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P2.10: AMBULATORY ARTERIAL STIFFNESS INDEX IN TURNER SYNDROME: THE IMPACT OF SEX HORMONE REPLACEMENT

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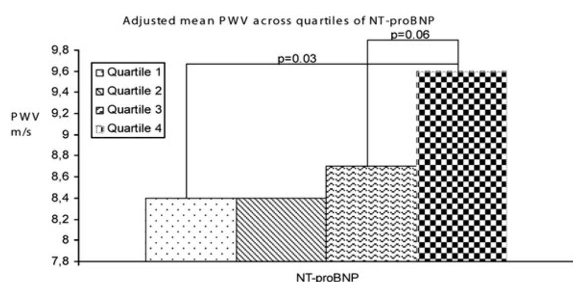

Conclusion: NT-proBNP is associated to levels of PWV in patients with RA.

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P2.07
INTERRELATIONSHIP BETWEEN AORTIC STIFFNESS AND PROTEINURIA IN CHRONIC KIDNEY DISEASE

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Aortic stiffness and proteinuria are cardiovascular risk factors. In several populations an association has been described between these factors. However, age is a strong determinant for both risk factors complicating the insight in dependencies. Therefore, we aimed to investigate whether dependencies between aortic stiffness and proteinuria exist in patients with chronic kidney disease (CKD) as in these patients renal disease is the leading cause for proteinuria.
In a cross-sectional setting 144 patients with severe to mild CKD (estimated Glomerular filtration rate (eGFR): >15 - ≤90 ml/min/1.73m^2 or bioptically proven renal disease) were investigated for aortic stiffness measured by carotid-femoral pulse wave velocity (C-F PWV) and proteinuria as determined by protein-creatinine ratio from morning spot urine. In stepwise linear regression analysis, C-F PWV predicted protein-creatinine ratio and *vice versa*. The diagnosis of proteinuria (≥ 200 mg protein/g creatinine) was an independent predictor of C-F PWV, whereas C-F PWV did not predict the diagnosis of proteinuria.
This study demonstrates that the extent of aortic stiffness and proteinuria predict each other in a cohort of CKD similar to other populations. However, if the diagnosis of proteinuria is used as variable only apparent proteinuria predicts aortic stiffness, but not *vice versa*. This suggests that aortic stiffness is not consistently predicting proteinuria in CKD patients.

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P2.08
PREMATURE VASCULAR AGEING IN CYSTIC FIBROSIS?

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Background: Cystic Fibrosis (CF) is the most common autosomal recessive condition affecting Caucasians. Improved survival paralleled with a high prevalence of risk factors (diabetes and systemic inflammation) suggest that cardiovascular disease may become an important co-morbidity in CF, yet currently cardiovascular risk profiling is lacking. We hypothesised that augmentation index (Aix), a marker of arterial stiffness, would be increased in CF.
Methods: We studied 50 (33 male) adults with stable CF, mean (range) age 28.0 (16-46) yrs and 26 age/gender/BMI matched controls. We measured heart rate adjusted Aix, aortic pulse wave velocity (PWV) (SphygmoCor), blood pressure, spirometry (FEV_1 & FVC), glucose tolerance status, serum CRP and lipids.
Results: Height, MAP and PWV were similar however Aix was increased in patients and the difference to controls persisted following adjustment for gender, age, MAP and height. Aix was greatest in diabetic patients (n=13), 13.1 (4.3)%, but the non-diabetic sub-group still had greater Aix: 6.9(12.3)% than controls (ANOVA, p<0.05). CRP was increased in patients (p<0.005). In patients, Aix was inversely related to FEV_1 (r=-0.43) and FVC (r=-0.54), and directly with age (r=0.54), all p<0.01 and $\log_{10}$CRP (r=0.33, p<0.05).

	Controls	Patients
Total cholesterol (mmol/L)	4.4 (0.7)	3.7 (0.7)*
Peripheral MAP (mmHg)	91.7 (8.6)	94.1 (8.3)
Aix (%)	-1.8 (13.1)	8.5 (11.1)*
Aortic PWV (m/s)	6.1 (0.8)	6.4 (1.5)

Mean(SD).*P<0.05.
Conclusions: Aix was increased in adults with CF, independent of glycaemic status. This apparent vascular ageing may have important implications for surveillance and cardiovascular risk stratification of these patients.

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P2.09
INCREASED AUGMENTATION INDEX IN POST-COARCTECTOMY PATIENTS WITHOUT SIGNIFICANT RESTENOSIS

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Objectives: Despite successful surgical repair, post-coarctectomy patients suffer from early onset cardiovascular disease (CVD). Enhanced pressure wave reflections and increased arterial stiffness have been proposed to explain the increased risk of CVD. We therefore assessed arterial wave reflections and arterial stiffness in post-coarctectomy patients and matched controls.
Methods: We examined 10 post-coarctectomy patients aged 29 ±7 yrs, 7 males, without significant restenosis and without antihypertensive treatment. Ten healthy age and gender matched subjects served as controls (age 26 ±2 yrs, 6 males). Radial artery waveforms were recorded non-invasively by applanation tonometry using the Sphygmocor device. Aortic augmentation index (AIx) was calculated using a validated transfer function and corrected for heart rate. Pulse wave velocity (PWV) was measured between carotid and femoral arteries. All measurements were performed three times on the right and left side and were averaged.
Results: Post-coarctectomy patients had a higher right-sided (11.4±16.8 vs -12.4±8.8, p <0.01) and left-sided (22.5±7.9 vs -10.5±10.4, p <0.01) AIx compared to healthy controls. Carotid-femoral PWV showed no difference between patients and controls (right 5.7±0.9 vs 5.8±0.9, p =0.70; left 5.5±0.7 vs 5.7±0.8, p 0=.44).
Conclusions: Augmentation index is increased in post-coarctectomy patients. The finding of normal arterial stiffness combined with a distinct right to left difference in augmentation suggests that the enhanced wave reflection likely arises from early pulse wave reflection on the reconstructed aorta despite the absence of significant restenosis.

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P2.10
AMBULATORY ARTERIAL STIFFNESS INDEX IN TURNER SYNDROME: THE IMPACT OF SEX HORMONE REPLACEMENT

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Objective: Women with Turner syndrome (TS) face increased morbidity and mortality from congenital and acquired cardiovascular (CV) diseases. Traditional indices of unfavourable CV risk are increased in TS. However, the single most common syndrome-related feature remains estrogen deficiency. The present trial therefore aimed to investigate total CV risk in TS as expressed by ambulatory arterial stiffness index (AASI) and the influence of female sex hormone replacement therapy (HRT).
Design and Methods: Randomly recruited women with TS receiving HRT (n=26) were examined following wash-out and during 6 months of HRT in the form of cyclical estrogen and progestin. Age-matched normally menstruating female controls (n=24) were examined once. Parameters of effect

were 24-hour ambulatory blood pressures, AASI in addition to various metabolic and anthropometric indices of CV risk.
Results: Besides being takykardic TS women displayed relative systolic and diastolic hypertension with diminished circadian variation, while pulse pressures were similar. HRT in TS brought on a significant fall in diastolic pressures and borderline significant reduction in diurnal pulse variability. AASI was significantly elevated in TS prior to HRT when compared to controls (T_b vs. C: 0.36 (0.02) vs. 0.26 (0.03), P = 0.01) and unaffected by HRT. Individual status, i.e. being TS or not, was the major explanatory variable to AASI followed by age, insulin sensitivity and the degree of diurnal pulse variability.
Conclusion: AASI was elevated in TS following HRT wash-out which possibly indicated a syndrome-associated elevated CV risk with no direct impact of HRT during 6 months.

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P2.11
WHEN DOES THE REFLECTED WAVE ARRIVE — SYSTOLE OR DIASTOLE? A SYSTEMATIC LITERATURE REVIEW

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Background: The arterial waveform in young adults is ascribed to the combination of a forward wave from the ventricle and a reflection arriving at the aortic root in diastole. With ageing, the reflected wave is proposed to arrive earlier, augmenting systolic pressure and increasing afterload. This view has been recently disputed[1] and it is suggested that pressure in diastole is attributable to an arterial 'reservoir'. We undertook a systematic review to ascertain whether reflected waves arrive in diastole.
Methods and Results: We searched the literature using PubMed and Cochrane. We identified 67 studies describing 139 cohorts totalling 13,957 subjects (mean age 53 years, range 4-91). The arrival time of waves was calculated from the time of the shoulder on the pressure waveform and the end of systole was estimated by the time of the dicrotic notch.
The arrival time of the reflected wave was 135.5 (95% CI 131.7-139.4) ms. In comparison, the end of systole occurred at 328.1 (314.0-342.2) ms. All reflection times were in the first two-thirds of systole. The peaks of the reflected pressure arrived at an average of 217.6 (207.8-227.4) ms, well within systole, across the age spectrum.
Conclusion: The mean time of arrival of the reflected wave is in systole even in the youngest subjects. These observations do not support the view that reflected waves typically arrive in diastole.

1. Wang JJ *et al*. Time-domain representation of ventricular-arterial coupling as a windkessel and wave system. *Am J Physiol Heart Circ Physiol* 2003;284(4):H1358-H1368.

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P2.12
INFLUENCE OF THE CENTRAL TO PERIPHERAL ARTERIAL STIFFNESS GRADIENT ON TIMING AND AMPLITUDE OF WAVE REFLECTIONS

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In younger individuals peripheral muscular arteries are stiffer and pulse wave velocity (PWV_m) greater than central elastic artery stiffness and PWV_e ($PWV_m > PWV_e$). The marked increase in aortic stiffness with age, with little change in peripheral stiffness, results in a reversal of the arterial stiffness gradient ($PWV_e > PWV_m$). It has been hypothesized[1] that this may reduce wave reflection amplitude and augmentation index (AI_a) due to movement of the major reflection site further from the heart. To test this hypothesis we investigated whether a reverse stiffness gradient ($PWV_e > PWV_m$) is associated with a reduced AI_a and an increased reflection site distance.
Studies were performed in subjects aged>50 years who were free of medication. Following 10mins supine rest, blood pressure, pulse wave analysis and carotid-femoral (PWV_e) and femoral-dorsalis-pedis (PWV_m) PWVs were measured. Distance to the major reflection site was calculated from PWV_e and reflected wave travel time (Tr/2)[2].
PWV_e and PWV_m were 7.8±1.0m/s and 9.7±1.0m/s, respectively, in subjects with a positive stiffness gradient ($PWV_m > PWV_e$) and 10.8±2.1m/s and 9.0±1.6m/s in subjects with a reverse stiffness gradient. Central pulse pressure and augmentation pressure were higher in subjects with a reverse stiffness gradient (38 ±18vs.48±9mmHg and 12±6vs.14±5mmHg,P<0.05), as was AI_a corrected for heart rate (23±8vs.27±6%.P<0.05) and reflection site distance (56±10vs.76±15cm.P<0.01). Time to reflection did not differ between groups (71.4±6.4vs.70.5±5.0ms).
Reversal of the stiffness gradient ($PWV_e > PWV_m$) is associated with increased central pulse pressure, reflected wave amplitude and AI_a and a paradoxical increase in reflection site distance.

1.Mitchell GF et al. Hypertension. 2004;43:1239-45.
2.Murgo JP et al. Circulation. 1980;62:105-16.

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P2.13
THE FORM FACTOR (FF) OF PRESSURE WAVEFORMS IN A YOUNG POPULATION: DIFFERENCE BETWEEN MEN AND WOMEN

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Background: Bos et al stated that the well known one-third rule for the calculation of mean arterial pressure (MAP) from diastolic (DBP) and pulse pressure (PP) underestimates the MAP. We calculated the percentage (form factor, FF) of the PP to be added to the DBP to assess MAP at the brachial artery in a population sample of young adults and compared middle-aged adults.
Methods: Brachial artery tonometer measurements were performed in 95 healthy subjects (18 men, 77 women; age 19-35 yr). The pressure waveforms were calibrated using sphygmomanometer SBP and DBP. MAP was assessed as the numerical average of this pressure wave curve.
Results: The table shows the FF as mean percentage ± SD. The FF at the brachial artery was 2.1±0.9 % higher in women compared to men (p<0.02).

FF % (SD)	Men	Women	Total
Age 19-35 yrs	37.2 (3.1)	39.2 (3.4)	38.9 (3.4)

FF based on published data from the Asklepios study (age 35-55) *

Age 35-55 yrs	41.3 (3.0)	43.7 (3.1)	42.4 (3.3)

* D. Mahieu et al. Validity of the One-Third Rule to Calculate Mean Arterial Pressure. Artery Research 2007;1(2):71.
Conclusions: The present study confirms the findings from the Asklepios Study that the form FF to calculate MAP is higher in women than in men. This study also suggests that the FF is age dependent being lower in the age range of 19-35 compared to the range 35-55. Further research is needed to define the influence of age on the form factor to calculate MAP.

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P2.14
INFLUENCE OF CALIBRATION OF PERIPHERAL PRESSURE ON THE ESTIMATION OF CENTRAL SYSTOLIC BLOOD PRESSURE

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Objective: We compared the accuracy with which central systolic aortic pressure (cSBP) can be estimated from the late systolic shoulder of the digital artery pressure waveform (SBP_2) when the digital waveform is calibrated using a validated non-invasive oscillometric device and when it is calibrated using mean (MAP) and diastolic (DBP) central blood pressure measurement.
Design: Subjects (n = 25) were studied at the time of cardiac catheterisation for diagnostic angiography and/or angioplasty. The study was approved by the local research ethics committee and all subjects gave written informed consent.
Methods: cSBP was measured with a Millar SPC-454D (Millar instruments Houston, Texas) catheter with the tip of the catheter in the proximal aortic root. Peripheral pressure waveforms were acquired from the digital artery using a Finometer (Finapres medical systems, Netherlands) and were calibrated from aortic mean and diastolic pressures and from systolic and diastolic pressures measured using an Omron 750IT (Omron Healthcare). Measurements of digital artery and aortic pressures were obtained at baseline and after nitroglycerin (NTG, sublingual spray 500 μg).