



## Artery Research

ISSN (Online): 1876-4401

ISSN (Print): 1872-9312

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

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### **P8.09: C-REACTIVE PROTEIN IS ASSOCIATED WITH ENDOTHELIUM-DEPENDENT ALTERATIONS OF MICROCIRCULATION IN PATIENTS WITH METABOLIC SYNDROME**

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**To cite this article:** L. Ryliskyte, J. Badariene, V. Dzenkeviciute, A. Cypiene, V. Skorniakov, A. Laucevicius (2009) P8.09: C-REACTIVE PROTEIN IS ASSOCIATED WITH ENDOTHELIUM-DEPENDENT ALTERATIONS OF MICROCIRCULATION IN PATIENTS WITH METABOLIC SYNDROME, Artery Research 3:4, 188–189, DOI: <https://doi.org/10.1016/j.artres.2009.10.115>

**To link to this article:** <https://doi.org/10.1016/j.artres.2009.10.115>

Published online: 14 December 2019

**Objective:** Which are aortic pulse wave velocity determinants in a diabetic population?

**Methods:** We studied 132 diabetic patients. They entered the day hospital to have a cardiovascular checkup. We measured brachial and central blood pressure, augmentation index, and pulse wave velocity (PWV). They also had extended biochemical tests.

**Results:** Among those 132 patients, 8% had type 1 diabetes and 92% had type 2 diabetes. Mean period of diabetes was 13 years. Treatments combined insulin (47%), biguanids (54%), acarbose (10%), sulfamids (31%), thiazolidinediones (11%), with 25 patients (19%) having both insulin and oral drugs. We compared patients with and without insulin, measured their PWV, and adjusted it to standard factors (age, gender, MAP, sex), but also to 3 time-related diabetes criteria (short term : plasma glucose; middle term : HbA1c; long term : insulin treatment).

Antihypertensive drugs such as ACEI also contribute to the model (-1.02;  $p = 0.0398$ ).

**Conclusion:** Insulin treatment is the most powerful diabetes-related parameter accepted in this PWV model.

Oral hypoglycemic drugs, HbA1C, plasma glucose do not contribute to the PWV model.

RAAS blockade drugs contribute to the PWV model.

Diabetes control quality over the time when coming to the point of having insulin as a treatment is an independent factor of arterial wall rigidification.

#### P8.06

##### REFERENCE VALUES FOR ARTERIAL STIFFNESS MEASURED WITH ARTERIOGRAPH

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Elevated aortic pulse wave velocity (aoPWV) is an independent predictor of cardiovascular morbidity and mortality. There are, however, no widely accepted normal or reference values for aoPWV. The aim of this work was to define these values.

**Patients and methods:** AoPWV was assessed in several patient populations using oscillometric device (TensioMed Arteriograph) by a numerous investigators and data were collected into a large database of 17173 subjects aged 2-92 years. AoPWV was studied in a group of 11024 normotensive individuals without antihypertensive medication which was divided into age decades in order to determine the age-specific reference values for aoPWV.

**Results:** Mean age was  $39.5 \pm 20.12$  and  $43.6 \pm 17.82$  ys in males and females, respectively ( $p < 0.001$ ). Mean aoPWV differed significantly between genders ( $7.9 \pm 2.3$  vs  $8.9 \pm 2.7$ ;  $p < 0.001$ ). Median aoPWV values in the age subgroups by decades were determined (5.44, 6.08, 6.69, 7.29, 8.38, 9.81, 10.15, 10.41, 11.02 m/s from the age under 10 to 80-90, respectively). The 75th and 95th percentiles of the samples were used to determine the upper limit of aoPWV reference values.

**Conclusions:** The value above 12 m/s suggested as a threshold for elevated aoPWV by ESH'07 can be questioned as PWV depends on the method used to calculate the travel distance. Our results derived from a huge healthy general population including wide range of age suggest that aoPWV values are highly dependent on age and gender. Therefore, these results might serve as age and gender specific reference values for aoPWV.

#### P8.07

##### AN OLD DOG WITH NEW TRICKS: URIC ACID LEVELS ARE ASSOCIATED WITH AORTIC STIFFNESS AND WAVE REFLECTIONS IN NEWLY DIAGNOSED, NEVER-TREATED HYPERTENSION

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**Background:** Serum uric acid (UA) plays a key role in the development and progression of hypertension. We investigated the association of UA levels and indices of arterial function in a cohort of newly diagnosed, never treated hypertensive subjects.

**Methods:** 1225 patients with a new diagnosis of mild to moderate arterial hypertension for which they had never received treatment were enrolled in the study (mean age 53 years, 728 men). Serum UA, carotid-femoral pulse wave velocity (cfPWV), an index of elastic-type, aortic stiffness and

augmentation index (Alx), a composite marker of wave reflections and arterial stiffness were measured.

**Results:** In univariable analysis, UA levels correlated with cfPWV ( $r = 0.199$ ,  $P < 0.001$ ) and Alx ( $r = -0.263$ ,  $P < 0.001$ ). In stepwise multivariable linear regression analysis, an independent positive association of cfPWV with UA levels was observed after adjusting for confounders (standardized regression coefficient  $\beta = 0.135$ ,  $P < 0.001$ , adjusted  $R^2 = 0.405$ ), indicating an increase in aortic stiffness with higher values of UA. In contrast, an independent negative association of Alx with UA levels was observed after adjusting for confounders (standardized regression coefficient  $\beta = -0.059$ ,  $P = 0.022$ , adjusted  $R^2 = 0.507$ ), indicating a decrease in wave reflections with higher values of UA.

**Conclusion:** Serum UA levels are independently associated with aortic stiffening and wave reflections in never treated hypertensives. This finding extends the theoretical underpinnings regarding the cardiovascular functions of UA, as it advocates a putative role in the development of hypertension via mechanisms regulating arterial function.

#### P8.08

##### HEMODYNAMICS AND LARGE ARTERY STIFFNESS IN YOUNG PREHYPERTENSIVE MEDICAL STUDENTS

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**Background:** Prehypertensive subjects have a markedly increased risk of developing hypertension compared to normotensive subjects. Prehypertension is therefore an excellent model to study hemodynamics and arterial stiffness in the development of hypertension.

**Methods:** We assessed hemodynamics and arterial stiffness in normotensive (NT, blood pressure  $< 120/80$  mmHg) and prehypertensive (PHT, blood pressure  $120-139/80-89$  mmHg) medical students. Blood pressure (BP) was measured with a validated oscillometric device on two separate visits. On a third visit cardiac output, cardiac index (cardiac output corrected for body surface area), stroke volume and heart rate were measured using the Nexfin monitor for continuous non-invasive finger BP monitoring. Carotid-femoral pulse wave velocity (cfPWV) was measured using the Sphygmocor system.

**Results:** We studied 15 prehypertensive subjects (BP  $127 \pm 8/69 \pm 6$  mmHg, 13 males, age  $21.5 \pm 2$  years) and 25 normotensive subjects (BP  $112 \pm 7/64 \pm 6$  mmHg, 8 males, age  $21.1 \pm$  years). Nexfin data were available for 31 subjects (22 NT and 9 PHT). Cardiac output and cardiac index were  $7.0 \pm 1.2$  and  $3.6 \pm 0.7$  L/min respectively in prehypertensive compared to  $5.7 \pm 0.9$  and  $3.1 \pm 0.4$  L/min in normotensive subjects ( $p = 0.002$ ,  $p = 0.02$ ). Stroke volume was 111 vs 101 ml ( $p = 0.13$ ) and heart rate was 65 vs. 57 bpm ( $p = 0.06$ ). cfPWV was higher in the prehypertensive group ( $5.5 \pm 0.5$  vs.  $5.2 \pm 0.5$  m/s  $p < 0.03$ ). Linear regression analysis showed that age ( $R^2 = 0.13$ ,  $\beta = 0.39$ ,  $p = 0.02$ ) and SBP ( $R^2 = 0.28$ ,  $\beta = 0.53$ ,  $p = 0.001$ ) are independent determinants of cfPWV.

**Conclusion:** Young prehypertensive medical students have higher cardiac output and cardiac index than normotensive students. The increased cfPWV in the prehypertensive subjects is partially determined by higher blood pressures.

#### P8.09

##### C-REACTIVE PROTEIN IS ASSOCIATED WITH ENDOTHELIUM-DEPENDENT ALTERATIONS OF MICROCIRCULATION IN PATIENTS WITH METABOLIC SYNDROME

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**Objective:** Inflammation and early arterial damage are the possible mechanisms responsible for increased cardiovascular risk (CVR) in patients with metabolic syndrome (MetS). The aim of this study was to investigate the relationship between C-reactive protein (CRP) and arterial parameters of macro- and microcirculation in MetS patients.

**Methods:** Subjects with MetS but without overt cardiovascular disease ( $n = 100$ ; age  $52.9 \pm 6.4$ ; 40% male) underwent detailed assessment of CVR factors. Measurements of local, regional and systemic arterial stiffness (AS) and endothelial function (EF) in brachial artery, finger and skin were performed.

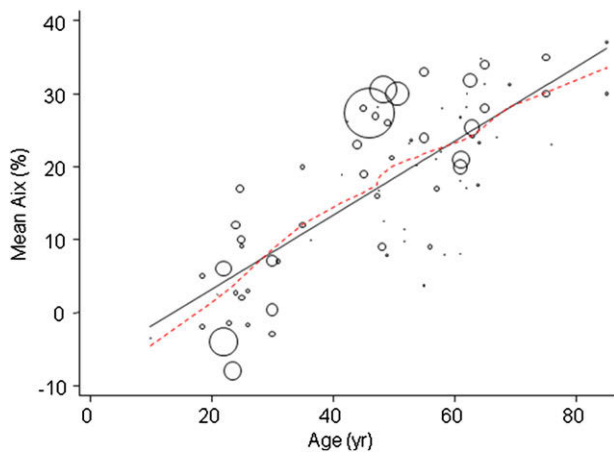
**Results:** Subjects were categorized according to CRP levels that relate to future CVR (<1, 1-3, and >3 mg/L). There was no significant difference in the mean age ( $51.2 \pm 5.3$ ,  $53.6 \pm 6.6$  and  $53.6 \pm 7.2$ ,  $p = 0.19$ ) and gender distribution ( $p = 0.44$ ) between the CRP categories. However, body mass index and waist circumference differed as did mean arterial pressure ( $p < 0.001$ ,  $p = 0.001$  and  $p = 0.016$  respectively). Carotid AS ( $2.86 \pm 1.09$ ;  $3.49 \pm 1.52$ ;  $3.77 \pm 1.68$ ,  $p = 0.028$ ) and several parameters of EF assessed by laser Doppler in microcirculation, e.g. percent change of skin perfusion ( $5090 \pm 2385$ ;  $3636 \pm 1777$ ;  $3885 \pm 2731$ ,  $p = 0.033$ ) and time to half before hyperaemia ( $9.76 \pm 15.10$ ;  $4.51 \pm 8.04$ ;  $3.47 \pm 5.69$  s,  $p = 0.036$ ), were significantly related to CRP category (Kruskal-Wallis Test). Multiple regression analysis revealed that CRP is independently associated only with alterations in microcirculation – percent change of skin perfusion (rest-to-peak flow,  $\beta = 0.27$ ,  $p = 0.016$ ) but not other arterial parameters.

**Conclusion:** In MetS patients CRP is independent predictor of endothelium-dependent alterations in skin microcirculation. Association between CRP categories and other parameters of microcirculation and carotid arterial stiffness was also observed.

#### P8.10 THE RELATIONSHIP BETWEEN AUGMENTATION INDEX AND AGEING: A META-REGRESSION ANALYSIS

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It has been reported that augmentation index ( $AI_x$ ) increases with age, but that the increase is more prominent in younger subjects [1], and may even decrease with age in individuals over 50yrs [2]. We undertook a meta-analysis of the published literature of 9,551 individuals (5,659 male), aged 4 to 91 years (mean 54.2 years) and undertook meta-regression to further investigate the relationship of  $AI_x$  with age.  $AI_x$  increased with age (0.51 (0.41, 0.61) %/yr; coefficient (95% CI); adjusted  $r^2 = 59.97\%$ ;  $p < 0.0001$ ) with little evidence of marked non-linearity over the life course (Figure).



*Meta-analysis of  $AI_x$  vs age (solid line) with LOWESS fit shown (dashed line).* This meta-analysis suggests that  $AI_x$  increases relatively uniformly with age, although there may be a small decline in the rate of increase at older ages.

1. McEniery et al. *J Am Coll Cardiol* 2005; 46:1753-60.
2. Mitchell et al., *Hypertension*. 2004;43:1239-1245.

#### P8.11 SUPINE BLOOD PRESSURE IS RAISED IN HYPERTENSIVE NON-DIPPERS: A NOVEL TEST TO DETERMINE DIPPER STATUS?

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**Introduction:** Patients with nocturnal blood pressure (BP) that fails to decline  $\geq 10\%$  compared with daytime BP (non-dippers) have increased mortality risk. This may be related to increased arterial stiffness and raised central BP whilst supine. This study aimed to test this hypothesis. We also sought to determine if non-dippers could be identified by the BP change from seated-to-supine positions.

**Methodology:** 24-hour-ambulatory BP was recorded in 95 treated hypertensive patients (aged  $62 \pm 8$  years), comprising 43 (45%) non-dippers and 52 (55%) dippers (nocturnal BP decline  $\geq 10\%$ ). Brachial and central BP (SphygmoCor) were recorded in the seated and supine positions after  $\approx 5$  minutes rest in each position. Arterial stiffness was estimated by augmentation index and aortic pulse wave velocity.

**Results:** Arterial stiffness was not significantly different between dippers and non-dippers, nor were brachial or central systolic BP (SBP) whilst seated ( $p > 0.05$  for all). However, non-dippers had significantly higher supine brachial SBP ( $132 \pm 14$  vs  $126 \pm 11$  mmHg;  $p < 0.05$ ) and central SBP ( $121 \pm 15$  vs  $115 \pm 11$  mmHg;  $p < 0.05$ ). Moreover, the changes in both brachial and central SBP to the supine position were also higher in non-dippers ( $p < 0.05$  for both). A brachial SBP increase of  $\geq 8$  mmHg from the seated-to-supine position predicted non-dipper status with 87% specificity ( $p < 0.05$ ). Night-time SBP correlated with clinic brachial SBP in the supine ( $r = 0.39$ ;  $p < 0.001$ ), but not seated ( $r = 0.19$ ;  $p > 0.05$ ) position ( $Z = 2.11$ ;  $p < 0.05$ ).

**Conclusion:** Supine central SBP is elevated in non-dippers, which may contribute to cardiovascular risk. Increased supine, relative to seated, brachial SBP may be a useful clinical test to identify non-dipper status.

#### P8.12 ASSOCIATION BETWEEN ASYMMETRIC DIMETHYLARGININE AND THE INDICES OF VASCULAR FUNCTION IN PATIENTS WITH ESSENTIAL HYPERTENSION

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**Background:** Asymmetric dimethylarginine (ADMA) is an inhibitor of nitric oxide production and is associated with endothelial dysfunction. Elevated plasma levels of ADMA have been demonstrated in patients with hypertension. The aim of the present study was to investigate the relationship between ADMA and the structural and functional indices of arteries in patients with hypertension.

**Methods and results:** Eighty middle-aged ( $47 \pm 1.0$  years, 41 male and 39 female) untreated mild to moderate essential hypertension patients underwent routine medical examination, pulse wave analysis (PWA) with salbutamol and nitroglycerin test, carotid-femoral pulse wave velocity (PWV) and duplex ultrasound measurements of the carotid artery intima media thickness (IMT). PWA with the administration of salbutamol and nitroglycerin was used to assess endothelium dependent (EDV) and independent vasodilation.

In patients with hypertension ADMA was significantly associated with EDV ( $r = -0.26$ ;  $p = 0.02$ ) and IMT ( $r = 0.32$ ;  $p = 0.007$ ). In multiple regression analysis ADMA was significantly independently correlated with peripheral diastolic blood pressure, EDV and IMT ( $R^2 = 0.28$ ;  $p < 0.01$ ). No correlation was detected between ADMA and  $AI_x$  ( $p = 0.48$ ) or PWV ( $p = 0.54$ ). In multiple regression analysis IMT was independently associated with age, peripheral pulse pressure, LDL cholesterol, WBC and ADMA concentration ( $R^2 = 0.4$ ;  $p < 0.01$ ).

**Conclusion:** Present study demonstrated independent associations between ADMA levels and the structural and functional indices of arteries in patients with untreated hypertension. Plasma levels of ADMA were associated with increased carotid artery IMT and with reduced EDV. Thus, ADMA is a potential marker of endothelial dysfunction and intima media thickening in hypertensive patients.

#### P8.13 CORONARY IMPLANTATION OF SIROLIMUS-ELUTING STENT IMPAIRS THE PERIPHERAL VASCULAR COMPLIANCE IN PATIENT WITH CORONARY ARTERY DISEASE

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