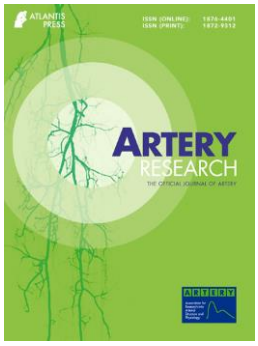

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3.5: DIFFERENTIAL EFFECTS OF BNP AND NO DONORS ON HUMAN FOREARM MUSCULAR CONDUIT ARTERIES

H. Fok, B. Jiang, A. Donald, P. Chowienczyk

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Methods: From the cohort of EPP3 study, 2211 patients were included in this report (age 59±6 years). The baroreceptor sensitivity (BRS) was defined as the ratio between variations in the carotid distension rate and variations in R-R interval in the low-frequency range (0.04-0.15Hz). The CHD risk was estimated according to the Framingham risk score.
Results: We studied 2088 patients with GFR>60ml/min/1.73m^2 and 123 patients with CKD (GFR 45-60ml/min/1.73m^2). The prevalence of 10 years CHD risk≥20% was significantly higher in patients with CKD than in those with normal renal function (30% and 14%, respectively). In fully adjusted model, in the total population, the increase of BSA, IMT and carotid PP, the reduction of carotid strain and BRS, and the presence of CKD were independently associated with 10 years CHD risk≥20% (Table 1).
Conclusions: The spontaneous BRS is a predictor of CHD risk in patients with moderate CKD and in those with normal renal function.

Predictors of 10 years CHD risk ≥ 20%	OR	95%CI	P value
Body surface area, m^2 x 10^{-1}	1.20	1.13-1.27	<0.001
Intima-media thickness, μm x 10^2	1.29	1.16-1.43	<0.001
Carotid pulse pressure, *10 mm Hg*	1.62	1.47-1.79	<0.001
Carotid strain, *%*	0.80	0.74-0.86	<0.001
Baroreflex sensitivity, *Log [(ms/(μm/s)^2) x 10^2]*	0.36	0.23-0.59	<0.001
Moderate chronic kidney disease	2.15	1.38-3.37	<0.001

3.3
NORMAL AND REFERENCE VALUES FOR CAROTID INTIMA-MEDIA THICKNESS

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Increased carotid artery intima-media thickness (IMT) has been widely used as a surrogate marker of atherosclerosis and has been shown to predict cardiovascular disease (CVD). However, the interpretation of IMT values, as measured across different age, sex and risk groups, has been hampered by the absence of normal and reference values comparators. The aim of the present study is therefore to establish normal and reference values for IMT based on a wide population.
We combined common carotid IMT data from 25 research centres worldwide as obtained with the use of an echo-tracking system. The total population consisted of 29,975 individuals (54% men), with ages ranging from 15 to 101 years-old, of whom 21% had established CVD, 56% had hypertension, 11% had diabetes, 25% had hypercholesterolemia, 20% was current smoker and 32 and 16% were on blood pressure (BP)- and/or lipid lowering treatment respectively. Sex- and age-specific normal values of IMT were established in the 'normal population', which consisted of 2,762 individuals without overt CVD, *and* who had optimal or normal BP (i.e. <130/85 mm Hg) *and* no acquired cardiovascular risk factors [i.e. diabetes, use of BP- and/or lipid lowering medication, hypercholesterolemia, current smoking] (Fig 1). Multiple linear regression analyses will be used to investigate the influence of, and establish reference IMT values across categories of the cardiovascular risk factors mentioned above.
In conclusion, this unique study enables the definition of normal and reference values for IMT to help interpretation of such measures as obtained in both research and clinical settings.

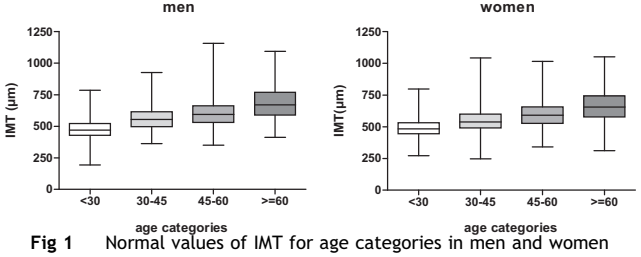

Fig 1 Normal values of IMT for age categories in men and women

3.4
ESTABLISHING REFERENCE VALUES FOR CENTRAL BLOOD PRESSURE IN A GENERAL HEALTHY POPULATION AND ESTABLISHED DISEASE GROUPS

A. Herbert [1,2,3,4], Reference Values for Arterial Stiffness Collaboration
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Background and Objective: Estimated central blood pressure is a non-invasive outcome regarded as a prognostic marker of cardiovascular disease. Reference values have been calculated previously in specific populations, for example, in 5,648 healthy subjects from East Anglia and Cardiff in the ACCT study (*Hypertension* 2008;51;1476-1482). These values are useful not only for assessing flow properties, but for study design in investigating treatments or adverse events longitudinally. This study aimed to establish reference values for a worldwide general population, increasing the flexibility of their use.
Methods: Existing data from individual studies were combined, comprising of central pressure data from clinical trials and population surveys, whether published or not. Main inclusion criteria were that these studies used validated methods of applanation tonometry or distension measurement and could provide a minimum pre-defined set of variables and information on the individual study.
Results: Data of 63,107 subjects were gathered from 52 centres in total and values standardised across different study methods. Of these subjects, 29,882 were declared as healthy and valid for analysis (median (IQR) age = 53 (40.5 to 63) years, 15,290 being female (51%) with median (IQR) SBP = 108 (103 to 115) mmHg. Reference ranges were calculated for these subjects, stratified by age, sex and peripheral pressure. This analysis was repeated for the 18,524 valid non-healthy subjects, by established disease-groups.
Conclusions: Average central pressures per subject-characteristic group were provided, as well as disease-type, across a very broad population with an increased precision.

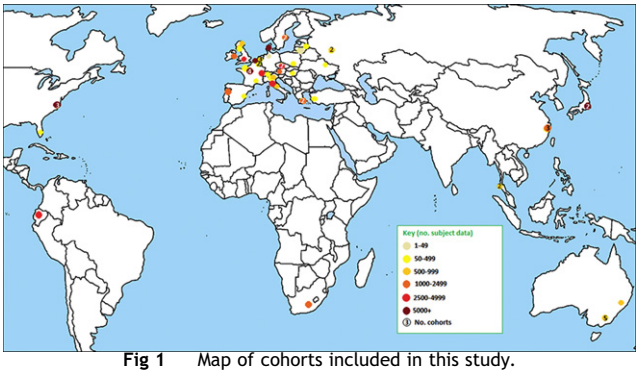

Fig 1 Map of cohorts included in this study.

3.5
DIFFERENTIAL EFFECTS OF BNP AND NO DONORS ON HUMAN FOREARM MUSCULAR CONDUIT ARTERIES

H. Fok, B. Jiang, A. Donald, P. Chowienczyk
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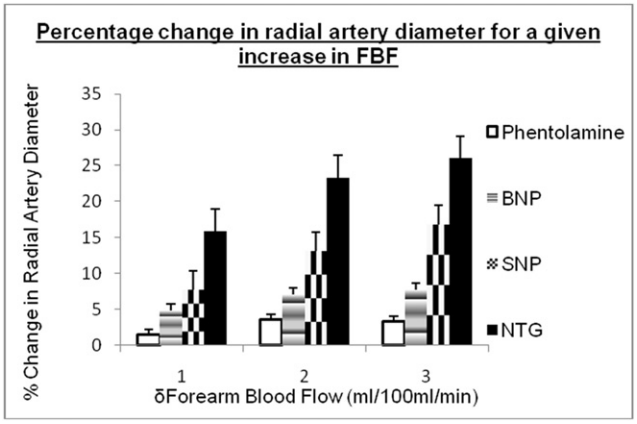
Nitroglycerin (NTG) selectively vasodilates muscular conduit arteries. Whether other nitric oxide (NO) donors and natriuretic peptides have similar effects is unknown. The aim of this study was to compare effects of NTG, sodium nitroprusside (NP) and brain natriuretic peptide (BNP) on the radial artery (a muscular conduit artery) and forearm resistance vasculature. Phentolamine (PHT), a vasodilator with minimal vasodilator effects on conduit arteries was used as a control. Healthy normotensive men aged 19-45 years were studied. The right brachial artery was cannulated using a 27 gauge needle and an intra-arterial infusion of each vasodilator (PHT, 10, 30 and 100µg/min, n = 9; NTG 0.03, 0.1, 0.3, 1.0, 3.0 µg/min, n = 8. NP, 0.3, 1, 3 µg/min,n = 11; BNP 0.03, 0.1, 0.3, 1, 3 µg/min n = 8) given on separate occasions or after washout. Forearm blood flow (FBF) was measured by venous occlusion plethysmography and change in radial artery diameter by ultrasound. The percentage change in diameter for different drugs was compared at doses producing the same change in FBF (DFBF). The

efficacy of dilation of the radial artery was NTG>NP >BNP>PHT. Radial artery dilation by NTG and NP but not BNP was greater than that by PHT ($P<0.05$) and radial dilation by NTG greater than that by BNP ($P<0.05$). These results demonstrate that drugs acting on the guanylyl cyclase — cGMP pathway have differential actions on muscular conduit arteries.



3.6
THE "MARATHON PARADOX": DECREASED INTIMA-MEDIA THICKNESS AND IMPROVED FLOW-MEDIATED DILATATION, BUT INCREASED AORTIC STIFFNESS

D. Kardara, C. Vlachopoulos, D. Terentes-Printzios, P. Xaplanteris, N. Ioakeimidis, C. Stefanadis
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Background: Arterial stiffness, wave reflections, endothelial dysfunction and carotid intima-media thickness (cIMT) are predictors of cardiovascular events. Marathon running is an extremely vigorous aerobic exercise.
Methods: We enrolled 3 groups of regularly-trained marathon runners and 3 groups of matched recreationally-active controls. Aortic stiffness was evaluated with carotid-femoral pulse wave velocity (PWV), wave reflections with augmentation index (AIx), endothelial function with flow-mediated dilation (FMD) and nitroglycerine-mediated dilatation (NMD) of the brachial artery and early atherosclerosis with cIMT. PWV was studied in 49 runners (trained for 11.6±9.1 years) and 46 controls. IMT was measured in 36 runners (trained for 13.1±9.5 years) and 19 controls. FMD and NMD were assessed in 21 runners (trained for 14.5±8.5 years) and 17 controls.
Results: Marathon runners had significantly higher systolic, diastolic, pulse (aortic and brachial) and mean pressures ($P<0.05$ for all) and higher PWV compared to controls (6.89±1.0m/s vs. 6.33±1.03m/s, $P<0.01$). Athletes exhibited lower cIMT (0.58±0.10mm vs 0.63±0.80mm, $P<0.05$) and higher FMD (8.59±4.1% vs 6.25±1.6%, $P<0.05$). AIx, AIx@75 and NMD did not differ.
Conclusion: While marathon runners have higher FMD and decreased IMT compared to controls, indicating better endothelial function and lower subclinical atherosclerosis, they also have increased PWV. Increased aortic stiffness may be the result of elastic component damage due to excessive exercise burden; however, it may also represent an adaptive process that leads to a higher, but favorable -for this type of running- travel for waves, and possibly relates to why marathon runners reach their peak later in life compared to other athletes.

Oral Session 5
Free Oral Communications
In association with 'Pulse of Asia'

5.1
COMMON CAROTID ARTERY PROPERTIES ARE RELATED TO SYMPATHETIC OUTFLOW AND CARDIOVASCULAR VARIABILITY

D. Hering [1], K. Czechowicz [1], R. Nowak [1], W. Kucharska [1], P. Brands [2], P. Boutouyrie [3], S. Laurent [3], K. Narkiewicz [1]
[1]*Department of Hypertension and Diabetology, Medical University of Gdansk, Gdansk, Poland*
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Objective: The relationship between sympathetic activity and common carotid artery (CCA) properties is unknown. We therefore tested the hypothesis that mechanical properties of arterial wall are independently linked to muscle sympathetic nerve activity (MSNA) and cardiovascular variability.
Design and Methods: We measured MSNA (microneurography), heart rate (ecg), arterial pressure (Finapres) and CCA properties (ART.LAB system) in 20 subjects with high normal blood pressure and newly detected stage 1 hypertension (18 males, age 36±2 years, BMI 27±1 kg/m^2, mean±SEM). SBP and RR-interval variabilities were defined as the standard deviation of the means.
Results: MSNA averaged 27±3 bursts/min., mean CCA intima-media thickness (IMT) was 0.57±0.03 mm, carotid distension was 499±27 μm, systolic (S) Carotid Wall Stress (CWS) was 119±6 kPa, pulsatile (P) CWS was 46±3 kPa. CCA IMT was related to MSNA ($r=0.54$; $P<0.01$), and SCWS ($r=-0.84$; $P<0.0001$), but not to variability of SBP ($r=-0.27$; P=NS) or RR-interval ($r=-0.26$; P=NS). MSNA was associated with reduction in carotid distension waveform ($r=-0.54$; $P<0.01$), SCWS ($r=-045$; $P<0.05$) and PCWS ($r=-0.57$; $P<0.01$). CWS was not linked to variability of SBP or RR-interval. Changes in CCA diameter were positively related to RR-variability ($r=0.49$; $P<0.05$), but not to variability of SBP ($r=0.3$; P=NS). The correlations between MSNA and CCA properties remained significant after adjustment for age, body mass index and blood pressure.
Conclusions: (1) Distension of the common carotid artery is related to muscle sympathetic nerve activity and cardiovascular variability. (2) Intima-media thickening and carotid wall stress are linked to sympathetic activation, but not to altered cardiovascular variability.

5.2
ARTERIAL STIFFNESS IS A MAJOR INDEPENDENT DETERMINANT OF VISIT-TO-VISIT VARIABILITY IN SBP: A 9.1 YEAR FOLLOW-UP IN TREATED HYPERTENSIVES

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Department of Pharmacology and INSERM U970, HEGP, Paris, France

Objective and background: Aortic stiffening, which favours the wave propagation generated by changes in cardiac output, and exaggerates the early return of wave reflection generated by changes in vasomotor tone, can increase the variability in SBP.
Methods: Aortic stiffness was determined through carotid-femoral pulse wave velocity (PWV) in 95 patients (age 62.9±10.8 years) who attended the outpatient hypertension clinic at Pompidou hospital during a total follow-up of 9.1±3.6 yrs. PWV was determined after 5.5±2.7 yrs. Visit-to-visit variability in office SBP was expressed as standard deviation (SD) of measurements and SD/mean, and calculated during the entire follow-up (FU). 8.5±4.8 visits occurred before PWV measurements, and 6.4±5.4 visits after.
Results: SD of SBP was 13.5±4.3 mmHg during FU. PWV was 11.4±2.7 m/s. In univariate analysis, SD-SBP during FU was significantly related to PWV (P=0.0007), age (P=0.021), SBP (P=0.033), MBP (P=0.0016) and diabetes (P=0.045). In multivariate robust regression analysis, PWV was a major determinant of SD-SBP (P=0.018) during FU, explaining 11.2% of SD-SBP variance (and 51% of explained variance), independently of age, gender, SBP, HR, BMI, diabetes, and dyslipidemia, which were not significantly associated with SD-SBP. Similar findings were observed when SD/mean of SBP was used instead of SD-SBP.
Conclusion: Aortic stiffness was a strong independent determinant of visit-to-visit variability in SBP, whereas no classical CV risk factor was associated with SD-SBP in multivariate models. These results suggest that antihypertensive treatment should aim at normalizing aortic stiffness to better reduce visit-to-visit SBP variability.

5.3
DISTANCE MEASUREMENT FOR PULSE WAVE VELOCITY CALCULATION — COMPARISON WITH INVASIVE FINDINGS

T. Weber [1], A. Haiden [1], S. Wassertheurer [2], C. C. Mayer [2], B. Hametner [2], J. Kropf [2], B. Eber [1]
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[2]*Austrian Institute of Technology, Vienna, Austria*

Background: A more simple yet accurate method for assessing travel distance (TD) for calculation of carotid-femoral pulse wave velocity (cfPWV) is desirable to improve acceptance of the method in clinical routine.
Methods: We compared the following methods for assessment of TD, as performed during non-invasive measurement of cfPWV with the SphygmoCor