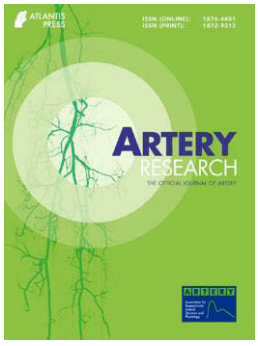

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2.8: RELATIONSHIPS BETWEEN ADIPOSITY AND LEFT VENTRICULAR FUNCTION IN ADOLESCENTS: MEDIATION BY BLOOD PRESSURE AND OTHER CARDIOVASCULAR MEASURES

Hannah Taylor, Alun D. Hughes, Abigail Fraser, Laura Howe, George Davey Smith, Debbie Lawlor, Nishi Chaturvedi, Chloe Park

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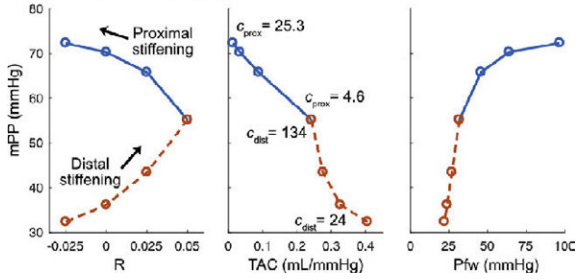
keeping average wave speed in all terminal vessels constant ("proximal-stiffening", see Figure). An elastance heart model was applied at the inlet and simulations were performed with a one-dimensional flow solver (2).
Results: Proximal-stiffening and distal-stiffening had opposing effects on R but the same effects on mPP, whereas mPP increased monotonically with decreasing TAC and increasing Pfw in both settings (Figure).
Conclusion: Wave reflection per se does not provide protection from high mPP since greater reflection also entails greater transmitted pressure. Although a decreased R may accompany proximal arterial stiffening, the likely mechanism of increased mPP with aging is decreased TAC and greater Pfw.

Figure. Reflection coefficient, R (at every junction), TAC and Pfw vs mPP with proximal and distal stiffening. Arrows indicate effect of stiffening. c_{prox} and c_{dist} are wave speeds (m/s) in the proximal inlet segment and distal terminals (mean).



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2.6
FEASIBILITY OF AORTIC WAVE INTENSITY ANALYSIS FROM SEQUENTIALLY ACQUIRED CARDIAC MRI AND NON-INVASIVE CENTRAL BLOOD PRESSURE

Anish Bhuva [1,2], Niro Nadarajan [3], Andrew D'Silva [4], Camilla Torlasco [5], Redha Boubertakh [2], Siana Jones [3], Paul Scully [3,2], Rachel Bastiaenen [4], Guy Lloyd [2], Sanjay Sharma [4], James Moon [3,2], Kim Parker [6], Charlotte Manisty [3,2], Alun Hughes [3,7]
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Background: Wave intensity analysis (WIA) in the aorta offers important clinical and mechanistic insights but is difficult non-invasively. We performed WIA by combining high temporal resolution cardiovascular magnetic resonance (CMR) flow velocity and non-invasive central blood pressure (BP) waveform data.
Method: 206 healthy volunteers (36 $\pm$ 11 years, 47% male) underwent sequential phase contrast CMR (Siemens Aera 1.5T, 1.97 x 1.77 mm^2, $\sim$9 ms temporal resolution) and supra-systolic oscillometric central BP (Uscom Ltd BP+) measurement. Velocity (U) and central pressure (P) waveforms (200 Hz) were aligned using the wave foot, and local wave speed was calculated both from the P-U slope during early systole (c) and the sum of squares method (cSS) (Figure 1), and compared with CMR aortic arch pulse wave velocity (PWV) by transit time.
Results: The peak intensity of the initial compression wave (dI+1), backward compression wave (dI-) and protodiastolic decompression wave (dI + 2) were 69.5 $\pm$ 28, -6.6 $\pm$ 4.2 and 6.2 $\pm$ 2.5 W/m^2 respectively. PWV correlated with c or cSS (r = 0.60, and 0.68 respectively; bias -1.3 [limits of agreement: -3.8 to 1.2 m/s], and bias -0.64 [limits of agreement: -3.0 to 1.7 m/s] respectively), Figure 1.
Conclusion: Wave intensity patterns and values are similar to those measured using invasive methods. Local wave speed showed good agreement with PWV. CMR and central blood pressure provides a novel non-invasive technique for performing wave intensity analysis and is feasible for large scale studies.

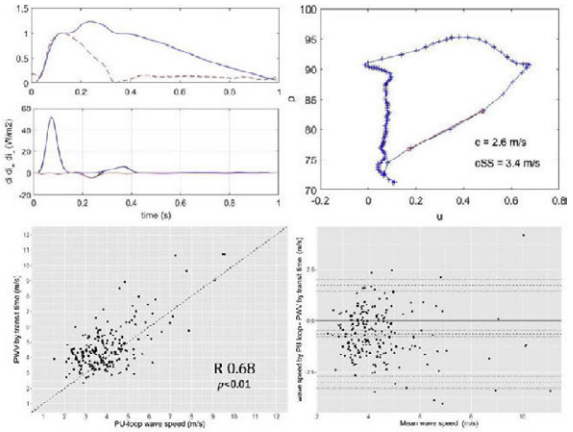

Figure 1. Calculation of wave speed from a pressure – velocity (P-U) loop and comparison with pulse wave velocity by transit time. Top left: alignment of scaled pressure (blue) and velocity (red) waveforms and example of wave intensity analysis showing initial compression (dI+1), backward compression (dI-) and protodiastolic decompression (dI+2) waves. Top right: P-U loop showing wave speed measurement in early systole (c); and using sum of squares (cSS). Bottom left and Bottom right: Correlation and Bland- Altman analysis of cSS and PWV from phase-contrast MRI showing good correlation and slight underestimation.

2.7
FITNESS MODIFIES THE ASSOCIATION BETWEEN EXERCISE BLOOD PRESSURE AND LEFT-VENTRICULAR MASS IN ADOLESCENCE

Zhengzheng Huang [1], Ricardo Fonseca [2], James Sharman [2], Nish Chaturvedi [3], George Smith [4], Deborah Lawlor [4], Laura Howe [4], Chloe Park [3], Alun Hughes [3], Martin Schultz [2], Martin Schultz [2]
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Objective: Exaggerated exercise blood pressure (BP) is associated with higher left-ventricular mass index (LVMI). Paradoxically, exercise BP and LVMI may be higher with greater fitness, but underlying factors are poorly understood. This study aimed to determine the influence of fitness on exercise BP and its relationship with LVMI in adolescents.
Methods: 4835 adolescents from the Avon Longitudinal Study of Parents and Children, aged 15.4(0.3) years, 49% male completed a submaximal cycle test. Exercise BP was measured immediately on test cessation and fitness calculated as physical work capacity 170 adjusted for lean body-mass. LVMI (n = 1589), cardiac output (CO, n = 1628) and total peripheral resistance (TPR, n = 1628) were measured by echocardiography 2.4 (0.4) years later.
Results: Each unit of fitness was associated with a 6.46 mmHg increase (95% CI: 5.83, 7.09) in exercise systolic BP. Exercise systolic BP increased step-wise by third of fitness (difference 6.06 mmHg, 95% CI:4.99, 7.13 first vs. middle; 11.13 mmHg, 10.05, 12.20 middle vs. highest). Each 5 mmHg increase in exercise systolic BP was associated with 0.25 g/m^2. 7 (0.16—0.35) greater LVMI, attenuated with adjustment for fitness. There was evidence of an interaction between fitness and exercise BP on LVMI, more-marked in the middle fitness third (difference -0.27g/m2.7, -0.51,0.04 vs. first third), but similar in lowest and highest fitness thirds. CO increased (difference 0.06 L/min, -0.05,0.17; 0.23 L/min, 0.12,0.34), TPR decreased (difference -0.13AU, -0.84,0.59; -1.08AU, -0.1.80,-0.35 with fitness.
Conclusion: Fitness may modify associations between exercise BP and LVMI in adolescence. Higher CO, but lower TPR suggests a physiological exercise BP-LVMI relationship with higher fitness, rather than pathological elevations in exercise BP and LVMI.

2.8
RELATIONSHIPS BETWEEN ADIPOSITY AND LEFT VENTRICULAR FUNCTION IN ADOLESCENTS: MEDIATION BY BLOOD PRESSURE AND OTHER CARDIOVASCULAR MEASURES

Hannah Taylor [1], Alun D. Hughes [2,3], Abigail Fraser [4], Laura Howe [4], George Davey Smith [4], Debbie Lawlor [4], Nishi Chaturvedi [3,2], Chloe Park [2]
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Introduction: Increased adiposity is associated with poorer left ventricular (LV) function but the mediating role of blood pressure (BP) and other cardiovascular measures is unknown. We investigated the roles of potential mediators in adolescents in a UK birth cohort, the Avon Longitudinal Study of Parents and Children.
Methods: Fat and lean mass were assessed by dual energy X-ray absorptiometry (DXA) in 2,068 individuals (age 17.7(SD 0.32) years; 45% male; weight 67(SD 13) kg). BP was measured and echocardiography performed. Tissue Doppler systolic (s'), early diastolic longitudinal function (e') and transmitral E/A were used as measures of LV systolic and diastolic function respectively. Mediation was estimated using structural equation modelling; height, sex, socioeconomic position, lean mass and smoking were included as potential confounders in all models.
Results: Table 1 shows the total and direct (total − indirect (mediated)) effects (standardized β) for each potential mediator, alongside %mediation. No convincing associations were found between fat mass and s' or e'.
Conclusions: MAP, HR and EDV, an indicator of preload, are important mediators of the effect of adiposity on diastolic function in adolescence, while TPR appears to account for none of the effect. Absence of mediation by PP, in combination with the mediation by TAC, suggests that stroke volume contributes some mediative effect. These findings emphasise the importance of adiposity and risk factor control in adolescence.

Table 1. Mediation of the association between fat mass and E/A

Mediator	Direct effect (standardized β)	Total effect (standardized β)	% mediation
None	-0.15 *(95%CI -0.20, -0.10)*		
Mean arterial pressure (MAP)	-0.11	-0.14	21
Pulse pressure (PP)	-0.13	-0.13	0
Heart rate (HR)	-0.11	-0.14	21
Total arterial elastance (TAE)	-0.15	-0.14	-7
Total peripheral resistance (TPR)	-0.15	-0.15	0
End-diastolic volume (EDV)	-0.17	-0.15	-13

Oral Session III − Clinical Aspects, Hypertension & Diabetes

3.1
STRAIN DISCONTINUITIES IN CAROTID ATHEROSCLEROTIC PLAQUES − A NOVEL MARKER FOR PLAQUE VULNERABILITY?

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Objective: Rupture of atherosclerotic plaques is ultimately a biomechanical event. We aim to develop and validate a novel method using ultrasound radiofrequency (RF) measurements to determine intraplaque inhomogeneities in the strain distribution with a high axial resolution which may identify rupture-prone plaques.
Methods: Ultrasound examinations were performed on CCAs and ICAs of 17 patients with recent stroke/TIA and 5 asymptomatic patients (39 CCAs and ICAs). Strain distribution was computed from RF data with a depth resolution <0.5 mm. In the plaque-free CCA, radial wall strain was compared with distension for validation. Two observers analyzed the data. In the ICAs, strain inhomogeneities in the plaque were studied.
Results: Within the CCA wall, the strain (observer 1: -7.4 ± 2.7%, observer 2: -6.4 ± 2.6%) had good intra-subject precision (1.6%), accuracy (correlation with relative distension, observer 1: $r = 0.69$; $p < 0.0001$, observer 2: $r = 0.68$; $p < 0.0001$) and intra-observer variability (ICC of 0.681). In the ICA, strain inhomogeneities demarcated in 58% of cases the plaque-adventitia boundary. The percentage of ICAs with ≥1 strain inhomogeneities was increasing with the degree of stenosis ($p = 0.03$, 95%-CI). Strain inhomogeneities were more frequent in ICAs at the symptomatic side of stroke/TIA (odd's-ratio = 4.7; $p = 0.07$). Strain in the deviating strain regions was higher at the symptomatic compared to the asymptomatic side ($p = 0.02$).
Conclusion: The proposed method to assess local radial strain distribution proved to be accurate and precise. In ICA, areas with high strain inhomogeneities were more frequent in symptomatic plaques vs asymptomatic plaques. These strain inhomogeneities could be a promising novel marker for plaque vulnerability.

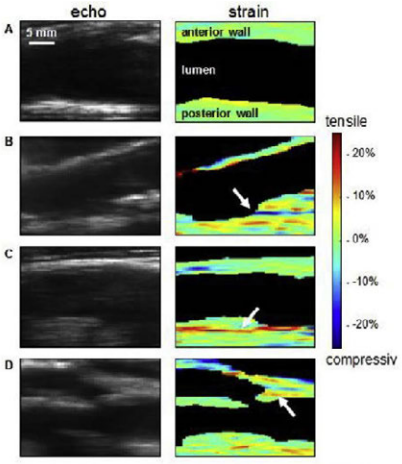

Figure 1. Examples of strain distribution in carotid plaques
Crude B-mode (echo, left panels) and corresponding strain distribution in the ICA (right panels); blood flow direction is from right to left. Note that in some cases the strain distribution is rather homogeneous (A), whereas in other cases a more heterogeneous distribution of strain is observed (B-D). Narrow but elongated regions with highly deviating strain (indicated by the white arrows) are often found near the boundary between the plaque and the supporting adventitia layer (B and D) and can appear either as diastolic-to-systolic wall compression (B) or as wall tension (C and D).

3.2
RESERVOIR PRESSURE INTEGRAL IS INDEPENDENTLY ASSOCIATED WITH THE REDUCTION IN RENAL FUNCTION IN AN OLDER POPULATION

Kunihiko Aizawa [1], Francesco Casanova [1], David M. Mawson [2], Kim M. Gooding [1], W. David Strain [1], Phillip E. Gates [1], Gerd Östling [3], Faisel Khan [4], Helen M. Colhoun [5], Carlo Palombo [6], Kim H. Parker [7], Jan Nilsson [3], Angela C. Shore [1], Alun D. Hughes [8]
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Background: Central haemodynamic parameters derived from reservoir pressure analysis (RPA-parameters) exhibit prognostic utility. Alterations in reservoir function could have an unfavourable influence on target organs, such as the kidneys. We determined in older adults whether these RPA-parameters would be associated with the reduction in estimated glomerular filtration rate (eGFR) during a 3-year follow-up period.
Methods: We studied 544 individuals (69.4 ± 7.9 yrs, 195F, 235CVD) at baseline and after 3 years. RPA-parameters including reservoir pressure integral (INTPR), peak reservoir pressure, excess pressure integral, systolic and diastolic rate constants were obtained by radial artery tonometry.
Results: After 3 years, 95 individuals (72.4 ± 7.6 yrs, 26F) had an eGFR reduction of more than 5 ml/min/1.73 m^2/year. A multivariate logistic regression analysis revealed that baseline INTPR was independently associated with the eGFR reduction after adjusting for conventional risk factors and baseline renal function [odds ratio 0.975 (95% CI, 0.958−0.993), $p < 0.01$]. When the eGFR reduction was expressed as a continuous variable, baseline INTPR was also independently associated with changes in eGFR ($\beta = 0.115$, $p < 0.01$; multivariate linear regression with adjustment for