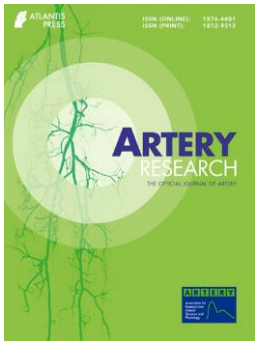

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3.2: ORIGINS OF THE BACKWARD TRAVELING WAVE IN THE ARTERIAL TREE

Ye Li*, Henry Fok, Benyu Jiang, Sally Epstein, Marie Willemet, Jordi Alastruey, Kim Parker, Phil Chowienczyk

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Conclusion: Ambulatory aPWV, estimated by an operator-independent method, provides additional information to cfPWV regarding the associations of arterial stiffness with the retinal microcirculation.

2.5
IN SINGLETONS BORN AT TERM, LOWER GESTATIONAL AGE IS ASSOCIATED WITH INCREASED AORTIC PULSE WAVE VELOCITY IN YOUNG ADULTHOOD: THE NORTHERN IRELAND YOUNG HEARTS PROJECT (NIYHP)

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Decreases in the mean gestational age of babies born at term have been reported over the past decade in several developed countries, linked to increases in the rates of planned births by labour induction and/or pre-labour caesarean sections. In contrast to the effects of pre-term birth, the extent to which lower gestation age within the 'at-term' range (i.e. $\geq$37−$\leq$42 weeks) affects individuals' cardiovascular heath is largely unknown, however. We have therefore examined the association between gestational age (obtained from the Northern Ireland Child Health Services' records) and aortic pulse wave velocity (aPWV) in 351 young adults from the NIYHP (50.4% women, mean age of 22.4 $\pm$ 1.6 years, all singletons and born at term, 98% with birth weight>2.5 kg). In analyses adjusted for age, sex, birth weight (in SDs relative to UK's 1990 reference), birth order, breast-feeding, maternal and paternal age at child's birth, and social economic status, we found that each week increase in gestational age was significantly associated with lower levels of aPWV [standardized ß = −0.11 (95% CI:−0.21;−0.01, p = 0.039)]. Additional adjustments for individuals' adult BMI and mean arterial pressure did not appreciably affect this association. None of the other birth covariates were independently associated with aPWV. These findings suggest that lower gestational age, even within the at-term range, may be a key determinant of early vascular ageing as each additional week conferred benefits. This aspect may have been neglected by the over-simplistic characterization of individuals as 'born at-term' and may have clinical implications for policies around planned deliveries, given the current trends.

2.6
PULSE WAVE VELOCITY AND GAIT PERFORMANCE IN OLDER SUBJECTS

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Background: Arterial stiffening is an age-related change and is a well-known cardiovascular risk factor but its association with physical decline is rarely evaluated.
The aim of this analysis was to assess the association of arterial stiffness as carotid-femoral pulse wave velocity (PWV) with gait performance in older subjects.
Methods: PWV was measured with Complior device. In all subjects was assessed: gait speed (V), Timed Up&Go test (TUG), handgrip strength, personal (ADL) and Instrumental Activities of Daily Living (IADL). Body composition was assessed with DXA, nutritional status with Mini Nutritional Assessment. Standard blood laboratory tests and markers of inflammation (hsCRP, IL-6, pentraxin3-PTX3, osteoprotegerin-OPG, TNFα soluble receptor2-sTNFR2) were determined.
Results: Mean age of 69 subjects (53—96 yrs) was 72.5 $\pm$ 9.8 yrs. Mean number of diseases was 5.3 $\pm$ 2.2, and of used medications was 7.0 $\pm$ 2.5. Subjects with PWV < 10 m/s and $\geq$10 m/s did not differ in systolic (SBP) and diastolic blood pressure, heart rate, number of diseases and medications, IADL, ADL, handgrip strength. Patients with PWV < 10 m/s were younger (67.8 $\pm$ 6.4vs74.8 $\pm$ 10.4 yrs; p = 0.004), had higher V (1.02 $\pm$ 0.31vs0.798 $\pm$ 0.23 m/s; p = 0.006), lower TUG (9.69 $\pm$ 2.6vs11.81 $\pm$ 4.56; p = 0.02), higher mdrd (76.3 $\pm$ 21.4 vs 62.87 $\pm$ 20.3 ml/min/m^2) and lower legs' fat content (LEfat) (6433.1 $\pm$ 1934.2vs 8046.4 $\pm$ 3187.5g; p = 0.047). PWV correlated positively with age (r = .47, p < 0.0001), TUG (r = 0.26, p = 0.037), negatively with V (r = −0.37, p = 0.003), handgrip strength (r = −0.30, p = 0.015), ADL (r = −0.28, p = 0.02).
In multiple regression analysis gait speed was negatively associated with PWV (β = −0.37; p = 0.0075), female gender (β = −0.36; p = 0.045) and TUG (β = −0.443; p = 0.0038), and positively with Hb (β = 0.30; p = 0.045), PTX3 (β = 0.608; p = 0.001), sTNFR2 (β = 0.374; p = 0.035).
Conclusions: Artery stiffness, apart from female gender and inflammation, may be associated with poorer gait performance in older subjects.

3.1
PREDIABETES IS ASSOCIATED WITH IMPAIRED RETINAL VASODILATION: THE MAASTRICHT STUDY

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Aim: Type 2 diabetes (DM2) causes microvascular dysfunction (MVD). In addition, MVD can contribute to insulin resistance, predisposing to DM2. This hypothesis predicts that MVD should be present in impaired glucose metabolism (IGM; prediabetes). However, population-based studies of MVD and glucose metabolism are not available. We investigated this using the retinal arteriolar dilator response to flicker light.
Methods: In a population-based study (n = 2205), we determined retinal %-dilation (Dynamic Vessel Analyzer; Imedos, Germany) and glucose metabolism status (OGTT; classified as normal (NGM), IGM or DM2). Differences were compared with multivariable regression adjusted for age, sex, BMI, smoking, systolic-BP, lipid profile, retinopathy, (micro)albuminuria, the use of lipid-modifying and/or blood-pressure-lowering medication and prior cardiovascular disease.
Results: 1263 individuals had NGM (42% men, aged 58 $\pm$ 8 years (mean $\pm$ SD)), 336 IGM (61% men, aged 61 $\pm$ 7 years) and 606 (due to oversampling) DM2 (69% men, aged 63 $\pm$ 8 years). Arteriolar %-dilation was median 3.51, IQR 1.47 to 5.95, range −5.69 to +19.71. %-dilation (mean $\pm$ SD) was 4.42 $\pm$ 3.45 in NGM, 3.77 $\pm$ 3.06 in IGM, and 3.26 $\pm$ 3.27 in DM2. Adjusted analyses showed decreased %-dilation in IGM (β = −0.461, p = 0.03) and DM2 (β = 0.559, p = 0.01) vs NGM.
Conclusion: IGM and DM2 are associated with reduced flicker-light-induced retinal arteriolar dilation, independently of major cardiovascular risk factors. These findings support the concept that MVD precedes and thus may contribute to DM2.

3.2
ORIGINS OF THE BACKWARD TRAVELING WAVE IN THE ARTERIAL TREE

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Backward traveling waves, an important determinant of central haemodynamics, are usually regarded as being due to reflections from discontinuities in the arterial tree. However, consideration of a single tube model of the arterial with a single site of reflection shows that a backward pressure wave may be generated by elastic recoil of large arteries, in which case the magnitude of the backward wave is proportional to that of the forward wave. A 55-segment 1-D model of the arterial which allows reflection as a continuum along the arterial tree and, for a given prescribed aortic flow, generates physiological aortic pulse waveforms was used to examine the relation of the backward to forward pressure waves in 4107 "virtual subjects" with arterial parameters spanning the physiological range. Backward pressure wave was closely correlated with the forward wave (R = 0.931, P < 0.001). Clinical data was obtained by carotid tonometry and aortic Doppler sonography during modulation of cardiovascular function in healthy volunteers (n = 13, age 46.5 $\pm$ 10.1 years with inotropic, vasopressor and vasodilator drugs (dobutamine, norepinephrine phentolamine and nitroglycerin). The magnitude of backward pressure was highly correlated with forward pressure over a range 5—15 mmHg (R = 0.824, P < 0.001) with a constant ratio of backward to forward wave magnitude except during treatment with nitroglycerin, a vasodilator known to be highly selective for large muscular arteries. These numerical and experimental data suggest that backward pressure waves can

be generated by elastic recoil of large arteries independent of pressure wave reflection and this effect dominates in human physiology.

3.3
AN EASY AND INTUITIVE WEB INTERFACE FOR THE ASSESSMENT OF MEASUREMENTS OF CAROTID-FEMORAL PULSE WAVE VELOCITY AND LOCAL ARTERIAL STIFFNESS RELATIVE TO THE REFERENCE VALUES DATABASE

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Objective: The use of different devices and methods still hampers the widespread clinical use of the reference values for arterial stiffness. The aim of this work was therefore to create a web-based application that allows easy assessment - for different methodological approaches - of a given measured value of arterial stiffness, with the application providing the percentile reference associated with that specific value.
Methods: Reference values of carotid-femoral pulse wave velocity (cf-PWV) (11,092 individuals; age range: 15—97 years, 49.8% men) and local carotid (22,708 individuals; age range 15—99 years; 54% men) and femoral (5,069 individuals; age range: 15—87 years; 49.5% men) arterial stiffness were obtained from The Reference Values for Arterial Stiffness' Collaboration 2010 and the database of The Reference Values for Arterial Stiffness' Collaboration. Data from healthy subpopulations were used to establish equations for percentiles of cf-PWV and sex-specific percentiles of carotid and femoral distensibility coefficient (DC) across age. Using these established equations, an application was created (in JavaScript) to provide the percentile reference value from routine parameters obtained in clinical practice.
Results: The tool can be found at: http://bit.do/referencevalues. The user selects the parameter to be determined (or standardized): carotid DC, femoral DC or cf-PWV. Subsequently, a number of inputs are required to calculate the selected parameter, the percentile and, when relevant, additional information. The tool also allows conversion of cf-PWV following different methods.
Conclusions: An easy and intuitive interface was created to assess a given measurement of arterial stiffness relative to know reference values.

3.4
EVALUATION OF THE MUTUAL RELATIONSHIPS AMONG THE DEVELOPMENT OF HYPERTENSION, ARTERIAL STIFFENING AND RENAL FUNCTION DECLINE BASED ON REPEATED LONGITUDINAL MEASUREMENTS

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Background: The mechanisms underlying the development of hypertension have not yet been fully clarified. The mutual relationships among the development of hypertension and the longitudinal changes of arterial stiffness and renal function, and also the effect of maintenance of a normal body weight on these relationships were evaluated by a linear mixed-effects regression model analysis (LMM).
Methods and Results: In 3932 middle-aged Japanese subjects without hypertension (41 ± 9 years old), an 11-year prospective observational study was conducted by repeated annual measurements of the blood pressure (BP), brachial-ankle pulse wave velocity (baPWV), and serum creatinine-derived estimated glomerular filtration rate (eGFR). The mean number of measurements per patient was 6.5. The LMM analysis revealed that higher values of the baPWV were associated with annual elevation of the SBP, and higher values of the SBP were associated with annual increase of the baPWV (estimate = 0.2103, $p < 0.001$). These associations were also significant in the subjects in whom the body mass index was maintained at <25.0 at the end of observation period (n = 2815). However, no significant relationships were observed between the eGFR/proteinuria and the annual change of the baPWV/BP.
Conclusions: The results of LMM analysis in this study revealed that, while a vicious cycle may exist between the development of hypertension and the progression of arterial stiffening, mild renal dysfunction as reflected by eGFR decline and/or proteinuria may not affect this vicious cycle. Furthermore, maintenance of a normal body weight may not be effective for interrupting this vicious cycle.

3.5
ASSOCIATION OF VASCULAR RISK FACTORS WITH BRAIN STRUCTURE AND FUNCTION

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Background: Vascular risk factors have been associated with brain aging. We aimed to determine the associations between blood pressure (BP), atherosclerosis, arterial stiffness and microvascular damage with both structural and functional measures of the brain.
Methods: A community-based sample of 1287 individuals (69 ± 6 yrs) underwent cognitive function testing and MRI to measure hippocampal brain volumes. Brachial and central systolic BP (SBP, cSBP) and pulse pressure (PP, cPP), diastolic BP (DBP), arterial stiffness (cfPWV), atherosclerosis (cIMT) and microvascular disease (composite from retinopathy, ACR and eGFR measures) were measured.
Results: After adjusting for age, sex and ethnicity hippocampal volume was significantly associated with SBP ($\beta \pm SE$: -0.004 ± 0.002; $p = 0.01$), PP ($\beta \pm SE$: -0.008 ± 0.002; $p < 0.0001$), cPP($\beta \pm SE$: -0.01 ± 0.003; $p < 0.0001$) and cfPWV ($\beta \pm SE$: -0.02 ± 0.01; $p = 0.04$). Cognitive function (z-score) was significantly associated with PP ($\beta \pm SE$: -0.004 ± 0.002; $p = 0.003$) and cPP ($\beta \pm SE$: -0.005 ± 0.002; $p = 0.02$). After further adjustment for concomitant risk factors (heart-rate, diabetes, hypertension, previous stroke, coronary artery disease, waist-to-hip ratio, years of education and smoking) only the associations with PP (Hippocampal volume $\beta \pm SE$: -0.005 ± 0.002; $p = 0.02$, cognitive function $\beta \pm SE$: -0.004 ± 0.001; $p = 0.01$) and cPP (Hippocampal volume $\beta \pm SE$: -0.008 ± 0.003; $p = 0.004$, cognitive function $\beta \pm SE$: -0.004 ± 0.002; $p = 0.048$) remained significant.
Conclusion: In this community based sample brachial and central PP were significantly associated with measures of brain structure and function, not explained by concomitant risk factors.

3.6
AORTIC STIFFNESS IS RELATED TO CEREBRAL LESION GROWTH IN PATIENTS WITH ACUTE ISCHEMIC STROKE

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Objective: Cerebral lesion growth in acute ischemic stroke leads to secondary neurological deterioration and poor outcome. Whether cSBP and arterial stiffness are related to the early brain infarct growth in patients after ischemic stroke is unknown.
Design and Methods: We enrolled 65 patients (43 males, age 62.9 ± 12.2 years, mean ± SD) with acute ischemic stroke (NIHSS at admission 6.0 ± 4.6 points). Carotid-femoral pulse wave velocity (CF-PWV), central systolic blood pressure (cSBP) and central augmentation index (cAIx) were measured (Sphygmocor®) within few (5 ± 2) days after stroke onset. Serial brain MRI were analysed. Cerebral lesion growth was assessed on diffusion-weighted imaging (DWI) by comparing baseline and follow-up scans. Marked cerebral lesion growth was determined as the highest tertile in a standardized measure of DWI lesion volume increase, and compared with the lowest tertile used as the reference group. Data were analysed with multivariate logistic regression.
Results: CF-PWV was higher in patients with marked cerebral lesion growth than that in patients of the reference group (10.9 ± 3.1 vs. 9.1 ± 1.9 m/s,