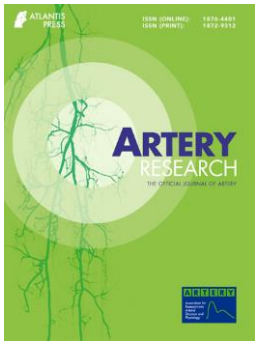

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6.3: DETERMINING EARLY CARDIOVASCULAR RISK PROFILES IN PAEDIATRIC RHEUMATIC DISEASE

T.J. Bradley, P.N. Tyrell, L. Ng, C. Slorach, J. Beyene, R. Schneider, B.M. Feldman, E.D. Silverman

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Oral Presentation Abstracts

6.1
LOW-GRADE INFLAMMATION AND ENDOTHELIAL DYSFUNCTION PRECEDE THE INCREASE IN PULSE PRESSURE IN TYPE 1 DIABETES:A 20-YEAR LONGITUDINAL STUDY

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Purpose: To investigate, longitudinally, whether increases in markers of inflammation (CRP, sICAM-1) and endothelial dysfunction (sICAM-1, sVCAM-1) are associated with and *precede* the increase in pulse pressure (PP) in individuals with type-1 diabetes (DM1).
Methods: Inception cohort of 277 DM1 patients (114 women; mean age at diagnosis: 27.5 ± 13.8 yrs) who were consecutively admitted, upon diagnosis, between Sep'79-Aug'84 to an outpatient diabetic clinic (Gentofte, Denmark). Throughout a follow-up period of >20 yrs, patients' PP, other risk factors, and CRP, sICAM-1 and sVCAM-1 were measured repeatedly (at 3-4 months intervals). Associations were analysed with generalized estimating equations (GEEs) and adjusted for sex, age at diagnosis, smoking, anti-hypertensive treatment and MAP.
Results: PP increased by 0.53 mmHg/yr, CRP by 0.033 mg/L/yr, sICAM-1 by 1.8 ng/ml/yr and sVCAM-1 by 1.8 ng/ml/yr over the 20-yr longitudinal period (all $p < 0.001$). Higher levels of ln-CRP, sICAM-1 and sVCAM-1 were all significantly associated with higher levels of PP: 0.53 mmHg (95%CI: 0.05-1.00), 1.09 mmHg (0.53-1.66) and 0.94 mmHg (0.40-1.48) per SD increase in marker, respectively. In addition, levels of sICAM-1 and sVCAM-1, but not ln-CRP, at any time point, were also associated with increases in PP occurring in the 2 yrs thereafter: 0.56 mmHg (0.18-0.94), 0.53 mmHg (0.17-0.90) and -0.01 mmHg (-0.38-0.35) per SD increase in marker, respectively. Adjustments for other risk factors did not change these associations.
Conclusion: Life-course increases in low-grade inflammation/endothelial dysfunction are associated with and *precede* increases in PP, supporting the view of their involvement in the development of premature arterial stiffening in diabetes.

6.2
IMPACT OF CHANGES IN SMOKING BEHAVIOUR BETWEEN ADOLESCENCE AND YOUNG ADULTHOOD ON ARTERIAL STIFFNESS IN YOUNG ADULTS. THE NORTHERN IRELAND YOUNG HEARTS PROJECT

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Purpose: to investigate 1) the extent to which young adults who started smoking during adolescence and persisted doing so during young adulthood ('persistent smokers'—PS), and those who started smoking in young adulthood only ('starters'—SS) had greater aorto-iliac PWV than never smokers (NS); and 2) whether any such differences could be explained by greater levels of inflammation and/or endothelial dysfunction (ED) associated with smoking.
Methods: We studied 408 young adults *(age 22.6 ± 1.6 yr*; 209 women) from the NIYHP in whom PWV and plasma levels of inflammation (i.e. CRP and fibrinogen) and ED (i.e. vWF and tPA-antigen) were measured during young adulthood, and smoking status was assessed during adolescence (age 15) and young adulthood. Data were analysed using linear regression with adjustments for potential confounders and/or mediators.
Results: After adjustment for age, sex, height and MAP, and other lifestyle risk factors, PS, but not SS, had higher levels of PWV compared with NS [+0.20 m/s (95%CI: 0.07; 0.33), $p = 0.003$, and -0.02 m/s (-0.13; 0.08), $p = 0.667$, respectively]. Further adjustments for inflammation and ED did not materially attenuate the differences between PS and NS [to +0.19 m/s (0.06; 0.33), $p = 0.006$], despite the fact that PS had higher levels of inflammation [+0.29 SD (0.05; 0.52), $p = 0.017$] and ED [+0.20 SD (0.01; 0.39), $p = 0.037$].
Conclusion: Persistent smoking between adolescence and young adulthood adversely impacts on arterial stiffness, as well as on levels of inflammation and endothelial-dysfunction. However, these pathophysiological mechanisms did not explain the increased arterial stiffness related to persistent smoking.

6.3
DETERMINING EARLY CARDIOVASCULAR RISK PROFILES IN PAEDIATRIC RHEUMATIC DISEASE

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Objectives: Increased cardiovascular risk in adults with systemic lupus erythematosus (SLE) and rheumatoid arthritis, not explained by exposure to traditional factors alone, have prompted investigation into the role of chronic inflammation. This study aimed to determine early cardiovascular risk profiles and their correlates in children with SLE, systemic juvenile inflammatory arthritis (SJIA) and juvenile dermatomyositis (JDM).
Methods: Disease activity and drug therapy were recorded, fasting lipid, glycemic and inflammatory profiles performed, and vascular testing including carotid intima-media thickness (CIMT), flow-mediated dilatation (FMD) and pulse wave velocity (PWV). Data within groups were compared to normal controls and between groups using parametric methods.
Results: Of 137 subjects, SLE ($n = 88$) were older and more predominantly female than SJIA ($n = 21$) and JDM ($n = 28$) age 15.4 ± 2.5 vs. 13.9 ± 2.4 and 13.9 ± 2.3 years, and female 83% vs. 57% and 50%, respectively. At testing, most had relatively healthy BMI, normal lipid and glycemic profiles and over mean follow-up 3.1 ± 3.0 years, 91% received corticosteroids (mean cumulative dose/kg 0.24 ± 0.30 g). Higher ESR, but lower complement C3 and C4 and albumin were found in SLE vs. SJIA and JDM, while CRP was lower in SLE vs. SJIA. Lower CIMT in SJIA ($p < 0.05$) and higher PWV in SLE and JDM (both $p < 0.001$) were found vs. controls. No between group differences for CIMT, FMD or PWV were found, even when adjusting for sex, age, BMI, disease duration or cumulative corticosteroid dose.

Conclusions: Early cardiovascular risk profiles vary in paediatric rheumatic diseases. Disease-specific inflammatory factors likely modify these cardiovascular risk profiles and warrant further investigation.

6.4
LONGITUDINAL FOLLOW-UP OF ARTERIAL DISTENSIBILITY IN EARLY CHILDHOOD: ROLES OF BIRTH WEIGHT, GROWTH, BLOOD PRESSURE AND EARLIER (AORTIC) 'STIFFNESS'

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Background: Although blood pressure (BP) 'tracks' from early life in humans, little is known of how arterial stiffness develops over time in early childhood.
Methods: UK born European (n = 208) and South Asian (SA, n = 99) origin infants had standardised measures of anthropometry, BP (Dynamap Critikon) and pulse wave velocity (aPWV — Doppler method, aortic arch to bifurcation) taken within 72 h of birth and at any of 3-6 months, 1,2,3 and 4 years later. Data were analysed using mixed cross-sectional/longitudinal (MXLS) and fully longitudinal (FL) regression models in STATA.
Results: SA neonates averaged 330 g lighter and 1.2 cm shorter at birth than Europeans. After increasing between 0-3 months, neither mean (95%CI) aPWV (6.1 (5.7-6.5) m/sec) nor systolic or diastolic BPs (±86/ 45 mmHg) changed greatly from 1-4 years. However, in MXLS, aPWV was related to weight ($\beta = 0.85$ $p < 0.001$), subscapular skinfold ($\beta = 0.21$, $p < 0.001$), systolic ($\beta = 0.02$, $p = 0.04$) or diastolic ($\beta = -0.26$, $p = 0.03$) BP, weakly to height ($p = 0.07$) but not to age, gender, ethnicity, pulse pressure nor heart rate.
In FL models, aPWV at 3 years (n = 77) and 4 years (n = 59), was not determined by BPs, birth weight, weight change, skinfold, length nor prior aPWV readings.
Conclusion: These first longitudinal data in early childhood suggest that previous data, even on BP, ignoring genuine within-person change or *lack of* change, may be confounded. While weight and central fat (skinfold) affect overall MXLS results, early arterial distensibility & BPs appear not to alter much from 3 months to 4 years.

6.5
THE EPICURE STUDY: BLOOD PRESSURE AND ARTERIAL STIFFNESS IN RELATION TO BIRTH BEFORE 26 WEEKS OF GESTATION

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Background: Antenatal and postnatal growth are associated with increased arterial stiffness and cardiovascular risk (e.g. myocardial infarction and stroke) in adults born at term.
Aim: We investigated cuff blood pressure (BP) and arterial waveforms in 70 extremely preterm (EP) children and in 91 age and sex matched term-born classmates.
Methods: Arterial waveforms were evaluated by carotid and femoral applanation tonometry using the SphygmoCor device (Atcor™) by trained researchers blind to EP status. BP was measured using an automated Omron BP monitor. Data quality was assessed according to preset criteria and questions of pulse waveform quality jointly resolved by JF and an independent assessor (CM).
Results: There were no differences in cuff systolic or diastolic BP, mean BP or derived central BP in EP children compared to controls. However, EP children had lower systolic and higher diastolic BP after correcting for height differences. In contrast EP children had higher augmentation indices (AIx) than classmates; this remained significant after correcting for heart rate, height and mean BP.

	EP children Mean (sd)	Controls Mean (sd)	Difference of means (95%CI)
Augmentation index %	7.5(9.6)	2.1(8.5)	5.3 (2.5;8.1)***
Pulse Wave Velocity m/s	4.5(0.5)	4.7(0.9)	0.2 (0.1-0.4)
Systolic BP mmHg	108.6(10.3)	109.3(9.8)	0.98(0.52;1.42)***†
Diastolic BP mmHg	65.3(7.5)	62.5(7.2)	0.12(0.46;0.19)**†

† Difference after correcting for height; **p = .001; ***p<.001

Conclusion: This first report of increased augmentation index in EP children raises the possibility of future increased cardiovascular risk, not indicated from examination of peripheral blood pressure.

6.6
WAIST CIRCUMFERENCE IS A BETTER PREDICTOR OF SUBCLINICAL ATHEROSCLEROSIS THAN ADIPONECTIN LEVEL

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Objective: Waist circumference is clinical marker of obesity and a well-established risk factor for cardiovascular disease. Adiponectin, an adipocyte-derived hormone and new biomarker of obesity, has recently been proposed to be the missing link between obesity and increased cardiovascular risk. We evaluated waist circumference and adiponectin level in a middle-aged population-based cohort to determine which marker of obesity was the best predictor of subclinical atherosclerosis.
Methods and Results: Seven non-invasive measurements of atherosclerosis(-NIMA), as surrogate markers of subclinical atherosclerosis, were determined in 1517 participants of the Nijmegen Biomedical Study, aged 50-70 years who were drawn from the Dutch community.
Both men and women with a high waist(M > 104 cm;F > 95 cm) showed deteriorated outcomes of NIMA as reflected by increased pulse wave velocity(PWV)(M:+12.6%;F:+13.1%) and thicker intima-media thickness (IMT)(M:+9.0%;F:+6.6%) and in women an increased plaque thickness(+22.1%). However, participants with a low adiponectin level(M < 2.2 mg/L;F< 3.5 mg/L) showed no changes in the outcomes of NIMA; in both sexes only after adjustment for age a decreased ankle-brachial index after exercise(M:-9%;F:-3.5%) and an increased IMT(M:3.7%;F:3.6%) and in women an increased PWV(+6.8%) was observed. Interaction between the effect of waist and adiponectin on NIMA was found only in women.
Conclusions: Waist circumference was a better predictor of subclinical atherosclerosis than adiponectin level in our large population-based cohort. Measurement of waist circumference in clinical practice is a valuable tool in cardiovascular risk profiling, but our data does not support the measurement of adiponectin level.