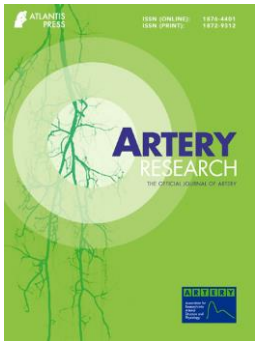

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P3.07: OXYGEN CONSUMPTION KINETICS IN SUPRA-ANAEROBIC THRESHOLD CONSTANT LOAD EXERCISES ALLOW TO QUANTIFY IN TRAINED AND UNTRAINED SUBJECTS CYTOCHROME C-OXIDASE INHIBITION BY NITRIC OXIDE AND SHOW THIS DIRECT EFFECT AFTER NITRATE

D. Maione, S. Bacchelli, E. Cosentino, S. D'Addato, D. Degli Esposti, R. Senaldi, E. Ambrosioni, C. Borghi

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P3.04
IS MALADAPTIVE CAROTID REMODELING A FEATURE OF TYPE 2 DIABETES?

R. M. Bruno [1], E. Bianchini [2], G. Cartoni [1], F. Stea [1], G. Penno [1], S. Del Prato [1], S. Taddei [1], L. Ghiadoni [1]
[1]*University of Pisa, Pisa, Italy*
[2]*National Research Council, Pisa, Italy*

A maladaptive carotid remodeling was described in type 2 diabetes mellitus. However, it is still unknown whether it is a feature of diabetes per se, or rather a consequence of the frequent comorbidity with hypertension. We therefore studied the impact of diabetes, hypertension, and their combination on carotid geometry and remodeling, recruiting to this aim 139 subjects (31 normotensives-NT, 38 hypertensives-HT, 24 diabetic normotensives-DMNT, and 46 diabetic hypertensives-DMHT). Common carotid diameter, intima-media thickness (IMT) and distension were determined using a real-time echo-tracking system "Carotid Studio". Local pulse pressure was obtained by applanation tonometry. Carotid static and pulsatile circumferential wall stress was calculated by Lamé equations. IMT was increasingly higher in the four groups, reaching the highest value in DMHT. As compared to NT, carotid lumen diameter was increased in HT and DMHT, but not in DMNT. HT showed significantly higher circumferential static wall stress than DMHT, while DMNT and NT had similar and significantly lower values. Carotid pulse pressure was similarly increased in DMHT and HT. In a logistic regression model adjusted for confounders, hypertension carried an increased risk (OR 2.33; CI-95% 1.02-5.63) of a widened lumen diameter, whereas diabetes carried an increased risk of IMT above the median value (OR2.49; 1.09-5.68). Hypertension, but not diabetes, was associated to an increased static and pulsatile stress (OR7.74; 2.76-21.72, and 4.86; 1.95-12.10). In conclusion, maladaptive remodeling, previously reported in diabetic patients, is conceivably attributable to the concomitant presence of hypertension.

Parameter	NT	HT	DMNT	DMHT	p (trend)
Lumen diameter (mm)	5.6±1.0	6.3±1.1*	5.9±0.6	6.3±1.1*	0.02
IMT (mm)	0.72±0.09	0.76±0.18	0.78±0.13*	0.81±0.14*	0.04
Static wall stress (kPa)	48.7±12.7	60.4±13.3‡*#	48.8±12.6†	54.6±12.2‡*†	0.001
Pulsatile wall stress (kPa)	27.0±6.2	36.0±12.3‡*	27.6±6.3†	32.5±9.0‡*	0.001
Pulse pressure (mmHg)	43.6±8.9	54.2±15.9‡*	44.7±8.9	53.8±11.8‡*	<0.001

*$p<0.05$ vs NT; † $p<0.05$ vs HT; ‡$p<0.05$ vs DMNT; # $p<0.05$ vs DMHT.

P3.05
DERANGED VASCULAR-VENTRICULAR COUPLING IN HEART FAILURE PATIENTS WITH DEPRESSED LEFT VENTRICULAR CONTRACTILITY: IMPORTANCE OF AORTIC CHARACTERISTIC IMPEDANCE

A. Sahlén [1], M. Norman [1], A. Manouras [2], L.Å. Brodin [2], R. Winter [2]
[1]*Karolinska Institutet, Stockholm, Sweden*
[2]*Royal Institute of Technology (KTH), Stockholm, Sweden*

Deranged vascular-ventricular coupling (VVC) occurs in heart failure (HF) when arterial elastance (Ea) is increased and/or left ventricular (LV) elastance (Elv) is depressed, leading to increased coupling ratio Ea/Elv. While calculation of Ea is simple (below), it represents the 'lumped' elastance of the arterial tree some of which is attributable to aortic characteristic impedance (Zc) which is more difficult to quantify. We examined the importance of Zc for VVC in 22 patients (7 with HF, 31%; 15 non-HF controls) who underwent echocardiography and analysis of central pressure waveform synthesised from radial artery pressure (SphygmoCor, AtCor Medical, Sydney, Australia). LV outflow tract Doppler recordings were digitised (custom software) and Zc was calculated as the ratio between pressure and flow in early systole before onset of wave reflections. Ea (LV end-systolic pressure / stroke volume (SV)) and Elv (single-beat method) were estimated; compliance (SV / brachial pulse pressure) and total peripheral resistance (TPR: mean arterial pressure / cardiac output) were computed. We found that HF patients had deranged VVC largely due to higher Ea (Table 1). Zc correlated strongly to Ea ($r=0.65$; $p=0.02$) and to Ea/Elv (0.80; $p=0.001$) but neither to Elv ($p=0.81$) nor higher age ($p=0.12$). In conclusion, elevated Zc contributes to the deranged VVC seen in systolic HF.

Variable	HF	Non-HF	p-Value
Age (years)	70 ± 11	54 ± 18	0.045
LVEF (%)	29 ± 15	52 ± 17	0.023
Compliance (mL/mmHg)	0.7 ± 0.3	1.1 ± 0.5	0.07
TPR (mmHg·s/mL)	0.03 ± 0.01	0.04 ± 0.04	0.84
Ea (mmHg/mL)	3.0 ± 1.5	1.7 ± 0.4	0.029
Zc (mmHg·s/mL)	0.39 ± 0.08	0.20 ± 0.06	0.01
Elv (mmHg/mL)	1.7 ± 1.0	2.3 ± 0.3	0.07
VVC ratio: Ea/Elv	0.75 ± 0.17	2.3 ± 1.5	<0.001

P3.06
AORTIC STIFFNESS AND VITAMIN D ARE INDEPENDENT MARKERS OF AORTIC CALCIFICATION IN PATIENTS WITH PERIPHERAL ARTERY DISEASE

M. Zagura [1,2], M. Serg [2,3], P. Kampus [1,2,3], M. Zilmer [1,2], J. Eha [2,3], E. Unt [4,5,6], J. Lieberg [7,8], J. Kals [1,2,7]
[1]*Department of Biochemistry, Tartu, Estonia*
[2]*Endothelial Centre, Tartu, Estonia*
[3]*Department of Cardiology, Tartu, Estonia*
[4]*Institute of Exercise Biology and Physiotherapy, Tartu, Estonia*
[5]*Department of Sports Medicine and Rehabilitation, Tartu, Estonia*
[6]*Sports Medicine and Rehabilitation Clinic, Tartu, Estonia*
[7]*Department of Vascular Surgery, Tartu, Estonia*
[8]*Department of Surgery, Tartu, Estonia*

Background: Arterial stiffness is a significant determinant of cardiovascular risk and is related to vascular calcification. Vitamin D may regulate arterial calcification and has been associated with cardiovascular survival benefits. However, data about the relationship between arterial stiffness, aortic calcification, and vitamin D levels in patients with peripheral artery disease (PAD) are limited.
Aim: To examine association between aortic calcification, arterial stiffness, and vitamin D levels in patients with symptomatic PAD and in healthy individuals.
Materials and methods: We studied 78 males with PAD (mean age 63±7 years) and 69 healthy men (mean age 54±7 years). Aortic pulse wave velocity (aPWV) and augmentation index (AIx@75) were determined by applanation tonometry using the Sphygmocor device. Aortic calcification score (ACS) was quantified by computed tomography. Serum 25-hydroxyvitamin D ((25(OH)D) level was measured using a radioimmune assay.
Results: ACS (6.4±5.3 *vs* 0.7±1.7(cm^3); $p<0.001$), aPWV (10.1±2.5 *vs* 7.6±1.6(m/s); $p<0.001$), AIx@75 (28.2±8.1 *vs* 13.7±11.0(%); $p<0.001$), and 25(OH)D (37.7±14.0 *vs* 50.3±16.3(nmol/L); $p<0.001$) were different for the study groups. There was linear relationship between aPWV and ACS for the patients ($p=0.02$) and for the controls ($p=0.049$). 25(OH)D was associated with ACS only in the patient group ($p=0.05$). In multivariate analysis ACS was independently determined by aPWV and 25(OH)D in patients with PAD ($R^2=0.42$; $p<0.0001$).
Conclusion: These results indicate that calcification of the thoracic and abdominal aorta is independently associated with aortic stiffness and serum 25(OH)D level in patients with PAD. Aortic stiffness and abnormal vitamin D level may contribute to vascular calcification in these patients.

P3.07
OXYGEN CONSUMPTION KINETICS IN SUPRA-ANAEROBIC THRESHOLD CONSTANT LOAD EXERCISES ALLOW TO QUANTIFY IN TRAINED AND UNTRAINED SUBJECTS CYTOCHROME C-OXIDASE INHIBITION BY NITRIC OXIDE AND SHOW THIS DIRECT EFFECT AFTER NITRATE

D. Maione [1], S. Bacchelli [1], E. Cosentino [1], S. D'Addato [1], D. Degli Esposti [1], R. Senaldi [2], E. Ambrosioni [1], C. Borghi [1]
[1]*Internal Medicine University of Bologna, Bologna, Italy*
[2]*Sports Medicine Institute of Bologna, Bologna, Italy*

This work aims to highlight by VO_2 kinetics in constant load supra anaerobic threshold (AT) tests, the nitric oxide (NO) reversible direct inhibitory action on cytochromeC oxidase (cox). This results in decreased ability to oxidise electron flow (EF), by cytochromeC carried, in water, compensated by electron turnover (ET) increment via cox not yet NO bound, thus giving EF continuity along the respiratory chain O_2 ward. When NO production is increased and/or O_2 mitochondrial concentration decreased, as during intense effort, this compensation gradually weakened, owing to cox NO free oxidative capacity end limit, which approaches its saturation, but at the same time allows an O_2 saving and its diffusion deeper in tissues around vessels. O_2 saving effect is quantifiable in two bicycle constant load exercises by VO_2

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 seen as effective physiological means that allow one to reach the obtained enhanced functional capacity, by longer exercise owing to O_2 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 heamodynamic 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 99th 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 viability (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. Kyyak
National Medical University n.a. Danylo Halitskyy, 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 aneurizm 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 necropcies from infarction zone.
Results: According to electron microscopic investigation in infarction zones of the left ventricle exept necrotic, hibernated and apoptotic myocytes, as well as apoptotic endothelial and plasmatic cells,macrophages and fibroblasts, with features of pycnosis, nuclear chromatin condensation and cytoplasma vacualization where detected. As the result of prominent interstitial fibrosis, very poor vascularization and moderate matrix edema,CMC usually were dissociated and myocardium loses its synthityal 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 $\pm$ 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 an 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
Hippokration 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$\pm$11.7 years, 728 males). Arterial stiffness was determined with carotid-femoral pulse wave velocity (PWV) using the Complior® device. Total cholesterol, LDL cholesterol, non-HDL cholesterol, and apolipoprotein B, as well as ratios of total/HDL cholesterol, LDL/HDL cholesterol, and apolipoprotein B/A-I were measured or calculated, accordingly.
Results: In multivariable regression analysis, apolipoprotein B/A-I ratio, LDL and total/HDL cholesterol ratio exhibited significant positive association with PWV, which was independent of age, gender, mean blood pressure, smoking, BMI, diabetes, triglycerides, CRP and all the aforementioned measures of lipid profile ($p<0.001$, $p<0.001$ and $p<0.05$, adjusted R2 of model$=0.402$). In further analyses we employed dichotomous outcome variable (PWV $\geq$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 $\geq$75th percentile [9.1 m/s]) were AUC$=0.64$ ($p<0.001$), AUC$=0.53$ ($P=0.07$) and AUC$=0.58$ ($p<0.001$).