



## Artery Research

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### **P4.10: PRINCIPAL FINDINGS FROM THE FIRST RANDOMISED STUDY TO DETERMINE THE VALUE OF CENTRAL BLOOD PRESSURE FOR GUIDING MANAGEMENT OF HYPERTENSION: THE BP GUIDE STUDY**

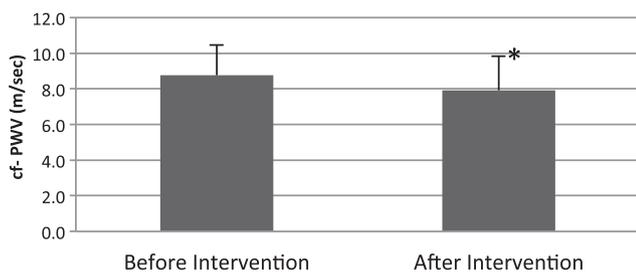
J.E. Sharman, M. Stowasser, W.P. Abhayaratna, T.H. Marwick

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**Conclusion:** A structured ambulatory rehabilitation program improves pulsatile hemodynamics in CAD patients and may, thus, improve prognosis.



**Figure** Arterial Stiffness before and after 5 week ambulant cardiology rehabilitation cf-PWV, carotid – femoral pulse wave velocity

#### P4.07 RELATIONSHIP BETWEEN CENTRAL AND PERIPHERAL AMBULATORY AND OFFICE BLOOD PRESSURE WITH LEFT VENTRICULAR MASS IN HYPERTENSIVE PATIENTS

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**Objectives:** The purpose of the present study was to assess the relationship of peripheral and central, systolic and diastolic blood pressure with left ventricular mass, both measured in the office and under ambulatory conditions.

**Methods:** Cross-sectional study that included 71 never treated hypertensives (37 men, 52.1%). 24 hours ambulatory peripheral and central (Mobil-O-Graph®) as well as office peripheral (OMRON®) and central blood pressure (Sphygmocor®) together with determination of left ventricular mass (LVM) by echocardiography were performed in all patients and adjusted for height<sup>2.7</sup> (LVM<sub>L2.7</sub>) and body surface area (LVM<sub>BSA</sub>).

**Results:** The mean age was 45.8±12 years with office peripheral BP of 140/90 (SD±15/10), office central BP of 130/91 (SD±16/13), ambulatory peripheral BP of 128/84 (SD±13/12) and ambulatory central BP of 120/85 (SD±15/10) mmHg. The mean LVM<sub>L2.7</sub> and LVM<sub>BSA</sub> was 49.3 g/m<sup>2.7</sup> and 104.2 g/m<sup>2</sup>, respectively. In bivariate analysis systolic ambulatory central BP showed the greatest correlation (r=608;p<0.0001) with LVM<sub>L2.7</sub>, followed by systolic ambulatory peripheral BP (SBPper\_24, r=508;p<0.0001). In multiple regression analysis, adjusting by age and gender, all systolic BP measurements were independently related to LVMI, but central, ambulatory SBP showed the closest association with LVMI, independently of adjustment for height<sup>2.7</sup> or BSA.

**Conclusions:** In our population of untreated middle aged hypertensives, systolic BP was more closely related to LVMI than DBP, peripheral BP showed a greater association than office BP, and central BP had a greater relationship to LVMI than peripheral BP. Variation of central systolic 24 hours blood pressure caused therefore the greatest variation of LVMI.

#### P4.08 AMBULATORY AND CENTRAL HAEMODYNAMICS ARE ELEVATED DURING HIGH-ALTITUDE HYPOXIA

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**Background:** High-altitude hypoxia may cause temporary increases in brachial BP, but the effect on more sensitive BP measures (24hr ambulatory and central BP) is unknown. This pilot study aimed to determine this, as well as the haemodynamic correlates of acute mountain sickness (AMS).

**Methods:** Measures of oxygen saturation (pulse oximetry), 24hr ambulatory BP (A&D-TM2430), brachial and central BP (including augmentation index; Pulsecor) were recorded in 10 adults (aged 27±4, 30% male) during a 16-day trek to Mt. Everest base camp, Nepal. Data was recorded at sea level (stage 1; <450m above sea level [ASL]) and at progressive ascension to 3440m ASL (stage 2), 4350m ASL (stage 3) and 5164m ASL (stage 4). The Lake Louise Score (LLS) was used to quantify AMS symptoms.

**Results:** Total LLS increased step-wisely from sea level to stage 4 (0.3±0.7vs.4.4±2.0, P=0.012), whilst oxygen saturation decreased to 77±9% in a similar step-wise fashion (P=0.001). The highest recordings of 24hr ambulatory BP, daytime BP, night-time BP, brachial and central SBP and DBP, augmentation index and heart rate (HR) were achieved at stage

3, which was significantly greater than at sea level (P<0.005 for all). However, there was no difference in brachial or central PP, or PP amplification between stages (P>0.05 for all). Overall, 24hr ambulatory and night-time HR were strongly correlated with oxygen saturation (r=-0.741 and -0.608, both P<0.001) and LLS (r=0.648 and r=0.493, both P<0.001).

**Conclusion:** 24hr ambulatory BP, central BP and HR are elevated during high-altitude hypoxia, but AMS symptoms are only related to tachycardia.

#### P4.09 BASELINE AUGMENTATION INDEX AND PULSE PRESSURE AMPLIFICATION DETERMINE THE RESPONSE TO ANTIHYPERTENSIVE THERAPY

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**Objectives:** Essential hypertension is characterised by alterations in haemodynamics. Hence haemodynamic profiling could lead to improved blood pressure (BP) control in these patients. We tested if baseline haemodynamic indices predict the BP lowering effects of different classes of antihypertensive drugs in hypertensive patients.

**Methods:** In this double-blind placebo-controlled crossover study we randomised 53 treatment-naïve hypertensive patients to receive doxazosin 4 mg, candesartan 16 mg, bisoprolol 5 mg, isosorbide mononitrate (ISMN) 50 mg, and placebo daily for 6 weeks. Brachial and central BP, augmentation index (Alx), aortic pulse wave velocity (aPWV), stroke volume (SV), cardiac output (CO), peripheral vascular resistance (PVR), and pulse pressure amplification (PPA) were measured at baseline and after each drug.

**Results:** Baseline Alx and PPA determined brachial and central BP reduction with antihypertensive therapy, particularly with bisoprolol. In patients with low baseline Alx (1.7-28.9%) and high PPA (1.22-1.87), bisoprolol had a weak antihypertensive effect, while the opposite was observed in patients with high Alx (36.3-48.2%) and low PPA (1.05-1.11). With candesartan, BP reduction was the largest, regardless of baseline Alx or PPA levels. There were no significant differences in BP reduction between the baseline extremes of SV, CO, PVR or aPWV with any drug.

**Conclusion:** Our study suggests that haemodynamic profiling by Alx or PPA could serve as a valuable tool in management of hypertension, particularly if beta-blockers are considered for treatment. Among the drug classes and doses used, the angiotensin II receptor antagonist reduced BP the most regardless of the underlying haemodynamic profile.

#### P4.10 PRINCIPAL FINDINGS FROM THE FIRST RANDOMISED STUDY TO DETERMINE THE VALUE OF CENTRAL BLOOD PRESSURE FOR GUIDING MANAGEMENT OF HYPERTENSION: THE BP GUIDE STUDY

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**Introduction:** Central blood pressure BP could be a better method to assess risk related to BP because it predicts mortality independent of brachial BP. This current study is the first randomized trial to test the usefulness of central BP as a management tool for doctors treating patients with hypertension.

**Methods:** Participants with uncomplicated essential hypertension (n=284) were randomized to 12 months of treatment decisions guided by usual care (based on office, home and 24 hour ambulatory brachial BP) or, in addition, by central BP estimated using radial tonometry (based on age and sex-specific normal central systolic SBP values). Recommendations regarding titration of antihypertensive medication (increase, decrease or maintain dose) were provided to each participant and their general practitioner. Relevant clinical information (e.g. co-morbidities, LV mass, blood biochemistry and BP-related symptoms) were considered when making titration recommendations in all participants. The primary outcome measures are: 1) change in LV mass (by real time three dimensional echocardiography); 2) amount of medication used; and 3) quality of life. Analysis will be by intention to treat.

**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

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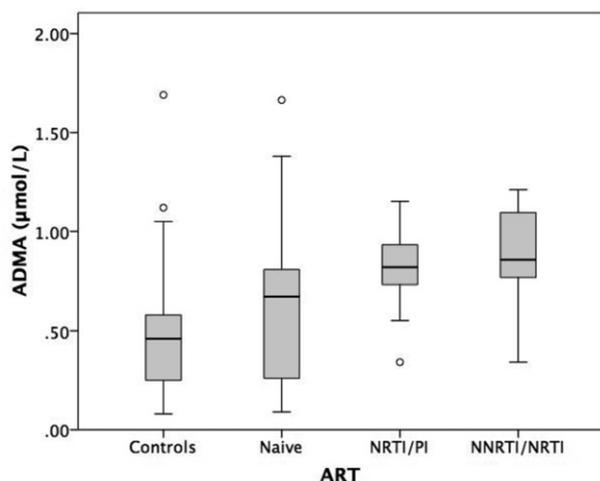
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**Background:** HIV infection is linked to higher cardiovascular risk. Adverse outcomes may be mediated through mechanisms of endothelial dysfunction attributed to nitric oxide (NO) inhibition. The aim of the study was to compare blood plasma levels 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)  $\mu\text{mol/L}$  for ART versus 0.67 (0.26, 0.86)  $\mu\text{mol/L}$  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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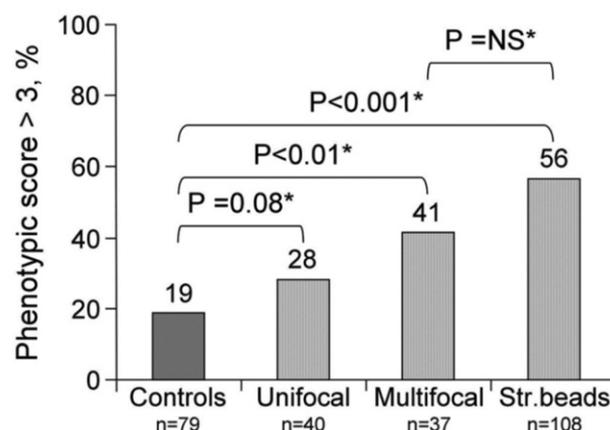
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The common carotid artery (CCA) is an unusual localization of fibromuscular dysplasia (FMD). However, we previously detected CCA phenotypic alterations in a small population of patients with renal FMD and validated a CCA score. We aimed to test this 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; alteration 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 (150 $\mu\text{m}$  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 (Alx) is associated with increased arterial stiffness. However, several reports have shown that Alx is not significantly raised in patients with type 2 diabetes (T2DM) despite having increased arterial stiffness. This suggests different mechanisms contributing to Alx in T2DM, although the exact cause is unknown. The aim of this study was to examine haemodynamic determinates of Alx in healthy people compared with T2DM.

**Methods:** Resting haemodynamics were recorded in 53 T2DM patients (aged 61 $\pm$ 8 years, 51% male) and 53 matched controls (aged 58 $\pm$ 6, 51% male). Tonometry was used to record Alx, 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 Alx (24 $\pm$ 11 vs 27 $\pm$ 9%,  $p=0.107$ ). T2DM patients had significantly higher aPWV (7.6 $\pm$ 1.6 vs 6.8 $\pm$ 1.9 m/s), heart rate (64 $\pm$ 9 vs 57 $\pm$ 7.0 bpm), CO (5.54 $\pm$ 1.15 vs 4.49 $\pm$ 0.71 L/min), and central SBP (114 $\pm$ 12 vs 107 $\pm$ 12 mmHg), but lower SVR (1326 $\pm$ 249 vs 1559 $\pm$ 281 d.s.cm<sup>-5</sup>) ( $p<0.05$  all). The strongest correlates of Alx 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 Alx in controls,