3.2: SPECTRAL ANALYSIS OF CAROTID DISTENSION RATE AND R–R INTERVAL (SPONTANEOUS BAROREFLEX ACTIVITY) PREDICTS CORONARY HEART DISEASE RISK IN PATIENTS WITH MODERATE CHRONIC KIDNEY DISEASE AND IN THOSE WITH NORMAL RENAL FUNCTION: THE EPP3 STUDY

L. Zanoli, M. Alivon, J.P. Empana, N. Estrugo, G. Ecriou, H. Ketthab, J.F. Pruny, P. Castellino, S. Yanes, D. Laude, K. Bean, F. Thomas, X. Jouven, S. Laurent, P. Boutouyrie

Conclusion: This study provides the first direct evidence that aortic stiffness not arterial remodeling is an independent predictor of fatal and non-fatal cardiovascular events in patients with CKD stage 2-5.

1.6

ARTERIAL STIFFNESS IS AN INDEPENDENT DETERMINANT OF COMPENSATORY HYPERFILTRATION AFTER KIDNEY DONATION

P. Fesler, J. Ribstein, du Cailar G., G. Mourad, A. Mimran
Department of Internal Medicine and Nephrology, Hopital Lapeyronie, Montpellier, France

After kidney donation, the remaining kidney tends to hyperfiltrate thus limiting the initial loss of renal function. However, the potential determinants of this compensatory hyperfiltration (CHF) and the possible influence of arterial function are not known.

In 26 normotensive healthy kidney donors (51 +/- 9 yrs [mean+/-SD], 22 females), glomerular filtration rate (GFR) was measured by the clearance of continuously infused Tc99m-DTPA and timed urine collections at baseline -i.e. before donation- and 1 year after donation. CHF was computed as post-donation GFR minus half of baseline GFR. Arterial function was assessed at baseline through carotido-femoral pulse wave velocity (PWV) and carotid augmentation index (AIx).

After kidney donation, there were no significant changes in blood pressure (BP), but 2 subjects became hypertensive. GFR decreased from 104+/-17 to 71+/-11 mL/min/1.73m^2 and mean CHF was 19+/-9 mL/min/1.73m^2. In univariate analysis, CHF was inversely correlated to baseline age (r^2=0.15, p=0.049) and PWV (r^2=0.23, p=0.012), but not mean BP or AIx. In multivariate analysis, CHF remained inversely correlated to PWV (p=0.020), independently of baseline age, mean BP and GFR (model r^2=0.45, p=0.002).

In conclusion, in healthy subjects, increased arterial stiffness seems to be associated with a limited magnitude of post-donation hyperfiltration. This could reflect an influence of arterial function on renal reserve, providing further insights into the relationship between macrocirculation and renal microcirculation.

Oral Session 3
Young Investigators' Presentations

3.1

PRE-PREGNANCY CARDIOVASCULAR RISK IN WOMEN WITH PREVIOUS PREECLAMPSIA (PET)/INTRAUTERINE GROWTH RESTRICTION (IUGR)

A. A. Mahendru [1], C. C. Lees [1], T. R. Everett [1], C. M. McEniery [2], I. B. Wilkinson [2]
[1]*Fetal Medicine Department, Addenbrooke's Hospital, Cambridge, United Kingdom*
[2]*Clinical Pharmacology Department, Addenbrooke's Hospital, Cambridge, United Kingdom*

Women with history of preeclampsia (PET) and delivery of intrauterine growth restriction (IUGR) babies are at increased risk of cardiovascular events later in life. This could be related to endothelial dysfunction, altered arterial stiffness or metabolic abnormalities resulting from pregnancy complications. Alternatively, pre-existing abnormalities in the cardiovascular system may predispose them to both pregnancy related complications and cardiovascular disease later in life. We compared pre-pregnancy arterial stiffness and central haemodynamics between women with previous PET/IUGR and those with previous uncomplicated pregnancies.

Method: 46 women planning to conceive were prospectively recruited in two groups: (1) 34 parous women with previous normal pregnancies (controls) (2) 12 women with previous PET (ISSHP guideline) requiring delivery at <34 weeks or requiring treatment for severe preeclampsia and/or who delivered an IUGR baby. Brachial and central blood pressures, pulse wave analysis (AIx), carotid-femoral pulse wave velocity (a PWV) and cardiac output were assessed along with routine biochemistry.

Results: Women with previous PET/IUGR had higher brachial diastolic blood pressure (*P*=0.03), central systolic blood pressure (*P*=0.02), MAP (*P*=0.01), and PVR (*P*=0.03) compared to controls but had lower PP amplification (*P*=0.04). There was no difference in the adjusted AIx, aPWV or in the cholesterol/lipid profile between the groups.

Conclusion: Vascular dysfunction as reflected by higher central blood pressure and peripheral resistance exists pre-pregnancy in women with previous PET/IUGR compared to normal healthy women. Further prospective pre-pregnancy studies prior to development of PET/IUGR are needed to assess the mechanism of the vascular dysfunction that persists following these pregnancy complications.

Table 1   Pre-pregnancy haemodynamics in two groups:

Cardiovascular parameter	Previous normal pregnancies (n=34)	Previous PET/IUGR (n=12)	P*
Age (yrs)	37 ± 4	34 ± 5	0.07
Brachial SBP (mm Hg)	108 ± 8	114 ± 9	0.07
Brachial DBP (mm Hg)	71 ± 7	77 ± 8	0.03*
Brachial PP (mm Hg)	37 ± 6	37 ± 4	0.7
Central SBP (mm Hg)	100 ± 9	107 ± 9	0.02*
PP (mm Hg)	28 ± 5	29 ± 5	0.4
PP amplification	1.4 ± 0.1	1.3 ± 0.1	0.04*
MAP (mm Hg)	84 ± 9	92 ± 9	0.01*
Heart rate (beats/min)	67 ± 9	67 ± 13	0.9
CO (L/min)	5.5 ± 1.0	5.1 ± 1.1	0.3
SV (ml)	77 ± 13	64 ± 25	0.1
PVR (dynes.s^{-1}.cm^{-5})	1258 ± 239	1508 ± 334	0.03*
AIx$_a$ (%)	23 ± 6	27 ± 7	0.06
aPWV$_b$ (m/sec)	5.4 ± 0.1	5.5 ± 0.2	0.8

Data are means ± S.D. a=adjusted for age, height and heart rate. b=adjusted for MAP. *P <0.05 is statistically significant. (SBP= Systolic blood pressure, DBP= Diastolic blood pressure, PP= pulse pressure, MAP=Mean arterial pressure, CO=cardiac output, SV= stroke volume, PVR= peripheral vascular resistance)
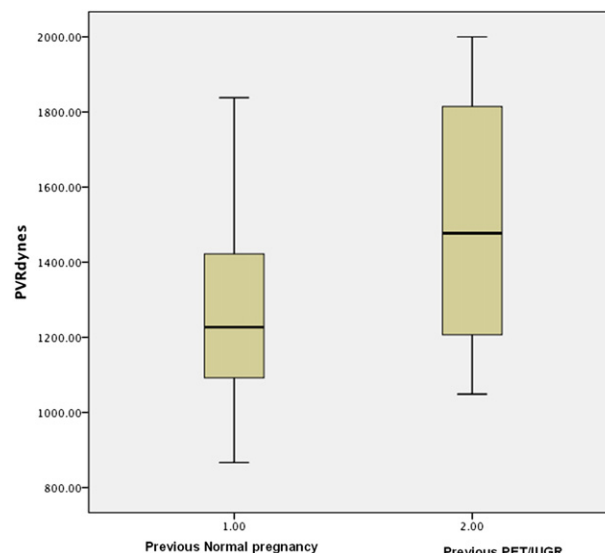
Figure 1   Differences of mean PVR in the two groups (*P*=0.03)

3.2

SPECTRAL ANALYSIS OF CAROTID DISTENSION RATE AND R−R INTERVAL (SPONTANEOUS BAROREFLEX ACTIVITY) PREDICTS CORONARY HEART DISEASE RISK IN PATIENTS WITH MODERATE CHRONIC KIDNEY DISEASE AND IN THOSE WITH NORMAL RENAL FUNCTION: THE EPP3 STUDY

L. Zanoli [1,2], M. Alivon [1], J. P. Empana [1], N. Estrugo [1], G. Ecriou [1], H. Ketthab [1], J. F. Pruny [1], P. Castellino [2], S. Yanes [1], D. Laude [1], K. Bean [1], F. Thomas [3], X. Jouven [1], S. Laurent [1], P. Boutouyrie [1]
[1]*Université Paris Descartes, Department of Pharmacology, HEGP, APHP, Paris, France*
[2]*University of Catania, Department of Internal Medicine, Catania, Italy*
[3]*Institut Prévention cardiovasculaire, Paris, France*

The classic technique to evaluate the spontaneous baroreflex is the spectral analysis of finger blood pressure and heart rate. However, baroreceptors respond to deformation and not to pressure per se and the results obtained with this technique can be influenced by the vascular component of the baroreflex. Recently, the spectral analysis of carotid distension rate has been used to study the neural baroreflex. The aim of this study is to test this new technique to predict the coronary heart disease (CHD) risk in patients with moderate chronic kidney disease (CKD) and in those with normal renal function.

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

L. Engelen [1,2], P. Boutouyrie [1], I. Ferreira [2], C. Stehouwer [2], S. Laurent [1]
[1] Hôpital Européen Georges Pompidou, Paris, France
[2] Maastricht University Medical Centre, Maastricht, Netherlands

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.
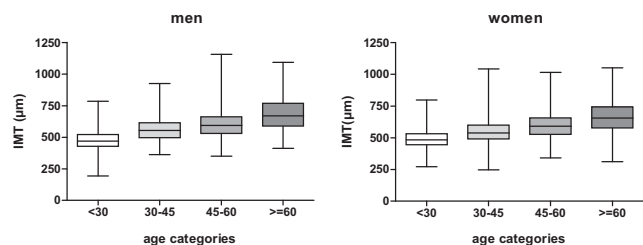

Fig 1   Normal values of IMT for age categories in men and women

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
[1] INSERM Team U970, Paris, United Kingdom
[2] Biostatistics, University of Manchester, Manchester, United Kingdom
[3] Research & Development, Pennine Acute Hospitals NHS Trust, Manchester, United Kingdom
[4] Research & Development, Salford Royal Hospitals NHS Trust, Salford, United Kingdom

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.
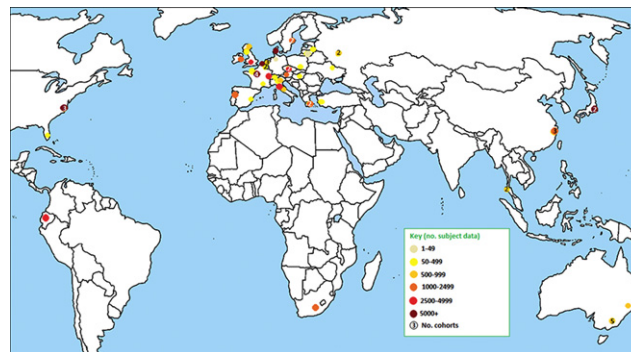

Fig 1   Map of cohorts included in this study.

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

H. Fok, B. Jiang, A. Donald, P. Chowienczyk
King's College London BHF Centre, Department of Clinical Pharmacology, St Thomas' Hospital, London, United Kingdom

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