



Artery Research

ISSN (Online): 1876-4401

ISSN (Print): 1872-9312

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

P8.05: DIABETES CONTROL QUALITY IS AN INDEPENDENT FACTOR OF ARTERIAL WALL RIGIDIFICATION

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To cite this article: A.L. Lieber, C. Vesin, M.E. Safar, B.I. Levy, J. Blacher (2009) P8.05: DIABETES CONTROL QUALITY IS AN INDEPENDENT FACTOR OF ARTERIAL WALL RIGIDIFICATION, Artery Research 3:4, 187–188, DOI: <https://doi.org/10.1016/j.artres.2009.10.111>

To link to this article: <https://doi.org/10.1016/j.artres.2009.10.111>

Published online: 14 December 2019

P8.02

IMPACT OF TRIGLYCERIDES AND INSULIN LEVELS ON WHOLE AND SURFACE CAROTID PLAQUE COMPOSITION IN PATIENTS WITH METABOLIC SYNDROME

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Introduction: Metabolic syndrome (MetS) is a cluster of metabolic abnormalities strongly associated with atherosclerosis and increased risk of CV events. Atherosclerotic plaques (AP) and its echolucency (ECL) can be detected using ultrasound (US) and evaluated by grey scale median analysis (GSM). ECL is associated with a higher plaque lipid content and vulnerability to rupture.

Aim: To assess the association between carotid plaques ECL and plasma markers of vascular inflammation, and disarray of lipid and glucose metabolism in patients (p.) with MetS.

Methods: After evaluating plasma lipids, glucose and insulin levels, blood pressure, and waist circumference in 700 p., 390 (56%) presented MetS (ATP III). Carotid US evaluation revealed AP in 185 (47%) of them (age 54.2 ± 11.1 , 33.3% females). AP were evaluated by GSM analysis, and divided in tertiles of ECL of the whole AP (whole plaque GSM, WGSM) and for the luminal first millimeter of the plaque (surface GSM, SGSM). The relation between tertiles of WGSM and SGSM and plasma lipids, glucose, insulin, CRP us, and HOMA were evaluated by multivariate regression analysis.

Results: Plasma triglycerides, insulin and HOMA were negatively related with WGSM and SGSM tertiles meaning a higher plaque lipid content and vulnerability. In multivariate analysis, triglycerides were significantly associated to low WGSM ($p < 0.003$) and SGSM ($p < 0.018$), whereas insulin only to low SGSM ($p < 0.012$).

Conclusion: The elevation in plasmatic triglycerides and insulin levels in patients with MetS are directly related with carotid plaques ECL, lipid content and vulnerability.

P8.03

INCREASED ARTERIAL STIFFNESS IN WOMEN WITH RHEUMATOID ARTHRITIS AND SYSTEMIC LUPUS ERYTHEMATOSUS IS NOT ASSOCIATED WITH LEVEL OF C-REACTIVE PROTEIN

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Introduction: The elevated level of C reactive protein (CRP) is associated with increased arterial stiffness in general population. However, it is uncertain whether CRP is related to arterial stiffness in rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE).

Methods: We studied 63 RA women (aged 41.48 ± 10.77 years) with disease activity (DAS28) 5.43 ± 0.93 , 31 SLE (aged 37.23 ± 9.09 years), disease activity index (SLEDAI) 18.40 ± 8.17 , organ damage index (SLICC) 1.0 (IQR 2.0) and 72 controls (aged 37.42 ± 9.15). Blood tests included serum lipid

profile, glucose and high-sensitivity CRP (hsCRP) measurement. The augmentation index (Alx), the measure of systemic arterial stiffness, was assessed by applanation tonometry (Sphygmocor v.7.01, AtCor Medical).

Results: In RA patients CRP (mg/l) was significantly higher as compared to SLE and controls (31.89 ± 40.44 vs. 5.80 ± 5.56 vs. 1.64 ± 3.18 ; $p < 0.001$), but it was not related to Alx. Alx was $24.71 \pm 11.52\%$ in RA vs. $20.81 \pm 12.29\%$ in SLE and $13.24 \pm 10.44\%$ in controls; $p < 0.001$. Significant influence of mean blood pressure (MBP) on arterial stiffness (Alx) was observed in RA patients ($r_{2adj.} = 0.365$; $p < 0.001$). In SLE patients MBP, SLICC and age were significant predictors of Alx ($r_{2adj.} = 0.508$; $p < 0.001$). **Conclusion:** Elevated CRP is present in RA and SLE, but it is not related to increased systemic arterial stiffness. Significant influence of MBP on arterial stiffness (Alx) was observed in RA patients. In SLE patients MBP, SLICC and age were related to increased Alx.

P8.04

ARTERIAL FUNCTION AND INSULIN SENSITIVITY: THEIR INTERPLAY IN EUGLYCAEMIC, NEVER-TREATED HYPERTENSIVES

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Background: Insulin resistance is a feature of essential hypertension. The interrelationships of indices of insulin resistance and arterial function in euglycaemic, never-treated hypertensives has not been addressed. To this end, we investigated the correlations of two insulin resistance indices (HOMA: homeostasis model assessment index; QUICKI: quantitative insulin sensitivity check index) and two arterial function indices (cfPWV: carotid-femoral pulse wave velocity; Alx: augmentation index) in a cohort of non-diabetic, never-treated hypertensives.

Methods: 998 patients with a new diagnosis of essential hypertension for which they had never received treatment were enrolled in the study (mean age 53 years, 600 men). HOMA and QUICKI were calculated from fasting glucose and insulin values. cfPWV and Alx were measured using validated devices.

Results: In univariable analysis, only cfPWV correlated with insulin resistance indices ($r = 0.245$, $P < 0.01$ for HOMA; $r = -0.245$, $P < 0.01$ for QUICKI). No statistically significant correlation was observed for Alx ($r = 0.015$, $P = NS$ for HOMA; $r = -0.015$, $P = NS$ for QUICKI). QUICKI is directly proportional to $1/\log\text{HOMA}$, thus explaining its negative correlation with cfPWV.

Conclusion: Aortic stiffness, as estimated by cfPWV correlates with insulin sensitivity in non-diabetic, newly diagnosed, never-treated hypertensives. A choice of an antihypertensive drug which improves arterial elasticity and insulin sensitivity could be of benefit in this setting.

P8.05

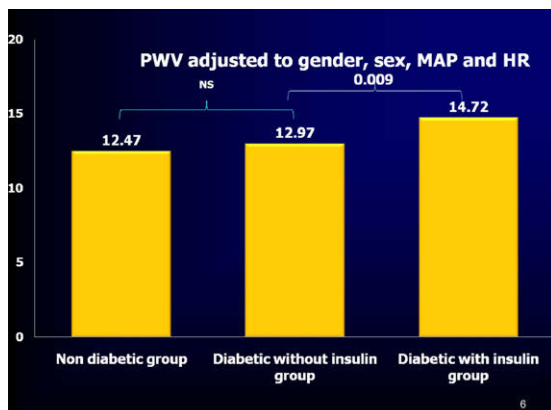
DIABETES CONTROL QUALITY IS AN INDEPENDENT FACTOR OF ARTERIAL WALL RIGIDIFICATION

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Introduction: Arterial tree alteration is the cornerstone of diabetes complications and its mechanical parameters are impaired.



• **FACTORS INFLUENCING PWV IN THE DIABETIC POPULATION (n=150)**

parameter	estimate	p
Intercept	-18.51	0.0257
Age	0.15	<.0001
log(HR)	4.49	0.0153
MBP	0.02	0.2123
Gender	-0.72	0.2346
Insulin treatment	1.58	0.0131
HbA1c	0.28	0.3292
Glycaemia	-0.04	0.7244

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 ± 20.12 and 43.6 ± 17.82 ys in males and females, respectively ($p < 0.001$). Mean aoPWV differed significantly between genders (7.9 ± 2.3 vs 8.9 ± 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 ± 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 ± 1.2 and 3.6 ± 0.7 L/min respectively in prehypertensive compared to 5.7 ± 0.9 and 3.1 ± 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 ± 0.5 vs. 5.2 ± 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 ± 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.