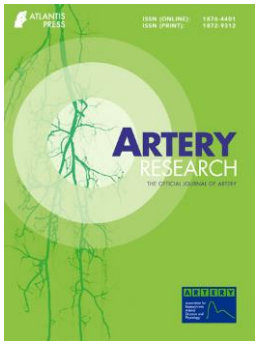

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P11.06: FIBRONECTIN, BUT NOT LAMININ CONTENT IS INCREASED IN THE TUNICA MEDIA OF SUBCUTANEOUS SMALL RESISTANCE ARTERIES OF PATIENTS WITH ESSENTIAL HYPERTENSION

C. De Ciuceis, L.F. Rodella, D. Rizzoni, E. Porteri, R. Rezzani, G.E.M. Boari, E. Borsani, G. Favero, C. Platto, G.A.M. Tiberio, S.M. Giulini, E. Agabiti Rosei

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with Scheltens' visual rating scale. Arterial wall parameters were measured by echo-tracking and applanation tonometry. RLS was assessed by contrast transcranial Doppler sonography with agitated saline. In order to explore the relationship between presence and load of DWMLs and possible risk factors logistic and linear regressions were applied.
Results: 29 (25.4%) migraineurs had DWMLs. They were significantly older ($p<0.001$), had more cardiovascular risk factors, thicker carotid intima-media ($p=0.006$), higher CS ($p=0.004$) and AIx (0.001) compared to migraineurs without DWMLs. The prevalence of large RLS was higher in patients with DWMLs, but not significant. The predictors of DWMLs were age (OR 1.11, $p<0.001$) and hypertension (OR 6.57, $p=0.001$). Higher DWMLs load was predicted by age, obesity, hypertension, and decreased HDL cholesterol. We established no relationship between presence and load of DWMLs and arterial wall parameters or RLS.
Conclusions: Age and traditional cardiovascular risk factors, but not arterial wall parameters, are predictors of DWMLs in patients with migraine.

P11.03
PULSE PRESSURE PARTIALLY EXPLAINS THE INCREASED INCIDENT CARDIOVASCULAR DISEASE ASSOCIATED WITH INFLAMMATION IN TYPE 1 DIABETES: A 12-YR FOLLOW-UP STUDY

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Objective: To investigate, in a prospective cohort of individuals with type 1 diabetes: 1) the association between an aggregated z-score of low-grade inflammation markers (CRP, IL-6, sPLA2 and sICAM-1) and pulse pressure (PP), as a marker of arterial stiffness, and 2) the association of low-grade inflammation with incident fatal and non-fatal cardiovascular disease (CVD) and the potential mediating role of PP herein.
Methods: We prospectively followed 339 individuals with type 1 diabetes who were free of CVD at study entry and in whom brachial PP and markers of low-grade inflammation were measured at baseline. Data were analysed with linear and Cox-regression models, and all results presented are adjusted for age, sex, duration of diabetes, eGFR, UAE, MAP, BMI, total cholesterol, smoking, endothelial dysfunction and the use of antihypertensive medication.
Results: PP increased with 3.2 mmHg (95%CI: 0.4-6.0, $p=0.025$) per SD increase in the inflammation score. During the course of follow-up [median duration: 12.3 yrs (IQR: 7.6—12.5)], 85 individuals suffered a fatal ($n=48$) and/or non-fatal ($n=53$) CVD event. Low-grade inflammation was associated with higher incidence of CVD [HR = 1.56 (1.02-2.40), $p=0.042$], as was PP (per 10 mmHg increase): HR = 1.27 (1.08-1.48), $p=0.007$. Additional adjustment for PP attenuated the association between inflammation and incident CVD with ~20% to HR = 1.45 (0.96-2.21), $p=0.106$.
Conclusions: Arterial stiffness, as expressed by PP, can partially explain the increased CVD associated with a higher low-grade inflammatory status in patients with type 1 diabetes. Treating inflammation may be a means to reduce the accelerated arterial stiffening that characterize these patients.

P11.04
VASCULAR STIFFNESS IS INCREASED IN ANTIPHOSPHOLIPID SYNDROME: SIGNIFICANCE AND CLINICAL ASSOCIATIONS

D. Wahl [1,2], P. Salvi [1], A. Kearney-Schwartz [1], V. Bravetti [1], T. Moline [1], E. Farese [1], V. Regnault [1], P. Lacolley [1], M. Valla [1], S. Zuily [1,2], C. Perret-Guillaume [1], T. Lecompte [1,2], A. Benetos [1,2]
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Vascular stiffness is an independent risk factor of cardiovascular events in the general population. While it is established that vascular stiffness is increased in patients with systemic lupus (SLE), studies investigating vascular stiffness in patients with antiphospholipid antibodies yielded conflicting results. In order to determine whether arterial stiffness was increased in patients with antiphospholipid antibodies we studied 53 patients with antiphospholipid antibodies and 109 controls matched for age and sex.
Patients were : 46.0±2.3 years-old, 40 female and 13 male. Twenty-six had primary antiphospholipid syndrome, 16 antiphospholipid syndrome associated with SLE. Clinical manifestations included arterial thromboembolic events n = 14, venous thromboembolism n = 28, obstetrical manifestations of APS n = 9 and 11 patients were asymptomatic. Pulse wave velocity (PWV) was used to investigate arterial stiffness and was determined by aplanation tonometry. PWV was increased in patients : 8.14 ± 0.40 m/s and 7.24 ± 0.20 m/s in controls ($p=0.036$). PWV was correlated with age ($r=0.75$;$p=0.0001$) and systolic blood pressure ($r=0.62$;$p=0.0001$). PWV was significantly increased in patients with arterial thrombosis than in controls (9.54±1.20 m/s and 7.23±0.20 m/s, respectively) or patients without arterial thrombosis (7.63±0.40 m/s;$p=0.0416$). PWV was not significantly different among various antiphospholipid profiles.
In summary patients with antiphospholipid syndrome have increased arterial stiffness, in particular patients with arterial thrombotic events. Arterial stiffness is significantly correlated with age and blood pressure but does not differ according to different antiphospholipid antibodies profiles.

P11.05
ASSESSING VENTRICULAR-VASCULAR INTERACTIONS AFTER STENTED COARCTATION

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Introduction: Stented coarctation is associated with increased ventricular and aortic stiffness. This study compared non-invasively determined ventricular-vascular interactions in patients after stented coarctation with healthy age/sex-matched controls.
Methods: Ventricular assessment included M-mode, B-mode, pulse and tissue Doppler echocardiography. Vascular assessment included carotid ultrasound, applanation tonometry and echo-Doppler assessment of the biophysical properties of the aorta. Ventricular-arterial coupling assessed as the ratio between arterial elastance (Ea) and end-systolic ventricular elastance (Ees), was calculated using SBP, DBP, echo-derived stroke volume and the ratio between aortic pre-ejection time and total systolic time. Between groups comparisons were performed using parametric methods with p-values>0.05 considered significant.
Results: Thirty patients after stented coarctation (4 females; median age 17.2 [range 8.1-28.2] years; 11 after initial surgical repair) were studied. Stented patients were slightly older, but of similar height and BMI to controls. Peripheral and centrally derived SBP and radial augmentation index were lower and CIMT higher in stented patients. Carotid, ascending and abdominal aorta distensibility, pulse wave velocities and biophysical properties of the aorta were all similar, except for input impedance which was lower in stented patients. LV mass was higher and diastolic parameters suggested abnormal relaxation in stented patients. Ea and Ees were both reduced in stented patients, but ventricular-arterial coupling ratio Ea/Ees was similar.
Conclusion: After stented coarctation, elevated central systolic and augmentation pressures can be shown in association with abnormal ventricular relaxation. Although arterial and end-systolic ventricular elastance are reduced the ratio is similar to controls, suggesting an adaptive response of the ventricular-arterial coupling.

P11.06
FIBRONECTIN, BUT NOT LAMININ CONTENT IS INCREASED IN THE TUNICA MEDIA OF SUBCUTANEOUS SMALL RESISTANCE ARTERIES OF PATIENTS WITH ESSENTIAL HYPERTENSION

C. De Ciuceis [1], L. F. Rodella [2], D. Rizzoni [1], E. Porteri [1], R. Rezzani [2], G. E. M. Boari [1], E. Borsani [2], G. Favero [2], C. Platto [1], G. A. M. Tiberio [3], S. M. Giulini [3], E. Agabiti Rosei [1]
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Objective: It was suggested that, in the development of hypertensive microvascular remodeling, a relevant role may be played by laminin and fibronectin vascular content Aim of this study was to evaluate the amount of fibronectin and laminin within the tunica media of subcutaneous small arteries of normotensive subjects and essential hypertensive patients.
Design and Methods: We have investigated 6 normotensive control subjects and 10 essential hypertensive patients. All subjects were submitted to a biopsy of subcutaneous fat from the gluteal or the anterior abdominal region. Subcutaneous small resistance arteries were dissected and mounted on an isometric myograph, and the tunica media to internal lumen ratio was measured. In addition, the fibronectin and laminin content within the tunica media was evaluated by immunohistochemistry, with image analysis (% of area stained).

Results: As expected, clinic blood pressure values and media to lumen ratio were higher in essential hypertensive patients than in normotensive controls. Fibronectin media content was significantly greater in essential hypertensive patients (7.41±2.28 %), compared with normotensive controls (5.62±0.40, $P<0.05$). A significant correlation was observed between fibronectin media content and media to lumen ratio ($r=0.49$, $p<0.05$). No significant difference in laminin media content was observed between groups (3.7±1.71 % in essential hypertensive patients, 5.63±1.79 % in normotensive controls).
Conclusions: Our results indicate that, in small resistance arteries of patients with essential hypertension, fibronectin, but not laminin media content is increased. Fibronectin might be therefore involved in the development of small resistance artery remodeling in humans.

P11.07
DIFFERENCE BETWEEN SYSTOLIC AND DIASTOLIC CAROTID ARTERY STIFFNESS IS INDEPENDENTLY ASSOCIATED WITH LEFT VENTRICULAR MASS INDEX IN HEALTHY MIDDLE-AGED SUBJECTS

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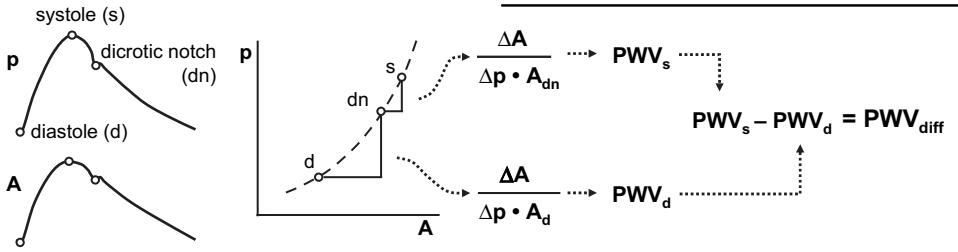
Background: Arterial stiffening potentially plays a role in cardiac hypertrophy. We recently demonstrated in patients that arterial stiffness can be substantially pressure dependent and, here, introduce a non-invasive measure to quantify the pressure dependence in the carotid artery, defined as the difference between systolic and diastolic pulse wave velocity (PWV_{diff}). Both PWV_{diff} and peripheral wave reflections (quantified by augmentation index, AIx) are biomechanically related to (late) systolic pressure increase. Therefore, we investigated the associations of PWV_{diff} and AIx with left ventricular mass index (LVMI).
Methods and Results: In 1522 subjects of the Asklepios cohort (age 35-55 yrs, healthy) PWV_{diff} was calculated from segmental distensibility coefficients, as obtained by carotid artery ultrasound and tonometry (Figure). PWV_{diff} ranged from 0.7 to 4.4 m/s. Linear regression analysis showed a significant association of PWV_{diff} with LVMI (β of 1.26 g/m$^{2.7}$ per m/s, 95% CI: 0.91-1.62), which remained significant after adjusting for covariates ($p=0.03$). AIx showed no consistent association with LVMI.
Conclusions: Carotid PWV_{diff} is independently associated with left ventricular mass index in presumed healthy middle-aged subjects. Non-invasive carotid artery ultrasound and tonometry enable assessment of the contribution of pressure dependent stiffness to LV pressure load, independently of wave reflections.



P11.08
EVALUATION OF ARTERIAL STIFFNESS IN CHRONIC KIDNEY DISEASE (CKD) STAGE 2-5 BY PULSE WAVE MEASUREMENTS AND AMBULATORY ARTERIAL STIFFNESS INDEX (AASI)

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Purpose: To study arterial stiffness in CKD by AASI compared to Augmentation Index (AIx) and aortic pulse wave velocity (aPWV). To study the intra-patient reproducibility of AASI in CKD.
Methods: Patients were studied 2 days within 2 weeks. Double applanation tonometry recordings of the radial pressure wave form and aPWV and 24-h ambulatory blood pressure measurements were done. AASI was calculated as 1 minus the regression slope of diastolic over systolic blood pressure. CKD stage was determined by estimated glomerular filtration rate. Spearman's correlation coefficient (SCC) was used for evaluating correlations. Day-to-day reproducibility was evaluated by the intra-class correlation coefficient (ICC).
Results: 68 patients (M50:F18), median age 63 years (range 30-79), with CKD stage 2 (n=17), stage 3 (n=22), stage 4 (n=20) and stage 5 (n=9) were studied. Mean(±SD) AASI was 0.44±0.15, mean AIx was 28.2%±10.4% and mean aPWV was 9.4m/s±1.0m/s with no significant differences among the stages. The SCC between AASI and AIx was 0.320 ($P=0.01$), between AASI and aPWV it was 0.643 ($P<0.0001$) and between AIX and aPWV it was 0.346 ($P=0.006$). ICC_{AASI} was 0.755 (95% CI: 0.630-0.841) with even greater reproducibility in CKD stages 4-5 (ICC>0.860).
Conclusions: The observed values of AASI in CKD patients were similar to those reported for the background population, while AIx and aPWV were higher. Despite good correlations between these parameters, the normal values of AASI found in the present study preclude its use as an index of vascular stiffness in CKD. Intra-patient reproducibility of AASI in CKD stage 2-5 was high.

P11.09
SYSTEMIC ARTERIAL PROPERTIES IN WOMEN 3 YEARS AFTER A PRE-ECLAMPTIC PREGNANCY

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Purpose: Pre-eclampsia is defined by hypertension and proteinuria, occurs in 3-10% of all pregnancies. The pathohysiological adaptation of systemic arterial properties has not been described. We performed a comprehensive study of systemic arterial properties in women with previous pre-eclamptic pregnancy (PPEP) as compared to women with previous normal pregnancy (PNP).
Methods: 35 women (37±4 years) with PPEP (3.5±1.0 years) and 65 (33±1 years) with PNP (6 months postpartum), were studied. Aortic root pressure and flow were obtained by calibrated right subclavian artery pulse trace, and aortic annular Doppler blood flow recordings. Systemic arterial properties were described by total arterial compliance(C), arterial elastance (Ea), characteristic impedance (Z0), and peripheral arterial resistance (R). Wave reflection was assessed as the ratio of the magnitude of the backward (Pb) to forward (Pf) pressure wave. Parameters were estimated by Fourier analysis of central aortic pressure and flow data and methods based on the 2-element windkessel model.
Results: (Table) Women with PPEP had significantly higher blood pressure than PNP. R was not significantly different between the groups, but Z_0 and Ea were significantly higher, and C trended lower in the PPEP group. There was significantly higher amplitude in both forward and backward.
Conclusions: The higher blood pressures in women with PEP is not explained by higher peripheral arterial resistance, but is likely related to a stiffer proximal aorta, and lower arterial compliance. This may relate to the higher risk for later cardiovascular events observed in women with PEP.

	PPEP	PNP	P
Mean arterial pressure (mmHg)	102±17	86±8	<0.001
Systolic pressure (mmHg)	129±21	110±9	0.002
Heart rate (min^{-1})	70±7	66±7	0.011
Cardiac output (l min^{-1})	5.5±1.2	4.9±0.9	0.020
R (mmHg ml^{-1} s^{-1})	1.16± 0.31	1.10±0.29	0.295
Z_0 (10^3–mmHg ml^{-1} s^{-1})	72±30	55±22	0.004