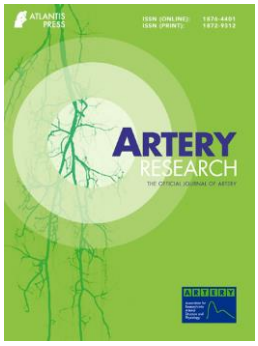

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P4.13: HIGH OUTPUT, LOW RESISTANCE HAEMODYNAMICS ARE ASSOCIATED WITH AUGMENTATION INDEX IN PATIENTS WITH TYPE 2 DIABETES

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Results: Recruitment began in January 2008 and will be completed in June 2012. It is hypothesized that there will be no significant difference in LV mass between groups. However, there will be significantly reduced use of medication and improved quality of life in the central BP group because more appropriate titration choices will be made to maintain normal central SBP.
Conclusion: Principal findings will be presented at ARTERY 12.

P4.11
ASYMMETRIC DIMETHYLARGININE LEVELS ARE INCREASED IN HUMAN IMMUNODEFICIENCY VIRUS INFECTED PATIENTS ON ANTIRETROVIRAL THERAPY COMPARED TO NAÏVE TO TREATMENT PATIENTS AND HEALTHY CONTROLS

P. Xaplanteris [1], C. Vlachopoulos [1], A. Synodinos [1], H. Sambatakou [2], E. Mariolis [2], A. Miliou [1], D. Pektasidis [2], C. Stefanadis [1]
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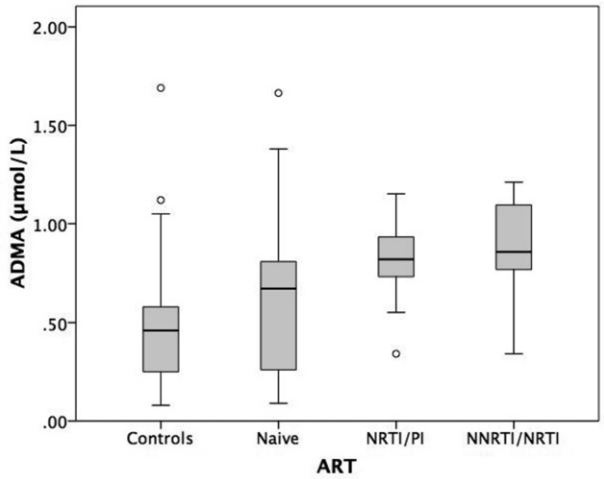
Background: HIV infection is linked to higher cardiovascular risk. Adverse outcomes may be mediated through mechanisms of endothelial dysfunction attributed to nitric oxide (NO) inhibition. The aim of the study was to compare blood plasma levels of asymmetric dimethylarginine (ADMA), a natural NO inhibitor, of HIV infected patients who are either naïve to treatment or on antiretroviral therapy (ART) and healthy controls.
Methods: 108 subjects were studied: 29 non-infected controls and 79 HIV infected patients [33 naïve to treatment, 30 on a nucleoside reverse transcriptase inhibitor plus non-nucleoside reverse transcriptase inhibitor combination (NRTI/NNRTI) and 16 on a nucleoside reverse transcriptase inhibitor plus a protease inhibitor combination (NRTI/PI)]. Plasma ADMA levels were measured using a commercially available ELISA kit. Between group comparisons were made using non-parametric tests.
Results: HIV infected patients had higher ADMA levels compared to controls ($P=0.003$). ADMA levels differed significantly across groups; non-infected controls had the lower levels of ADMA ($P=0.001$). Among HIV infected patients, those on ART exhibited higher ADMA levels versus ART-naïve patients [0.84 (0.77, 1.05) μmol/L for ART versus 0.67 (0.26, 0.86) μmol/L for ART-naïve patients, $P=0.002$]. ADMA levels did not differ between patients on NNRTIs [0.86 (0.77, 1.10)] or PIs [0.82 (0.71, 0.95)], $P=0.31$.
Conclusions: ART-naïve patients exhibit lower ADMA levels, denoting increased NO bioavailability compared to patients on ART; this may be attributed to their lower viral load that translates in a diminished inflammatory burden and better functional status. Patients on NNRTIs and PIs have comparable ADMA plasma levels.



P4.12
COMMON CAROTID ARTERY WALL SUBCLINICAL LESIONS ARE PRESENT IN SUBJECTS WITH RENAL FIBROMUSCULAR DYSPLASIA

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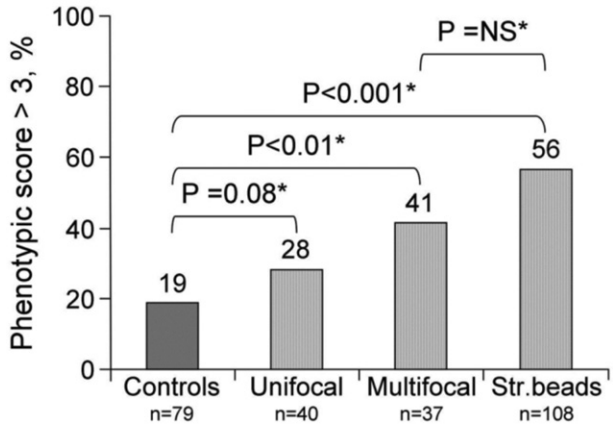
The common carotid artery (CCA) is an unusual localization of fibromuscular dysplasia (FMD). However, we previously detected CCA phenotypic alterations in a small population of patients with renal FMD and validated a CCA score. We aimed to test this score in a larger population of patients with renal FMD and hypertension.
Methods: CCA score was calculated with an high resolution echotracking device as the sum of B-mode and radiofrequency score as follows: *B-mode*. Normal=1; discontinuous blood-intima interface=2; discontinuous additional interface within the media=3; continuous interface within the media=4. *Radiofrequency signals*. Constant normal two-waved (double) signal=1; alternation of double and triple signal over successive acquisitions=2; constant three-wave (triple) signal=3.
Results: 185 hypertensive patients with renal FMD (40 patients with unifocal and 145 with multifocal lesions) and a control group of 79 hypertensive patients without renal FMD were enrolled. Prevalence of CCA score>3 was higher in patients with multifocal, with or without string of beads, than unifocal FMD and controls (Figure 1). In multivariate analysis, intima-media thickness (*150μm increase*: OR 1.83, 95%CI 1.27-2.64; $P=0.001$) and FMD distribution (*renal FMD alone*: OR 2.97; 95%CI 1.38-6.37; $P<0.01$. *Multisite FMD*: OR 6.03; 95%CI 2.62-13.89; $P<0.001$.) were associated with CCA score>3.
Conclusions: Phenotypic alterations of the CCA were reported in subjects with renal FMD with a higher prevalence in those with multifocal lesions. The CCA score>3 is associated with FMD distribution and intima-media thickness.



P4.13
HIGH OUTPUT, LOW RESISTANCE HAEMODYNAMICS ARE ASSOCIATED WITH AUGMENTATION INDEX IN PATIENTS WITH TYPE 2 DIABETES

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Objectives: Augmentation index (AIx) is associated with increased arterial stiffness. However, several reports have shown that AIx is not significantly raised in patients with type 2 diabetes (T2DM) despite having increased arterial stiffness. This suggests different mechanisms contributing to AIx in T2DM, although the exact cause is unknown. The aim of this study was to examine haemodynamic determinates of AIx in healthy people compared with T2DM.
Methods: Resting haemodynamics were recorded in 53 T2DM patients (aged 61±8 years, 51% male) and 53 matched controls (aged 58±6, 51% male). Tonometry was used to record AIx, central blood pressure (BP) and aortic stiffness (aPWV). Cardiac output (CO) and systemic vascular resistance (SVR) were measured using impedance cardiography.
Results: There was no significant difference between groups in AIx (24±11 vs 27±9%, $p=0.107$). T2DM patients had significantly higher aPWV (7.6±1.6 vs 6.8±1.9 m/s), heart rate (64±9 vs 57±7.0 bpm), CO (5.54±1.15 vs 4.49±0.71 L/min), and central SBP (114±12 vs 107±12 mmHg), but lower SVR (1326±249 vs 1559±281d.s.cm^{-5})($p<0.05$ all). The strongest correlates of AIx in T2DM patients were heart rate ($r=-0.632$), CO ($r=-0.604$) and SVR ($r=0.542$)($p<0.001$ all). However, these were not related to AIx in controls,

where the strongest correlate was central systolic BP ($r=0.587$; $p<0.001$). aPWV was not related to AIx in either group ($p>0.05$ both).
Conclusions: Haemodynamic determinants of AIx in T2DM patients are significantly different to healthy people where BP is a dominant factor. In patients with T2DM, however, a high output, low resistance haemodynamic environment is associated with AIx.

P4.14
EXERCISE AORTIC RESERVOIR FUNCTION IN PATIENTS WITH TYPE 2 DIABETES IS ASSOCIATED WITH BRAIN ATROPHY

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Objectives. Vascular mechanisms underlying brain atrophy and white matter lesions (WML) in patients with type 2 diabetes (T2DM) are unknown. Increased exercising blood pressure (BP) is associated with end-organ damage and could explain these brain abnormalities. This study examined associations between exercise central haemodynamics and brain structure.
Methods: Forty healthy participants (53±9 years; 50% male) and 40 T2DM (62±9 years; 50% male) were examined at rest and during light exercise. Resting and exercise central haemodynamics, including systolic BP (SBP), pulse pressure (PP) augmented pressure (AP), augmentation index (AIx), aortic stiffness and aortic reservoir function (including excess pressure integral [xsP]) were recorded by tonometry. Segmented grey (GM) and white matter (WM) and WML volumes were derived from magnetic resonance imaging.
Results: T2DM participants had lower WM ($p=0.004$) and GM ($p=0.07$) volumes, and significant elevation of all central hemodynamic variables during exercise ($p<0.01$ all). At rest, greater central (not brachial) haemodynamics (SBP, AP, AIx and PP) were independently associated with greater WML volume ($\beta=0.54$, $p=0.031$, $\beta=0.55$, $p=0.01$; $\beta=0.46$, $p=0.046$ and; $\beta=0.48$, $p=0.01$, respectively) in controls (not T2DM). During exercise, increased xsP was independently associated with reduced WM ($\beta=-0.54$, $p=0.006$) and GM ($\beta=-0.63$, $p=0.013$) volumes only in T2DM independent of age, sex, heart rate, and 24-hour ambulatory SBP.
Conclusions: In T2DM, aortic reservoir function and transmission of excess pressure during exercise is associated with brain atrophy. These findings suggest that vascular mechanisms underlying structural brain changes may differ between healthy individuals and those with T2DM.

P4.15
RELATIONSHIP BETWEEN ARTERIAL STIFFNESS, CARDIAC BAROREFLEX SENSITIVITY AND BLOOD PRESSURE VARIABILITY IN NORMOTENSIVE HEALTHY ADULTS

J. E. Ochoa [1,3], M. M. Correa [2], A. M. Valencia [2], J. G. McEwen [2], J. A. Gallo [2], G. Bilo [3], P. Salvi [3], D. Aristizabal [2], G. Parati [1,3]
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An increased arterial stiffness (AS) has been proposed as a likely mechanism for a reduced cardiac baroreflex sensitivity (BRS) and the associated increases in 24h blood pressure (BP) variability (BPV). Aim of the present study was to explore this issue in a group of 90 normotensive, non-obese, healthy adults (mean age 48±10 yrs, 50% F).
Methods: BRS was assessed by computer analysis of 10 min beat-to-beat BP and ECG recordings obtained in resting supine. The linear regression slope of spontaneous concomitant increases or decreases in systolic BP and RR interval were calculated, averaged and expressed as total slope of BRS (ms/mmHg). Simultaneous recordings of pulse waveform were obtained by means of a validated oscillometric device for ABPM (Mobil-O-Graph NG, IEM, Stolberg, Germany) with inbuilt transfer-function like method, and pulse wave velocity (PWV, m/s) calculated. BPV was assessed for systolic and diastolic BP as 24h standard deviation (SD), weighted 24h SD (wSD), daytime and night-time SD from 24h ABPM.
Results: In multiple linear regression analysis AS (assessed through PWV), had the strongest effect on BRS variation (beta:-0.50, $p<0.0001$), followed by HR and male sex. No significant effect was observed for age or MAP on BRS (See table). A similar independent analysis, showed a significant inverse relationship between BRS and daytime systolic BP SD (beta:-0,23; $p=0.036$)
Conclusion: Our findings suggest that in normotensive, otherwise healthy adults, decreased BRS and, indirectly, the associated increased day-time systolic BPV might be largely explained by an increased AS, independently of age and BP levels.

Predictors of cardiac BRS (Multiple linear regression analysis)

Variable (mean±SD)	Regression Coefficient	95% CI	Beta Coefficient	P value	R^2
PWV (6.12±1.53 m/s)	-3.619	-5.0, -2.2	-0,503	<0,0001	0,25
HR (64.2±9.4 bpm)	-0.426	-0.6, -0.2	-0,344	<0,0001	0,14
Sex (male)	-4.373	-8.4, -0.3	-0,212	0,029	0,04
Age (48±11 yrs)	-0.187	-0.7, 0,3	-0.187	0,547	-
MAP (97.9±8.8 mmHg)	-0.019	-0.4, 0.2	-0.077	0,759	-
R-Squared for the model including only significant variables (PWV, sex, HR)					**0,342**

P4.16
INSULIN RESISTANCE IS ASSOCIATED WITH INCREASED LARGE ARTERY STIFFNESS IN NORMOTENSIVE HEALTHY ADULTS

J. E. Ochoa [1,3], M. M. Correa [2], A. M. Valencia [2], J. G. McEwen [2], J. A. Gallo [2], G. Bilo [3], P. Salvi [3], D. Aristizabal [2], G. Parati [1,3]
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Aim: At present there is limited evidence on the relationship between insulin resistance (IR) and measures of large artery stiffness (AS) and wave reflections in normotensive healthy adults. Aim of the present study was to explore this issue in 90 normotensive (Systolic(S) blood pressure(BP) 107.1±9.3; diastolic (D) BP 69.6±7.7 mmHg), normoglycemic, non-obese, otherwise healthy adults (mean age 48 ± 10 yrs, 50% female).
Methods: IR was assessed with HOMA-Index and subjects were classified into IR tertiles, based on the distribution of HOMA-index values. Recordings of pulse waveform were obtained by means of a validated oscillometric device (Mobil-O-Graph NG, IEM, Stolberg, Germany) for ambulatory BP monitoring with in-built transfer-function like method. Aortic pulse wave velocity (PWV, m/s) and other measures derived from pulse wave analysis such as augmentation index (AIx, %), central SBP (cSBP), central DBP (cDBP) and central pulse pressure (cPP) were computed. Peripheral SBP and DBP, and heart rate (HR) were recorded and pulse pressure (PP) calculated as the difference between SBP and DBP.
Results: After multiple regression analysis adjusting for age, sex, HR and BMI, there was a significant overall effect of IR on measures of large artery stiffness and in central and peripheral BP levels. IR was associated with increased aortic PWV, and with higher central and peripheral SBP and DBP levels. See table.
Conclusion: our results indicate that in normotensive, healthy adults, IR may induce significant increases in large artery stiffness (as assessed with aortic PWV) and in central and peripheral BP levels.