit symbol substitution test score, gait speed, mean arterial pressure, heart rate and cardiovascular risk factors. Additional adjustment for white matter hyperintensity volume or subcortical infarcts attenuated the association between CFPWV and the GDS-15 score, which became statistically not significant. Formal mediation tests showed that the mediating effects of white matter hyperintensity volume and subcortical infarcts were statistically significant. Virchow-Robin spaces, cerebral microbleeds and cerebral atrophy did not mediate the association between CFPWV and depressive symptoms.

Conclusions: Higher arterial stiffness is associated with more depressive symptoms; this association is partly mediated by white matter hyperintensity volume and subcortical infarcts. This study supports the hypothesis that arterial stiffness leads to depression in part via cerebral small vessel disease.

P4.9

ASSOCIATION BETWEEN ARTERIAL STIFFNESS AND SKIN MICROVASCULAR FUNCTION IN INDIVIDUALS WITHOUT AND WITH TYPE 2 DIABETES: COMBINED REPORT OF THE SUVIMAX2 STUDY AND THE MAASTRICHT STUDY

T. Van Sloten^a, S. Czernichow^{b,c}, A. Houben^a, A. Protogerou^a, R. Henry^a, D. Muris^a, M. Schram^a, S. Sep^a, P. Dagnelie^a, C. Van der Kallen^a, N. Schaper^a, J. Blacher^d, S. Hercberg^e, B. Levy^b, C. Stehouwer^a

^aMaastricht University Medical Centre, Maastricht, The Netherlands

^bINSERM, Villejuif, France

^cUniversity of Versailles Saint Quentin, Versailles, France

^dHôtel-Dieu Hospital, Paris Descartes University, Paris, France

^eINSERM U557, Bobigny, France

Background: It has been hypothesized that arterial stiffness leads to generalized microvascular dysfunction, and that this may explain the association between arterial stiffness and different diseases, including

dementia, kidney dysfunction, neuropathy and osteoporosis. In addition, individuals with type 2 diabetes mellitus (T2DM) may be particularly prone to the detrimental effects of arterial stiffness. However, evidence for an association between arterial stiffness and direct markers of generalized microvascular dysfunction is lacking. The cutaneous microcirculation is a representative vascular bed to examine generalized microvascular phenomena. We therefore investigated the association between arterial stiffness and skin microvascular function in both individuals without and with T2DM.

Methods: Cross-sectional data was used of The SUVIMAX2 Study ($n = 284$; 62.2y; 48.6% women; 0% T2DM (by design)) and The Maastricht Study ($n = 737$; 59.7y; 45.2% women; 28.8% T2DM (by design)). Arterial stiffness was determined by carotid-femoral pulse wave velocity (cfPWV). Skin capillaroscopy was used to determine capillary density at baseline, during reactive hyperemia after arterial occlusion and during venous congestion. Laser Doppler flowmetry was used to assess acetylcholine- and local heating-induced vasoreactivity, and microvascular flowmotion.

Results: In both individuals without and with T2DM, cfPWV was not associated with baseline capillary density or capillary recruitment during reactive hyperemia or venous congestion. In addition, cfPWV was not associated with acetylcholine- or local heating-induced vasoreactivity, or microvascular flowmotion.

Conclusions: Arterial stiffness is not associated with skin microvascular function, irrespective of the presence of T2DM. This suggests that the association between arterial stiffness and different diseases cannot be explained by generalized microvascular dysfunction alone.

P4.10

PULSE WAVE VELOCITY UNDER THE CUT-OFF VALUE OF 10 M/S AND AORTIC AUGMENTATION INDEX CORRECTED TO HEART RATE MAY SIGNAL HIGHER EARLY CVD RISK IN MIDDLE-AGED MEN

I. Ceponiene, E. Tamuleviciute-Prasciene, R. Slapikas, J. Petkeviciene, J. Klumbiene

Lithuanian University of Health Sciences, Kaunas, Lithuania

Purpose: Arterial stiffness may have an added value in cardiovascular (CV) risk stratification. We aimed to evaluate association of CV risk factors and arterial stiffness in middle-aged subjects.

Methods: 238 Caucasian subjects (men 42.4%; mean age 48 years) free of known cardiovascular disease (CVD) were enrolled in a prospective cohort study in 1977. During the last evaluation in 2012-2013, arterial stiffness (carotid-femoral pulse wave velocity [cf-PWV] and aortic augmentation index [Alx]) were measured by applanation tonometry.

Results: cf-PWV was significantly higher in men than in women (8.1 ± 2.5 vs 7.5 ± 2.1 m/s; $p = 0.035$). cf-PWV was higher in subjects with MetS (8.8 ± 2.4 vs 7.5 ± 2.2 m/s; $p = 0.0003$), but was not associated with individual CV risk factors. Increased cf-PWV of >10 m/s was found in 10% of subjects with no significant differences between genders ($p = 0.22$), and was not related to any of the individual CV risk factors. Alx ($27.1 \pm 10.9\%$) was not associated with any of the CV risk factors or MetS, and did not differ between genders. However, when corrected to heart rate Alx (Alx@75) was significantly higher in men with MetS, compared to men without MetS (21.7 vs 16.7% ; $p = 0.02$), but not women, and was associated with hypertension ($p = 0.003$) and central adiposity ($p = 0.02$).

Conclusions: PWV was significantly higher in men than women, and in subjects with MetS. Alx@75, and not Alx, was related to worse cardiovascular risk profile. These findings suggest that higher PWV and Alx@75 values, although lower than currently established cut-off values, may signal of increased risk of early CVD in men.

P4.11

TYPE 2 DIABETES IS ASSOCIATED WITH GREATER CAROTID STIFFNESS AND GREATER PRESSURE-DEPENDENCY OF CAROTID STIFFNESS—THE MAASTRICHT STUDY

M. Veugen^a, T. Van Sloten^a, R. Henry^a, E. Hermeling^a, H.-P. Rocca^a,

M. Schram^a, P. Dagnelie^a, C. Stehouwer^a, K. Reesink^b

^aMUMC+, Maastricht, The Netherlands

^bMUMC+, Cardiovascular Research Institute Maastricht (CARIM), Maastricht, The Netherlands

Purpose: Arterial remodeling underlies the association between type 2 diabetes (T2D) and arterial stiffness. Remodeling may also affect the pressure-dependency of stiffness. Pressure-dependency can be quantified as the systolic-diastolic difference in pulse wave velocity (Δ PWV).