



## Artery Research

ISSN (Online): 1876-4401

ISSN (Print): 1872-9312

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

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### **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, G. Mitchell, S. Sigurdsson, M. Van Buchem, P. Jonsson, M. Garcia, T. Harris, R. Henry, A. Levey, C. Stehouwer, V. Gudnason, L. Launer

**To cite this article:** T. Van Sloten, G. Mitchell, S. Sigurdsson, M. Van Buchem, P. Jonsson, M. Garcia, T. Harris, R. Henry, A. Levey, C. Stehouwer, V. Gudnason, L. Launer (2014) P4.8: ARTERIAL STIFFNESS IS ASSOCIATED WITH DEPRESSIVE SYMPTOMS AND THIS ASSOCIATION IS PARTLY MEDIATED BY CEREBRAL SMALL VESSEL DISEASE: THE AGES-REYKJAVIK STUDY, Artery Research 8:4, 141–141, DOI: <https://doi.org/10.1016/j.artres.2014.09.131>

**To link to this article:** <https://doi.org/10.1016/j.artres.2014.09.131>

Published online: 7 December 2019

**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

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**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

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**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

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**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 ( $8.1 \pm 2.5$  vs  $7.5 \pm 2.1$  m/s;  $p = 0.035$ ). cf-PWV was higher in subjects with MetS ( $8.8 \pm 2.4$  vs  $7.5 \pm 2.2$  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

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**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 ( $\Delta$ PWV).