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P5.12
ARTERIAL STIFFNESS, WAVE REFLECTIONS AND PULSE PRESSURE AMPLIFICATION IN METABOLIC SYNDROME

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Background: the metabolic syndrome (MetS), an important contributor of insulin resistance and cardiovascular risk, is defined by three or more of the following clinical characteristics: abdominal obesity, hyperglycemia, hypertension, hypertriglyceridemia and hypo-HDL-cholesterolemia.

Aim: to review the existing data regarding the effect of Mets on peripheral and central blood pressure, stiffness and wave reflections.

Results: Increased aortic stiffness, a major mechanical factor predicting cardiovascular risk, is identified as participating to MetS. Its age-progression rate is proportional to the number of risk factors involved in MetS. Aortic stiffening with age is partly responsible for increased systolic blood pressure (SBP) and decreased diastolic blood pressure (DBP), the dominant hypertension phenotype in the elderly, which favors cardiac hypertrophy and coronary ischemia. Both parameters participate in the definition of pulse pressure (PP= SBP-DBP), which is of major importance in prognosis of subjects with MetS. Of note, beyond that of peripheral brachial parameters, central hemodynamic parameters associate to increased arterial stiffness reduced wave reflections and increased PP amplification, mainly attributed to enhanced heart rate. The latter findings are in the opposite direction than the one observed in essential hypertension in the absence of insulin resistance.

Conclusion: A diverging behavior of wave reflections and pulse pressure amplification, but not of arterial stiffness, is observed between hypertension alone and MetS. This might explain epidemiological findings on the reduced predictive value of MetS in the elderly and justify long term longitudinal studies relating central hemodynamics and mortality.

P5.13
ALKALINE PHOSPHATASE AND ARTERIAL STRUCTURE AND FUNCTION IN HYPERTENSIVE AFRICAN MEN: THE SABPA STUDY

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Background: Vascular calcification is believed to be due to the conversion of vascular smooth muscle cells into osteoblast-like cells and is associated with mortality. Since hypertension and related mortality in Africans is a concern, we investigated associations between a marker of osteoblastic activity, alkaline phosphatase (ALP), and measures of arterial structure and function in hypertensive African men.

Methods: This study included 79 hypertensive African men. We conducted 24h ambulatory blood pressure and carotid intima-media thickness (cIMT) measurements. The cIMT was obtained with an intra-observer variability of 0.04 mm and the cross-sectional wall area (CSWA) was calculated. ALP was measured in serum.

Results: ALP was within its reference range (101.6 vs. 30.0–120.0 U/L), however cIMT was higher compared to gender and age-specific reference values i.e., 25 to 40 years (0.63 vs. 0.43–0.53 mm), 40 to 50 years (0.71 vs. 0.50–0.61 mm) and older than 50 years (0.84 vs. 0.53–0.70 mm). In single and partial regressions, and confirmed with multiple regression analyses, 24h systolic blood pressure ($R^2=0.304$, $\beta=0.299$, $p=0.011$), 24h pulse pressure ($R^2=0.318$, $\beta=0.398$, $p<0.001$), but not 24h diastolic blood pressure ($R^2=0.164$, $\beta=0.078$, $p=0.54$), were positively associated with ALP. In addition, cIMT ($R^2=0.393$, $\beta=0.302$, $p=0.008$) and CSWA ($R^2=0.409$, $\beta=0.255$, $p=0.023$) also correlated positively with ALP after adjusting for significant covariates, and after excluding participants with diabetes and renal dysfunction.

Conclusion: Serum alkaline phosphatase in hypertensive African men is adversely associated with measures of arterial structure and function, independent of diabetes and renal dysfunction.

P5.14
ARTERIAL STIFFNESS IS ASSOCIATED WITH THE SEVERITY OF ATHEROSCLEROSIS AND SERUM OSTEOPOINTIN LEVELS IN PATIENTS WITH SYMPTOMATIC PERIPHERAL ARTERIAL DISEASE

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Background: Arterial stiffness is an independent predictor of vascular morbidity and mortality in the general population and in high-risk patients. Angiographic score (ASc) is closely related to the extent of atherosclerosis in patients with peripheral arterial disease (PAD). Osteopontin (OPN) is involved in the pathogenesis of atherosclerosis. The aim of the present study was to evaluate the association between arterial stiffness, ASc, and serum OPN in patients with symptomatic peripheral arterial disease.

Methods: Seventy-nine male patients with symptomatic PAD (mean age 64±7 years) were included into this study. The diagnosis of PAD was confirmed by ankle-brachial pressure index (ABPI) and digital subtraction angiography. Calculation of the ASc was based on the severity and location of atherosclerotic lesions in the lower extremity arteries. Aortic pulse wave velocity (aPWV) was evaluated by applanation tonometry using the Sphygmocor device. OPN level was determined by an enzyme-linked immunosorbent assay.

Results: The aPWV was significantly correlated with ASc ($r=0.35$, $p=0.002$), OPN ($r=0.34$, $p=0.004$), estimated glomerular filtration rate (eGFR) ($r=-0.36$, $p=0.002$), age ($r=0.4$, $p<0.001$), and mean arterial pressure (MAP) ($r=0.24$, $p=0.04$). In multivariate analysis, aPWV was independently associated with ASc, OPN, MAP and eGFR ($R^2=0.43$, $p<0.001$). Serum OPN was inversely correlated with ABPI ($r=-0.26$, $p=0.045$) but not with ASc.

Conclusion: In patients with symptomatic PAD, arterial stiffness is independently associated with the severity grade of atherosclerotic disease and serum OPN levels. These results suggest that aPWV might serve as a useful clinical marker of atherosclerosis in patients with PAD.

P5.15
THE INFLUENCE OF THE MEAN BLOOD PRESSURE ON ARTERIAL STIFFNESS PARAMETERS IN RHEUMATOID ARTHRITIS AND SYSTEMIC LUPUS ERYTHEMATOSUS WOMEN

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Introduction: The increased prevalence of premature atherosclerosis and stiffening of arteries in patients with rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) is well established.

However, it is uncertain which of risk factors has the greatest influence on arterial stiffness parameters from applanation tonometry.

Methods: 63 women with RA, 31 with SLE and 72 controls aged 18-55 years were examined. Parameters of arterial stiffness, augmentation index (AIx) and carotid-radial pulse wave velocity (PWV), were obtained by applanation tonometry (Sphygmocor (v.7.01) AtCor Medical).

Results: Women with RA and SLE differed from controls with respect to AIx ($p<0.001$; $p=0.008$) and did not differ between each other. SLE women differed from controls with respect to PWV ($p=0.018$) while RA - did not. By multiple regression analysis we have found that main explanatory factor for AIx and PWV was mean blood pressure (MBP) in RA patients. In SLE women PWV was not related to any of the pending parameters, AIx - to organ damage index, age and MBP.

Conclusion: The mean blood pressure was the major and the only one risk factor on arterial stiffening in rheumatoid arthritis while the disease damage index played the most important role in systemic lupus erythematosus group. Mean blood pressure in systemic lupus erythematosus was not as important as in rheumatoid arthritis group, though may have partial influence.

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P5.18 BRONCHOCONSTRICTION DOES NOT SIGNIFICANTLY ALTER CENTRAL HAEMODYNAMICS IN HEALTHY YOUNG ADULTS

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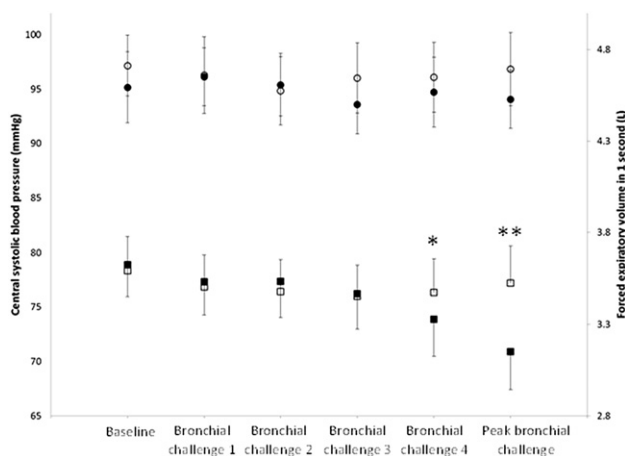
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Background: Cardiovascular disease is the most frequent cause of death in people with chronic respiratory disease. Whether this association is due to shared comorbidities or adverse respiratory function exerting detrimental cardiovascular effects is unknown. This study aimed to determine the cardiovascular effect of methacholine-induced acute airway obstruction.

Methods: Fifteen healthy young adults (aged 22.9 ± 2.5 years; 4 male; mean \pm SD) underwent a bronchial challenge test in which they were randomized in a blinded cross-over design to receive nebulized methacholine inhalation in serially increasing concentrations (from 0.39 to 25 mg/ml) or saline (0.9%; control) on two separate days. Airflow obstruction was assessed by forced expiratory volume at second (FEV1) and cardiovascular effects by brachial BP (oscillometry), central BP, augmentation index (Alx) and aortic stiffness (applanation tonometry).

Results: Methacholine caused a significant decrease in FEV1 (bronchoconstriction) from baseline to peak inhalation compared with saline (-0.48 ± 0.34 vs -0.07 ± 0.16 L; $p < 0.001$), but no significant between-group change in aortic stiffness (0.2 ± 1.3 vs 0.8 ± 1.8 m/s; $p = 0.20$), Alx (1.6 ± 7.0 vs $3.7 \pm 10.2\%$; $p = 0.49$), brachial SBP (-3.3 ± 7.6 vs -4.7 ± 5.7 mmHg; $p = 0.59$), central SBP (-1.1 ± 5.2 vs -0.3 ± 5.5 mmHg; $p = 0.73$), or heart rate (0.4 ± 7.1 vs -0.8 ± 6.6 bpm; $p = 0.45$). See figure for FEV1 and central SBP responses to inhaled methacholine (* $P = 0.012$, ** $P < 0.0001$).

Conclusions: Methacholine-induced bronchoconstriction does not change cardiovascular function, as assessed by aortic stiffness, brachial and central BP in healthy young adults. A comparison of the responses in people with airway disease would be of interest and may help to elucidate the connection between cardiovascular and respiratory disease.



P5.19 MATERNAL HEMODYNAMICS AT 11–13 WEEKS OF GESTATION AND THE RISK OF PRE-ECLAMPSIA

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Background: Women who develop preeclampsia (PE) are at increased risk of cardiovascular disease and stroke in the subsequent decades. In individuals with cardiovascular disorders there is increased central aortic systolic blood pressure (SBP_{AO}) and arterial stiffness, assessed by pulse wave velocity (PWV) and augmentation index (Alx). The aim of this screening study was to examine the potential value of assessment of SBP_{AO}, PWV and Alx at 11–13 weeks' gestation in identifying women who subsequently develop PE.

Methods: This was a screening study for PE in singleton pregnancies at 11^{–10}–13^{–6} weeks' gestation. Maternal history and characteristics were recorded and PWV, Alx and SBP_{AO} were measured by the Arteriograph. We compared these parameters in those that developed PE (n=146) with unaffected controls (n=4,436) and examined their performance in screening for PE.

Results: In the PE group, compared to unaffected controls, there was an increase in PWV (1.12 vs 1.00 MoM, $p < 0.0001$), Alx-75 (1.06 vs 1.00 MoM, $p < 0.0001$) and SBP_{AO} (1.10 vs 1.00 MoM, $p < 0.0001$). In screening for PE by a combination of maternal variables and log₁₀ Alx-75 MoM, log₁₀ PWV MoM and log₁₀ SBP_{AO}, the estimated detection rate was 61.6 (95% CI 51.8–70.5), at a false-positive rate of 10%.

Conclusion: A high proportion of women who develop PE have increased SBP_{AO} and arterial stiffness that is apparent from the first-trimester of pregnancy.

P5.20 ADDITIVE EFFECT OF CARDIOVASCULAR RISK FACTORS ON CAROTID AND AORTIC STIFFNESS IN ESSENTIAL HYPERTENSIVE PATIENTS

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Background: The role of other cardiovascular risk factors (RF) on top of hypertension in worsening arterial elastic properties is still unknown. The aim of the study was to evaluate whether cardiovascular RF can influence aortic and carotid stiffness in essential hypertensive patients.

Methods: 314 hypertensive patients and 110 age- and sex-matched healthy subjects were recruited. Carotid-to-femoral PWV and carotid pulse pressure were obtained by applanation tonometry, and carotid stiffness (CS) by automated system for ultrasound sequence images "Carotid Studio". Medical history, physical examination, and blood exams were used to identify the following RF: family history of premature cardiovascular disease, smoking, previous cardiovascular events, diabetes mellitus, obesity, hypercholesterolemia, hypertriglyceridemia, low HDL, metabolic syndrome, and chronic renal failure.

Results: Hypertensive patients had higher PWV and CS compared to healthy subjects (9.4 vs 7.4 m/s and 6.9 vs 6.2 m/s, $p < 0.0001$ for both). PWV and CS were classified as "increased" when greater than 90th percentile, calculated on the healthy subjects sample. Among hypertensives, age- and sex-adjusted multiple logistic regression, including all the above-mentioned RF, demonstrated that only diabetes mellitus (OR 5.4, CL95% 2.6–11.2) and chronic renal failure (OR 7.7, CL95% 2.2–25.6) are independently associated to an increased PWV while only diabetes mellitus is independently associated to an increased CS (OR 3.2, CL95% 1.4–7.1).

Conclusions: In hypertensive population, the additive presence of diabetes mellitus is associated with a further carotid and aortic stiffening, while the presence of chronic renal failure is associated to a further increased PWV. The other cardiovascular RF seem to exert a marginal role, when added to arterial hypertension.

P5.21 CHRONIC HYPOXEMIA PER SE INDUCES SYSTEMIC VASCULAR DYSFUNCTION IN HUMANS

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Cardiovascular (CV) morbidity and mortality are increased in patients suffering from diseases associated with chronic hypoxemia. The contribution of hypoxemia per se has proven difficult to determine, because these patients often present several additional CV risk factors. Chronic mountain sickness (CMS) is characterized by chronic hypoxemia, affects subjects with a low CV risk profile and thereby provides a unique opportunity to study the independent effects of chronic hypoxemia on vascular function. We measured arterial oxygen saturation (SaO₂), flow-mediated dilation (FMD) of the brachial artery, carotid-femoral pulse wave velocity (PWV) and carotid intima-media thickness (IMT) in 23 CMS patients and 27 controls permanently living at 3600 m. The main new finding was that CMS patients (SaO₂ 83 ± 3 vs. $90 \pm 3\%$ in controls, $P < 0.0001$) displayed marked systemic vascular dysfunction as evidenced by decreased FMD (4.6 ± 1.2 vs.