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### **P5.29: PULSE TIMING DIFFERENTIAL AS A MEASURE OF ARTERIAL STIFFNESS**

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## P5.26

**AMBULATORY BLOOD PRESSURE CORRELATES POSITIVELY WITH COGNITIVE SCORES IN ELDERLY PEOPLE WITH CHRONIC KIDNEY DISEASE (CKD) AND CARDIOVASCULAR DISEASE**

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**Background:** Studies have linked low blood pressure (BP) with adverse outcomes in CKD. Hypertension is treated to reduce cardiovascular events, however this may compromise cerebral perfusion by excessive lowering of blood pressure.

**Objectives:** To examine the relationships between ambulatory BP with cognitive performance.

**Methods:** 80 patients >65 years with CKD were recruited and were assessed using a range of neuropsychological tests. Scores were compared to daytime ambulatory BP. Linear correlations and multivariate regression analysis were used to measure associations. Results were recorded for those with a history of cardiovascular disease (CVD).

**Results:** 16 patients had a history of CVD. Mean age was 75.7 years (SD 5.8) and 75% were male. Mean BP was 123/70mmHg (SD 14.0/18.0). Univariate correlations showed an increase in BP was positively correlated with cognitive scores. Increasing systolic (B0.35 CI 0.11, 0.6 p<0.01) and mean arterial BP (B0.72 CI 0.33, 1.12 p<0.01) were predictive of improved Digit-Symbol Substitution test after correcting for age, while increasing systolic (B0.52 CI 0.16, 0.89 p<0.01) and mean arterial BP (B0.77 CI 0.15, 1.4 p=0.02) was predictive for improved Test of Every Day Attention (Map 1<sup>st</sup> min). Although diastolic BP was associated with MMSE (p=0.01), this was not significant when corrected for IQ.

**Conclusion:** Our results show that in patients with CVD an increase in BP was associated with better scores on tests of global cognition, attention and speed of processing. This raises the possibility that elderly people with CKD and cardiovascular disease may be vulnerable to cognitive impairment with aggressive lowering of blood pressure.

## P5.27

**PULSE PRESSURE IS A STRONG AND INDEPENDENT PREDICTOR OF INCIDENT ATRIAL FIBRILLATION IN TYPE 2 DIABETIC PATIENTS**

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**Introduction:** Atrial fibrillation (AF) is the most common cause of chronic arrhythmia in adults and is associated with an increased risk of mortality and stroke. Pulse pressure (PP), as a surrogate measure of aortic stiffness, is an important risk factor for incident AF in the general adult population. Currently, there is no information about the possible role of PP in the development of FA in people with type 2 diabetes mellitus (DM), who are at high risk of developing FA.

**Objective:** we examined whether PP is associated with the development of incident AF in type 2 DM.

**Methods:** we followed for a mean period of 6.4 years an outpatient cohort of 350 subjects with type 2 DM, who regularly attended our diabetes clinic during the years 2001-2002 and who were free from AF at baseline (age 63±10 years, 43% women). Plasma lipids, hemoglobin A1c, diabetes duration, body mass index, blood pressure, current use of medications and other risk factors for AF were measured. Electrocardiograms were performed annually.

**Results:** During the follow-up, 32 patients (9.4%) developed incident AF. Baseline clinical and biochemical characteristics of participants stratified by PP tertiles are presented in Table 1. In multivariable logistic regression analyses, PP but not systolic or mean blood pressure was independently associated with an increased risk of incident AF (adjusted-OR 1.64 for each SD increment [12.8mmHg]; 95% CI, 1.09-2.50; P: 0.019).

**Conclusions:** PP is a strong and independent predictor of new-onset AF in patients with type 2 DM.

**Table 1** Baseline characteristics of the sample stratified by tertiles of pulse pressure.

| Variables                            | I tertile<br>PP <53<br>(n=116) | II tertile<br>PP 53-60<br>(n=126) | III tertile<br>PP ≥60<br>(n=108) | P value<br>for trend |
|--------------------------------------|--------------------------------|-----------------------------------|----------------------------------|----------------------|
| Gender (M/F)                         | 67/59                          | 69/47                             | 61/47                            | 0.61                 |
| Age (years)                          | 59 ± 10                        | 63 ± 10                           | 69 ± 9                           | <0.0001              |
| Body mass index (kg/m <sup>2</sup> ) | 29.8 ± 4                       | 30.3 ± 5                          | 29.2 ± 5                         | 0.22                 |
| Diabetes duration (years)            | 5.5 ± 1.1                      | 5.9 ± 1.0                         | 6.3 ± 0.9                        | <0.0001              |
| Systolic pressure (mmHg)             | 125 ± 10                       | 141 ± 8                           | 156 ± 9                          | <0.0001              |
| Diastolic pressure (mmHg)            | 80 ± 8                         | 81 ± 8                            | 81 ± 7                           | 0.33                 |
| Mean pressure (mmHg)                 | 95 ± 8                         | 101 ± 8                           | 106 ± 7                          | <0.0001              |
| Hemoglobin A1c (%)                   | 7.6 ± 1.7                      | 7.9 ± 1.9                         | 7.7 ± 1.5                        | 0.21                 |
| Total cholesterol (mg/dl)            | 205 ± 37                       | 202 ± 41                          | 204 ± 38                         | 0.79                 |
| Creatinine (mg/dl)                   | 0.86 ± 0.2                     | 0.89 ± 0.3                        | 0.87 ± 0.2                       | 0.54                 |
| Current smokers (n)                  | 32                             | 28                                | 22                               | 0.058                |
| Obesity (n)                          | 52                             | 59                                | 40                               | 0.29                 |
| Hypertension (n)                     | 61                             | 85                                | 93                               | <0.0001              |
| Chronic kidney disease (n)           | 21                             | 36                                | 30                               | 0.11                 |
| Coronary heart disease (n)           | 10                             | 13                                | 14                               | 0.57                 |
| Left ventricular hypertrophy (n)     | 12                             | 19                                | 35                               | <0.0001              |
| Chronic heart failure (n)            | 1                              | 3                                 | 4                                | 0.33                 |
| Valvular disease (n)                 | 1                              | 2                                 | 1                                | 0.85                 |
| Incident atrial fibrillation (n)     | 3                              | 12                                | 17                               | <0.001               |

Cohort size, n=350. Data are expressed as means ± SD or absolute frequencies. P values for trends were determined by means of one-way ANOVA and chi-squared test (for categorical variables).

## P5.28

**GESTATIONAL HYPERTENSION – AN OVERLOOKED INDICATOR FOR FUTURE CARDIOVASCULAR RISK**

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**Background:** Hypertension in pregnancy affects 3-8% of women in the UK, accounting for ~ 6 maternal deaths each year, foetal growth restriction, prematurity and still birth. Both gestational hypertension (GHT) and pre-eclampsia (PET) are associated with increased cardiovascular (CV) risk in later life. Commonly, research excludes GHT or fails to investigate it separately to PET. Our study explores the haemodynamic consequences in later life, of hypertension in pregnancy.

**Method:** Data from 545 women, aged > 40 years (mean age 62 years) were analysed. Subjects underwent detailed anthropometric and haemodynamic measurement including blood pressure, aortic stiffness, wave reflections (SphygmoCor) and cardiac output (InnoCor) and completed a questionnaire regarding pregnancy. Subjects were categorised as Never pregnant (NEP), Normotensive in pregnancy (NOP), GHT and PET.

**Findings:** There was a positive association between hypertension in pregnancy and seated brachial diastolic blood pressure (SBDP; P=0.001), seated central systolic and diastolic BP (P= 0.015, P=0.001) and peripheral vascular resistance (P=0.031). Seated systolic BP was 7±17mmHg and 9±23mmHg higher and DBP was 6±9mmHg and 3±10mmHg for the GHT and PET groups respectively compared to the NEP and NOP groups. There was no association between hypertension in pregnancy and arterial stiffness or wave reflections in later life.

**Conclusion:** Our data supports GHT being a distinct phenomenon impacting adversely on blood pressure and peripheral vascular resistance in later life. Further detailed research is required to elucidate discrete mechanisms contributing to altered haemodynamics and the CV risk profile in later life, associated specifically with GHT.

## P5.29

**PULSE TIMING DIFFERENTIAL AS A MEASURE OF ARTERIAL STIFFNESS**

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A simple measurement technique for the estimation of the dilation of the brachial artery has been developed from a comparison of measurements of

pulse timing in a raised arm and a control arm kept at heart level. The artery expands in the raised arm leading to a decrease in blood velocity. An estimate of the dilation of the brachial artery is obtained from the assumption that the flow in the raised arm is unchanged due to the position of the arm. The pulse timing difference measured at similar points in the two arms (index finger or wrist) is due to the dilation of the artery. The square of the radial dilation  $d$  is given by the length of the brachial artery divided by the product of the systolic blood velocity in the control arm times the observed pulse timing difference. Measurements were obtained by placing transducers on the index fingers of both hand and the lower leg of the subject. Measurements are recorded at a 1 kHz rate using a laptop computer. Initially, the subject places both hands at heart level. After a period of 1 minute, the right hand is raised at an angle of 45° and supported by a platform. Pulse timing measurements are computed using the two sensors on the hands and the pulse wave velocity is computed using the left hand and leg sensors. Simultaneous measurements of pulse wave velocity are inversely correlated with the pulse timing difference.

### P5.30 VASCULAR EXPLORATIONS OF PATIENTS WITH ERDHEIM CHESTER DISEASE

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**Objectives:** To study structural and functional alterations of arteries in patients with Erdheim-Chester disease, a rare acquired idiopathic histiocytosis characterized by a circumferential fibrosis of the aorta and its main branches.

**Methods :** Fifteen patients underwent peripheral arteries assessment with measurement of intima media thickness (EIM), carotid femoral pulse wave velocity (PWV) by Complior®, radial augmentation index (AI) by Sphygmocor® and OMRON HEM9001®, and ankle brachial index (ABI) by SCVL®. Blood pressure was assessed by 24h measurement.

**Results:** Our population consisted in 85% of men from 30 to 76 years old. There was 45% of treated and controlled hypertensive, 57% of former smokers and 14% of diabetics. One third was under interferon, 30% under corticosteroids and the rest were untreated. IMTs were all normals but a periarterial carotid fibrosis was noted in 28% who also had aortitis on PET scan. An augmentation of the global aortic stiffness (PWV) was present in 90% of the patients. According to the nomograms, the radial distensibility was altered in 30% of the patients, especially in the youngest and the carotid distensibility was normal in 90% of the patients. The mean difference between central blood pressure and brachial blood pressure was -18 mmHg and -23.5mmHg for those with aortitis. All ABI were normal.

**Conclusion:** Arterial explorations of Erdheim-Chester patients unravel a periarterial fibrosis in 28% of the patients but an increased aortic stiffness in 90%. The absence of carotid augmentation indexes abnormalities suggests that those alterations may not influence central blood pressure

### P5.31 RELATIONSHIP BETWEEN WAVE REFLECTION AND RENAL VASCULAR DAMAGE IN HYPERTENSIVE PATIENTS

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**Background:** Arterial stiffness reduces buffering capacity, exposing the microcirculation to increased pulsatility. Wave reflection could be protective by reducing pulsatility transmitted to low resistance vascular beds such as the brain or the kidney, as suggested by recent data in retinal circulation. Therefore we explored the relationship between wave reflections, arterial stiffness, and renal resistive index.

**Methods:** We searched our databases of hypertensive patients for subjects who underwent both measurement of arterial stiffness and renal arteries ultrasound. Augmentation index (AIx) and carotid-femoral pulse wave velocity (PWV) as measures of wave reflection and arterial stiffness, respectively, were recorded using the SphygmoCor system. Intraparenchymal renal resistive index (RI), a measure of vascular damage, was obtained in the interlobar arteries by Duplex ultrasound.

**Results:** Analysis was performed in 175 hypertensive patients (52.9±11.7 yrs), without renal artery stenosis or primary kidney disease. Mean RI was 0.630±0.065, PWV 8.41±1.74 m/s, AIx 26.7±11.5 %. RI was positively associated with AIx ( $r=0.31$ ,  $p<0.001$ ) and PWV ( $r=0.43$ ,  $p<0.001$ ). Neither

AIx nor PWV remained significant predictors of RI in a model including age, gender, body mass index, blood pressure, heart rate, glucose, cholesterol, glomerular filtration rate. Stratifying patients according to tertiles of AIx and PWV, RI was not different between low AIx / high PWV and high AIx / low PWV ( $0.633\pm 0.062$  vs  $0.632\pm 0.059$ ,  $p=ns$ ).

**Conclusions:** This cross sectional analysis failed to demonstrate an independent relationship between wave reflection and renal resistive index, suggesting that wave reflection could not have a beneficial effect in the renal circulation of hypertensive patients.

## P6 – Techniques and Mechanisms 1

### P6.01

#### THE METHOD OF DISTANCE MEASUREMENT AND TORSO LENGTH INFLUENCES THE RELATIONSHIP OF PULSE WAVE VELOCITY TO CARDIOVASCULAR MORTALITY

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**Background:** The method of estimating distance traveled by the pulse wave, used in the calculation of pulse wave velocity (PWV), is not standardized. Our objective was to assess whether different methods of distance measurement influenced the association of PWV to cardiovascular mortality in hemodialysis patients.

**Methods** 98 chronic hemodialysis patients had their PWV measured using three methods for distance estimation; PWV1: suprasternal notch-to-femoral site minus suprasternal notch-to-carotid site, PWV2: carotid-to-femoral site, PWV3: carotid-to-femoral site minus suprasternal notch-to-carotid site. Carotid-to-femoral distance was used to approximate torso length. Patients were followed for a median of 30 months and the association of PWV and cardiovascular mortality was assessed using survival analysis before and after stratification for torso length.

**Results:** The three methods resulted in significantly different PWV values. During follow up 50 patients died, 32 of cardiovascular causes. In log-rank tests only tertiles of PWV1 was significantly related to outcome ( $p$ -values 0.017, 0.257, 0.137, for PWV1, PWV2 and PWV3, respectively). In adjusted Cox proportional hazards regression only PWV1 was related to cardiovascular mortality. In stratified analysis, however, among patients with below median torso length all PWV values were related to outcome, while in patients with above median torso length none of the PWV methods resulted in significant relationship to outcome. **Conclusions** PWV calculated using suprasternal notch-to-femoral distance minus suprasternal notch-to-carotid distance provides the strongest relationship to cardiovascular mortality. Longer torso weakens the predictive value of PWV, possibly due to more tortuosity of the aorta hence more error introduced when using surface tape measurements.

### P6.02

#### IN-VIVO ASSESSMENT OF THE ACCURACY OF CAROTID STRAIN ESTIMATES DERIVED FROM ULTRASONIC WALL TRACKING

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**Background:** Ultrasonic wall tracking is a common tool in cardiovascular screening, where it is applied to assess arterial diameter distension waveforms. However, using multiple tracking points within the arterial wall and under the assumption of planar deformation, circumferential and radial strain can be obtained as  $\epsilon_{\theta\theta} = D/D$  and  $\epsilon_{rr} = \partial D/\partial D$ .

**Methods:** We investigated the accuracy of these arterial strain estimates, using 10 representative data sets of the Asklepios population study. Tracking was done using a scanline perpendicular to the common carotid artery, far enough from the bulbous and showing clear intima-media and media-adventitia transitions. We started tracking from a designated point on the media-adventitia transition and from there on every 100 micrometer towards the lumen.

**Results & Discussion:** Data revealed an S-shaped curve of  $\epsilon_{\theta\theta}$  throughout the wall for all 10 subjects (fig.1, solid line), which was different from  $D/D$  calculated from conservation of mass (dashed line:  $1/D^2$ -trend). Radial strain strongly varied from inner to outer wall, limiting its use as strain or compressibility measure. Using a multiphysics simulation incorporating