



## Artery Research

ISSN (Online): 1876-4401

ISSN (Print): 1872-9312

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

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### **P4.02: LIPIDS AND APOLIPOPROTEINS ARE ASSOCIATED WITH PULSE WAVE VELOCITY IN NEVER-TREATED HYPERTENSIVES**

D. Terentes-Printzios, C. Vlachopoulos, G. Vyssoulis, N. Ioakeimidis, N. Alexopoulos, P. Xaplanteris, A. Siama, A. Samentzas, P. Pietri, C. Stefanadis

**To cite this article:** D. Terentes-Printzios, C. Vlachopoulos, G. Vyssoulis, N. Ioakeimidis, N. Alexopoulos, P. Xaplanteris, A. Siama, A. Samentzas, P. Pietri, C. Stefanadis (2010) P4.02: LIPIDS AND APOLIPOPROTEINS ARE ASSOCIATED WITH PULSE WAVE VELOCITY IN NEVER-TREATED HYPERTENSIVES, Artery Research 4:4, 161–162, DOI: <https://doi.org/10.1016/j.artres.2010.10.054>

**To link to this article:** <https://doi.org/10.1016/j.artres.2010.10.054>

Published online: 21 December 2019

kinetics supra AT, in previous triangular test identified, which describes two superimposed components, one rapid and one appreciably slower, allowing one to calculate area between them. After training, NO availability increasing, this area decreases in inverse ratio to treatment efficacy. Then the training is to be seen as effective physiological means that allow one to reach the obtained enhanced functional capacity, by longer exercise owing to O<sub>2</sub> saving, so delaying the critical moment when effort is no longer sustainable from cardiovascular and pulmonary systems. In 10 untrained subjects, giving the NO donor isosorbide 5 mononitrate before second constant load test, the area is diminished on average of 46%. Therefore, all cardiopath subjects are to treat with organic nitrates in order to improve effort tolerance.

### P3.08

#### CENTRAL BLOOD PRESSURE AND VASCULAR STIFFNESS IN OBESE CHILDREN. RELATIONS TO THE METABOLIC SYNDROME AND SUBCLINICAL CARDIOVASCULAR DAMAGE: EFFECT OF WEIGHT REDUCTION. A PHD STUDY, BEGINNING MEDIO 2010

K. Hvidt, H. Ibsen, J.-C. Holm

Holbaek University Hospital, Holbaek, Denmark

**Background:** Increasing prevalence of childhood obesity threatens future health with higher cardiovascular morbidity and thereby reduction of life expectancy. Obesity in childhood is significant related to the metabolic syndrome. Stiffness in the wall of the central arteries increases systolic blood pressure and is an independent risk factor for cardiovascular complications. Measurements of central vascular stiffness and central blood pressure profiles may contribute to define the best principles for treatment of hypertension. Another variable "ambulatory arterial stiffness index" (AASI) is also shown to be a predictor on its own for cardiovascular complications.

**Hypothesis:** Central haemodynamic variables in obese children are related to the extent of obesity, the metabolic syndrome and insulin resistance, and will predict those obese children who are at risk for developing hypertension and signs of subclinical cardiovascular damage.

**Objectives:** This study aims to predict those obese children with the highest risk of developing cardiovascular complications / subclinical cardiovascular damage.

**Methods:** The study group consists of 100 obese children in the age of 12-16 years with a BMI over the 99<sup>th</sup> percentile referred to a standardized weight loss programme. The design will be a cross-sectional study including 50 healthy controls and a prospective study of the obese children followed for one year of weight loss intervention. The following haemodynamic variables will be determined; central pulse wave velocity, central aortic blood pressure profiles, heart rate variability (Sphymocor), 24-hour blood pressure measurements including AASI, clinic blood pressure measurements, echocardiography, electrocardiography, urine albumin/creatinine ratio, and blood samples including metabolic and inflammatory parameters.

### P3.09

#### ULTRASTRUCTURAL EVIDENCE OF APOPTOSIS IN ACUTE MYOCARDIAL INFARCTION AND CHRONIC ANEURISM WALL

O. Barnett, Y. Kyvak

National Medical University n.a. Danylo Halitsky, Lviv, Ukraine

Acute myocardial infarction (AMI) is characterized by myocardial cell necrosis, inflammatory response and scar formation. The aim was to reveal whether cardiomyocyte (CMC) apoptosis is present in the infarction zone of the left ventricle compared with postinfarction chronic aneurism wall.

**Subject and methods:** Myocardial express necropsies from 24 patients (age range 39-71) who suffered mainly from hypertension (HT) and died from STEMI complicated with Heart Failure (HF) or Cardiogenic Shock were examined. Biopsies from postinfarction aneurism wall from five patients (38-61 y.o), suffering from HT and HF were obtained and their ultrastructure was compared with changes in necropsies from infarction zone.

**Results:** According to electron microscopic investigation in infarction zones of the left ventricle except necrotic, hibernated and apoptotic myocytes, as well as apoptotic endothelial and plasmatic cells, macrophages and fibroblasts, with features of pycnosis, nuclear chromatin condensation and cytoplasm vacuolization where detected. As the result of prominent interstitial fibrosis, very poor vascularization and moderate matrix edema, CMC usually were dissociated and myocardium loses its synthital organization. Separately located CMC were hibernated finally resulting in apoptosis. Numerous hibernated and apoptotic CMC were destroyed via secondary necrosis

predominantly during short time (three months) after AMI. In aneurism wall 14 years after AMI onset, hibernating and some viable CMC were still present as the result of myocardium neovascularization.

**Conclusions:** CMC necrosis is the main mechanism of cell death in acute aneurism wall, while apoptosis develops predominantly in subacute periods of AMI. In chronic aneurism wall viable CMC are present, but hibernating and apoptotic CMC prevalent.

### Pathophysiology 2

#### P4.01

#### ROLE OF PULSE WAVE VELOCITY IN DETECTING ORGAN DAMAGE AND IMPROVING CARDIOVASCULAR RISK STRATIFICATION IN HYPERTENSIVE PATIENTS

F. Stea, L. Ghiadoni, R. M. Bruno, A. Magagna, C. Benedetti, S. Taddei  
Department of Internal Medicine, University of Pisa, Pisa, Italy

**Objective:** Arterial stiffness as carotid-femoral Pulse Wave Velocity (PWV) has been included in the European guidelines for the management of arterial hypertension as target organ damage (TOD). This study is aimed at determining the usefulness of PWV beyond other measures of TOD in risk stratification of hypertensive patients.

**Design and Methods:** 234 patients (56.6 ± 12.0 years; 135 men; 85% already under antihypertensive therapy) were enrolled among those referring to the Hypertension unit for a program including medical history, physical examination, blood pressure (BP) measurement, blood and urine samples with lipid profile, glucose, creatinine, and microalbuminuria, EKG, echocardiography, carotid ultrasound and PWV. A threshold of 8.3 m/s was used as marker of increased PWV.

**Results:** With history, examination, BP, and blood and urinary exams, patients were classified at low (33%), moderate (33%), high (29%), or very high (5%) added risk. Median PWV was 7.88 (25th-75th percentile 7.05-8.95) m/s. Patients reclassified to a higher risk class were 21% by adding PWV, 14% by echocardiography, and 50% by carotid ultrasound. When all TOD markers except PWV were used, patients were classified as low (6%), moderate (23%), high (66%), or very high (5%) risk. Adding PWV detected TOD in 10 further patients, but only 3 of them were reclassified into higher category.

**Conclusions:** PWV is useful to classify low and moderate risk patients, but it adds little in patients already studied with cardiac and carotid ultrasound. Its advantage over other measures could be represented by the low cost and expertise required.

#### P4.02

#### LIPIDS AND APOLIPOPROTEINS ARE ASSOCIATED WITH PULSE WAVE VELOCITY IN NEVER-TREATED HYPERTENSIVES

D. Terentes-Printzios, C. Vlachopoulos, G. Vyssoulis, N. Ioakeimidis, N. Alexopoulos, P. Xaplanteris, A. Siama, A. Samentzas, P. Pietri, C. Stefanadis

Hippokraton Hospital, 1st Department of Cardiology, Athens Medical School, Athens, Greece

**Introduction:** Hypertension is associated with increased arterial stiffness, which is a predictor of cardiovascular risk and has been shown to correlate with lipid profile. However, the effect of alternative measures of lipid profile other than LDL remains unknown.

**Methods:** We enrolled 1225 consecutive essential hypertensives (mean age 52.9 ± 11.7 years, 728 males). Arterial stiffness was determined with carotid-femoral pulse wave velocity (PWV) using the Complior® device. Total cholesterol, LDL cholesterol, non-HDL cholesterol, and apolipoprotein B, as well as ratios of total/HDL cholesterol, LDL/HDL cholesterol, and apolipoprotein B/A-I were measured or calculated, accordingly.

**Results:** In multivariable regression analysis, apolipoprotein B/A-I ratio, LDL and total/HDL cholesterol ratio exhibited significant positive association with PWV, which was independent of age, gender, mean blood pressure, smoking, BMI, diabetes, triglycerides, CRP and all the aforementioned measures of lipid profile (p < 0.001, p < 0.001 and p < 0.05, adjusted R<sup>2</sup> of model = 0.402). In further analyses we employed dichotomous outcome variable (PWV ≥ 75th percentile [9.1 m/s]). Receiver operating characteristic (ROC) curves were generated to evaluate the ability of apolipoprotein B/A-I ratio, LDL and total/HDL cholesterol ratio to discriminate subjects with and without significant arterial stiffness. The area under the curve (AUC) and 95% CIs of the ROC curves for apolipoprotein B/A-I ratio, LDL and total/HDL cholesterol ratio for prediction of significant arterial stiffness (PWV ≥ 75th percentile [9.1 m/s]) were AUC = 0.64 (p < 0.001), AUC = 0.53 (P = 0.07) and AUC = 0.58 (p < 0.001).

**Conclusion:** Higher apolipoprotein B/A-I and total /HDL cholesterol ratios are independent predictors of increased arterial stiffness in never-treated hypertensives and predict increased arterial stiffness better than LDL.

#### P4.03

##### WOMEN WITH SYSTEMIC SCLEROSIS HAVE WORSE ENDOTHELIAL FUNCTION AS COMPARED TO WOMEN WITH RHEUMATOID ARTHRITIS AND SYSTEMIC LUPUS ERYTHEMATOSUS

A. Cypiene<sup>1,2</sup>, L. Ryliskyte<sup>1</sup>, R. Ruginė<sup>2</sup>, M. Kovaite<sup>1</sup>, J. Dadoniene<sup>2</sup>, Z. Petrulioniene<sup>1</sup>, A. Venalis<sup>2</sup>, A. Laucevicius<sup>1,2</sup>

<sup>1</sup>Centre of Cardiology and Angiology Vilnius University Hospital Santariškiu Klinikos, Vilnius, Lithuania

<sup>2</sup>State Research Institute Centre for Innovative Medicine, Vilnius, Lithuania

**Introduction:** The endothelial function has been repeatedly shown to be damaged in rheumatoid arthritis (RA), systemic lupus erythematosus (SLE) and systemic sclerosis (SSc) patients. However, it is uncertain which of diseases has the greatest influence on endothelial function.

**Methods:** We studied 60 women with RA (aged 40.47 ± 9.93 years) with disease activity (DAS28) 5.47 ± 0.94, 30 women with SLE (aged 37.33 ± 9.22 years), disease activity index (SLEDAI) 18.40 ± 8.17, organ damage index (SLICC) 1.27 ± 1.53 and 16 women with diffuse cutaneous SSc (aged 47.94 ± 10.46 years). Blood tests included serum lipid profile, glucose and high-sensitivity CRP (hsCRP) measurement. The endothelium-dependent flow-mediated dilatation (FMD) test in a brachial artery was performed by the ultrasound system (Logiq 700, General Electric).

**Results:** Direct comparison of FMD in RA, SLE and SSc groups has shown that there was overall difference between groups ( $p = 0.033$ ). This result was confirmed by application of linear models with adjustment for other confounding factors. FMD significantly differed in SSc and RA groups (5.69 ± 5.10 % vs. 8.37 ± 3.84 %;  $p = 0.021$ ;  $\beta = -0.2$ ) as well as in SSc and SLE groups (5.69 ± 5.10 % vs. 9.25 ± 5.15 %;  $p = 0.021$ ;  $\beta = -0.2$ ).

**Conclusion:** Results of our study have shown that FMD is lower in SSc group as compared to RA and SLE groups, thus the SS does greater damage on endothelial function as compared with RA and SLE.

#### P4.04

##### IMPAIRED ABDOMINAL AORTIC WALL INTEGRITY IN ELDERLY MEN CARRYING THE ANGIOTENSIN-CONVERTING ENZYME D-ALLELE

L. U. Ljungberg<sup>1,2</sup>, R. De Basso<sup>1</sup>, U. Alehagen<sup>1</sup>, H. M. Björck<sup>1</sup>, K. Persson<sup>2</sup>, U. Dahlström<sup>1</sup>, T. Länne<sup>1</sup>

<sup>1</sup>Linköping University, Dept of Medical and Health Sciences, Div of Cardiovascular Medicine, Linköping, Sweden

<sup>2</sup>Linköping University, Dept of Medical and Health Sciences, Div of Drug Research, Linköping, Sweden

**Objective:** A genetic polymorphism in the angiotensin-converting enzyme (ACE) gene (ACE I/D polymorphism) has been associated with abdominal aortic aneurysm. A link between aortic aneurysm and aortic stiffness has been suggested. However, no study has previously investigated the relationship between ACE and abdominal aortic wall integrity. The aim of this study was to explore the links between ACE I/D polymorphism, circulating ACE, and abdominal aortic wall integrity determined by abdominal aortic wall stiffness.

**Methods:** The study population consisted of 406 subjects (212 men and 194 women), 70-88 years. Diastolic lumen diameter, pulsatile diameter change and intima-media thickness were measured and used to calculate the cross-sectional compliance (CC), distensibility coefficient (DC), stiffness  $\beta$  and wall stress. ACE genotype was determined by PCR followed by gel electrophoresis, and circulating ACE level was measured using ELISA.

**Results:** Male carriers of the ACE D allele had a lower distensibility coefficient than II carriers (ID/DD 8.09 vs. II 10.38,  $p=0.017$ ). Multiple regression analyses adjusting for confounding factors showed significant associations between the ACE D-allele and increased stiffness  $\beta$  as well as reduced CC. No significant association between abdominal aortic stiffness and the ACE D-allele was found in women.

**Conclusion:** This study showed, for the first time, a gender-specific association between the ACE-D allele and abdominal aortic wall mechanics, with men carrying the ACE D-allele having stiffer abdominal aortas compared to II carriers. Increased abdominal aortic stiffness indicates impaired vessel wall integrity, which along with other local predisposing factors, may increase the risk of aneurysm formation.

#### P4.05

##### DERANGED ARTERIAL WALL REMODELLING IN CENTRAL ARTERIES OF PATIENTS WITH ABDOMINAL AORTIC ANEURYSMS – A REASON FOR THE HIGH COMORBIDITY/MORTALITY IN CARDIOVASCULAR DISEASE?

S. Ardil, T. Länne

Linköping University, Linköping, Sweden

**Objectives:** Patients with abdominal aortic aneurysm (AAA) have a high cardiovascular comorbidity besides the risk of aneurysmal rupture, the reasons being largely unknown. The aim of this study was to determine other possible vascular defects in the arterial system besides aneurysmal disease that might be of relevance for the increased comorbidity.

**Methods:** 23 male AAA-patients and 20 age-matched controls (C) were examined with tonometry using the Sphygmocore system, to determine aortic and brachial PWV. The relation between local common carotid artery (CCA) pressure and lumen diameter (LD) as well as IMT determined by ultrasound was studied as a measure of remodelling capacity of the carotid wall.

**Results:** AAA:s had higher aPWV than C (11,2±2 vs 9,9±2 m/s,  $p=0.03$ ). No difference in bPWV was seen. An increased LD in CCA was found in the AAA:s (7,5±1,3 vs 6,5±0,7 mm respectively,  $p<0,001$ ). In C there was a positive correlation between local pulse pressure (LPP) and CCA IMT ( $r=0,49$ ,  $p<0,001$ ), which was not seen in the AAA ( $r=0,03$ , NS). The expected negative correlation between LPP and LD/IMT ( $r=-0,44$ ,  $p=0,004$ ) indicating a remodelling response in the CCA was found in C but not in AAA ( $r=-0,25$ , NS).

**Conclusion:** A changed aortic wall structure in central elastic arteries with high PWV in patients with AAA is seen. Further, the remodelling of the common carotid artery in response to local pulse pressure is defect. This form a background explaining the high cardiovascular comorbidity besides the risk of aneurysmal rupture in these patients.

#### P4.06

##### ENDOTHELIAL VASOMOTOR FUNCTION AND ARTERIAL STIFFNESS IN YOUNG MEN WITH ARTERIAL HYPERTENSION, GRADE I, AND THEIR RELATION WITH RED BLOOD CELL DISTRIBUTION WIDTH

A. R. Zairova, A. N. Rogoza, E. V. Oscepkova

Russian Cardiology Research Complex, Moscow, Russian Federation

Endothelial dysfunction and arterial stiffness increasing are negative prognostic markers in arterial hypertension. Red blood cell distribution width (RDW) was shown as a new negative prognostic marker in some cardiovascular diseases.

**Objective:** To study the relation between endothelial function and RDW, arterial stiffness and RDW in young men with arterial hypertension.

**Materials and Methods:** 54 men, 29,9±0,9 ys ( $M\pm SE$ ), with arterial hypertension, Grade I were examined. Flow-mediated vasodilatation (FMD) was assessed by Vivid 7 (GE), arterial stiffness by brachial-ankle pulse wave velocity (PWV) (Vasera VS-1000, Fukuda Denshi), RDW by Cell Din 3500 (Abbot).

**Results:** FMD ranged from 18,4% to -1,8% (6,8±0,7%), PWV from 9,7 m/s to 16,3 m/s (12,1 ±0,2 m/s), RDW from 12,3% to 16,2 % (14,2 ±0,1%). Endothelial dysfunction was detected in 46% patients, increasing the arterial stiffness in 61% and elevated RDW in 37%. Patients with elevated RDW had lower FMD (4,6±0,4 % vs 8,0±0,4 %,  $p=0,01$ ), more prevalence of endothelial dysfunction (70% vs 33 %,  $p=0,01$ ) and higher values of PWV (12,6±0,3m/s vs 11,9±0,2 m/s,  $p=0,04$ ) in comparison with patients with normal RDW. RDW correlated with FMD:  $r = -0,4$ ,  $p=0,01$ . Chance of endothelial dysfunction in young men with arterial hypertension and elevated RDW is more in 5 times.

**Conclusion:** Endothelial dysfunction, increased arterial stiffness and elevated RDW have high prevalence in young men with arterial hypertension. Elevated RDW is associated with endothelial dysfunction and increased arterial stiffness and may be considered as a perspective prognostic marker in arterial hypertension.

#### P4.07

##### DIFFERENT IMPACT OF HYPERTENSION AND TYPE 2 DIABETES ON AORTIC, CAROTID AND PERIPHERAL VASCULAR STIFFNESS

R. M. Bruno<sup>1</sup>, E. Bianchini<sup>2</sup>, L. Landini<sup>1</sup>, G. Cartoni<sup>1</sup>, F. Stea<sup>1</sup>, G. Penno<sup>1</sup>, S. Del Prato<sup>1</sup>, S. Taddei<sup>1</sup>, L. Ghiadoni<sup>1</sup>

<sup>1</sup>University of Pisa, Pisa, Italy

<sup>2</sup>National Research Council, Pisa, Italy

Aim of the study was to evaluate the impact of diabetes, hypertension, and their combination on aortic, carotid and peripheral stiffening.