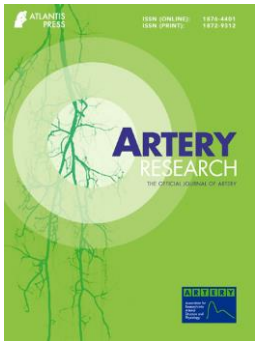

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3.6: AORTIC STIFFNESS IS RELATED TO CEREBRAL LESION GROWTH IN PATIENTS WITH ACUTE ISCHEMIC STROKE

Dariusz Gasecki*, Mariusz Kwarciany, Kamil Kowalczyk, Anna Gójska-Grymajło, Tomasz Nowicki, Edyta Szurowska, Pierre Boutouyrie, Stephane Laurent, Krzysztof Narkiewicz, Bartosz Karaszewski

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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

Dariusz Gasecki [1,*], Mariusz Kwarciany [1], Kamil Kowalczyk [1], Anna Gójska-Grymajło [1], Tomasz Nowicki [2], Edyta Szurowska [2], Pierre Boutouyrie [3], Stephane Laurent [3], Krzysztof Narkiewicz [4], Bartosz Karaszewski [1]
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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,

P = 0.035). By contrast, cAIx, as well as none of central and peripheral BP-derived parameters were significantly associated with cerebral lesion growth in univariate analysis. In multivariable regression logistic model, CF-PWV predicted cerebral lesion growth with an odds ratio of 1.43 [1.00—2.04], independently of age, and peripheral pulse pressure.
Conclusions: Increased aortic stiffness is independently associated with cerebral lesion growth in patients with acute ischemic stroke. Its deleterious effect is more important than that of BP.

4.1
EFFECT OF ALISKIREN ON VASCULAR REMODELING IN SMALL RETINAL CIRCULATION

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Background: In hypertension changes in small arterial structure are characterized by an increased wall-to-lumen ratio (WLR). These adaptive processes are modulated by the renin angiotensin system. It is unclear whether direct renin inhibitors exert protective effects on small arteries in hypertensive patients.
Methods: In this double-blind, randomized, placebo-controlled study (www.clinicaltrials.gov: NCT01318395) 114 patients with primary hypertension were after 4 weeks of standardized open-label treatment with valsartan 320 mg (run-in phase) randomized to additional therapy with either placebo or aliskiren 300 mg for 8 weeks. Parameter of arteriolar remodeling was WLR of retinal arterioles (80—140 μm) assessed non-invasively and in vivo by scanning laser Doppler flowmetry (Heidelberg Engineering, Germany). In addition, pulse wave analysis (SphygmoCor™, AtCor Medical, Australia) and pulse pressure (PP) amplification were determined.
Results: In the whole study population no clear effect of additional therapy with aliskiren on vascular parameters was documented. When analyses were restricted to patients with vascular remodeling, defined by median of WLR > 0.3326 (n = 57), WLR was reduced after 8 weeks by the treatment with aliskiren compared to placebo (−0.044 ± 0.07 versus 0.0043 ± 0.07, p = 0.015). Consistently, after 8 weeks of on-top treatment with aliskiren there was an improvement of PP amplification compared to placebo (0.025 ± 0.07 versus −0.034 ± 0.08, p = 0.013), indicative of less stiff arteries in the peripheral circulation.
Conclusion: Thus, our data indicate that treatment with aliskiren, given on top of valsartan therapy, improves altered vascular remodeling in hypertensive patients.

4.2
THE INHOMOGENEITY OF DIASTOLIC-SYSTOLIC RISE TIME OF THE DISTENSION WAVEFORM DISTRIBUTION IN THE COMMON CAROTID ARTERY IS ASSOCIATED WITH LIPID PRESENCE OF DISTAL PLAQUES

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Objectives: Diastolic-systolic rise time characteristics of the distension waveform distribution, i.e., mean and inhomogeneity, might be modified by wave reflections from distal plaques. The aim of this study is to investigate the association between rise time characteristics for the common carotid artery (CCA) and composition of distal plaques.
Methods: Longitudinal B-mode ultrasound (US) registrations of the CCA of 129 patients (age 69 ± 9) were performed with a Philips IU22 scanner. All patients had a plaque in the ipsilateral bifurcation and recently experienced a cerebrovascular accident. Distension waveforms were extracted by edge tracking and the diastolic-systolic rise time and its inhomogeneity, defined as standard deviation of systolic-diastolic rise time distribution for an artery segment, were derived. Plaque composition was extracted from 3T-MRI measurements (N = 125).
Results: 118 subjects had both an adequate MRI and US registration. 58% of the plaques had a lipid-rich necrotic core (LRNC) of which 68% had a thin fibrous cap (FC). Lipids were demonstrated in the proximal part in 51 plaques (43%). Mean CCA diastolic-systolic rise time (162 ± 26 ms) did not vary with plaque composition (Student t-test, p-value > 0.2). The inhomogeneity, however, was significantly lower for vulnerable distal plaques (mean difference LRNC: 8ms, FC: 11ms, Student t-test, p-value < 0.02) and, more specifically, when lipids were present in the proximal part of the plaque (mean difference 12ms, Student t-test, p-value < 0.001).
Conclusion: Diastolic-systolic rise time inhomogeneity of CCA distension is associated with the lipid presence of distal plaques.
This research was supported by the Center for Translational Molecular Medicine and the Dutch Heart Foundation.

4.3
THE EFFECT OF GLYCAEMIC STATE TRANSITION ON ACCELERATED AORTIC STIFFENING: A LONGITUDINAL STUDY IN THE WHITEHALL II COHORT

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In 4,759 participants from the Whitehall II study, we examined the impact of glycaemic history on aortic stiffening. Assessment of aortic stiffness by carotid-femoral pulse wave velocity (PWV) was performed twice with a 4 year interval (2007—2009 and 2012—2013). At the first aortic stiffness assessment and 5 years earlier (2002—2004 and 2007—2009 respectively), participants were categorised into 3 groups based on measurements of fasting plasma glucose (FPG), 2-hour plasma glucose (2hPG), and HbA_{1c}: normoglycaemia, dysglycaemia and type 2 diabetes. The impact of 5-year glycaemic state transition on PWV and PWV changes was analysed by mixed effect models adjusting for relevant confounders. In participants who had normoglycaemia on FPG, 2hPG and HbA_{1c} on both examinations, PWV was 8.3 m/s at baseline and increased by 0.4 m/s during 4 years. Those who progressed to dysglycaemia had a 0.3 m/s (95% CI: 0.1;0.5) steeper increase in PWV compared with stable normoglycaemia, whereas those who progressed to diabetes did not have a statistical significantly steeper increase in PWV (0.1 m/s (95% CI: −0.4; 0.6)). Participants with diabetes at both examinations had a markedly larger increase in PWV of 0.6 m/s (95% CI: 0.3;0.9) compared to participants with stable normoglycaemia. For other glycaemic state combinations there was a tendency towards a steeper increase in PWV compared with stable normoglycaemia, however not statistically significant. These results indicate that people with diabetes or deteriorating dysglycaemia, experience accelerated aortic stiffening; suggesting that prevention of dysglycaemic progression and diabetes may have a beneficial effect on the progression of aortic stiffness.

4.4
FORWARD AND BACKWARD WAVES AT THE AORTIC ROOT: STEADY-STATE AND WAVE RE-REFLECTION CONSIDERATIONS

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Background: The assumption of steady-state oscillation is often overlooked when arterial pressure and flow waveforms are decomposed into backward (P_b) and forward waves (P_f). This has led to various misinterpretations including a significant reflection-free time during early-systole and attribution of the P_f to solely a product of left ventricular contraction and proximal aortic properties.