



Artery Research

ISSN (Online): 1876-4401

ISSN (Print): 1872-9312

Journal Home Page: <https://www.atlantis-press.com/journals/artres>

P.074: VASCULAR STRUCTURAL AND FUNCTIONAL CHANGES IN PATIENTS WITH HEART FAILURE

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To cite this article: A. Shah*, E. Gkaliagkousi, B. Jiang, J. Ritter, A. Ferro (2006) P.074: VASCULAR STRUCTURAL AND FUNCTIONAL CHANGES IN PATIENTS WITH HEART FAILURE, Artery Research 1:S1, S44–S45, DOI: [https://doi.org/10.1016/S1872-9312\(07\)70097-2](https://doi.org/10.1016/S1872-9312(07)70097-2)

To link to this article: [https://doi.org/10.1016/S1872-9312\(07\)70097-2](https://doi.org/10.1016/S1872-9312(07)70097-2)

Published online: 21 December 2019

values ($CI = 0.57 \pm 0.07$ for group A and $CI = 1.23 \pm 0.19$ for group B) and differed statistically significant as at rest ($p < 0.05$, t-test).

These differences suggests that young healthy adults of group A could have increased sympathetic tonus compared to group B or there are changes in other peripheral mechanisms governing the small vascular behavior between both groups.

P.070

NON-INVASIVE QUANTITATIVE EVALUATION OF SYSTOLIC CARDIOVASCULAR INTERACTION BY CAROTID ARTERY ULTRASONOGRAPHY

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Introduction: We investigated non-invasive quantification of the systolic interaction between left ventricle and central arterial system by carotid artery distension waveform analysis.

Methods: ECG, finger-cuff pressure, and common carotid artery distension waveforms (M-mode ultrasound) were obtained in 14 young healthy volunteers in supine and sitting position.

Results: Distension waveform analysis enabled determination of isovolumic contraction period (ICP), ejection period (EP), aorta-carotid (TTa-c) and aorta-femoral (TTa-f) transit times with a precision of 3.2, 4.5, 3.1, and 7.9 ms, respectively. From supine to sitting position, diastolic arterial pressure (DAP) increased by 7 ± 4 mmHg ($p < 0.001$, paired t-test) and the R-R interval decreased by 70 ± 87 ms ($p < 0.05$) due to the baroreflex response. The decrease in carotid transmural pressure in sitting position was reflected by an increase in TTa-c of 15 ± 9 ms ($p < 0.001$). ICP increased from 42 ± 7 to 49 ± 5 ms ($p < 0.001$) while DAP/ICP, a load-independent measure of left ventricular contractility, decreased by 7% ($p = 0.058$). This implies that the cardiac response to the postural intervention is predominantly based on an increase in heart rate. EP decreased from 303 ± 18 to 267 ± 19 ms ($p < 0.001$) as a result of the earlier arrival of the lower body reflection wave (TTa-f decreased by 57 ± 25 ms, $p < 0.001$). The ejection period and the peripheral transit time exhibited a clear correlation ($R^2 = 0.66$).

Conclusions: Modest postural changes affect systolic cardiovascular interaction through changes in arterial transmural pressure and the baroreflex but leave left ventricular contractility unaltered. Carotid artery ultrasonography enables precise quantitative evaluation of systolic cardiovascular interaction. The application of this non-invasive method in patients appears promising.

P.071

ANGIOTENSIN RECEPTOR ANTAGONISM WITH VALSARTAN DECREASES ARTERIAL STIFFNESS IN HYPERTENSIVE PATIENTS WITH METABOLIC SYNDROME

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Background: Angiotensin II (AT II) plays a key role in the development of vascular disease. Arterial stiffness is an important, independent predictor of cardiovascular risk. We investigated the long-term effects of selective AT₁ receptor blockade with valsartan on arterial stiffness in patients with hypertension and metabolic syndrome (MS).

Study design and Methods: We have examined 30 patients (16 males and 14 females, aged 47 ± 1 years, BMI $29-46$ kg/m²) with the MS and mild essential hypertension in the double blind, placebo controlled study. We measured brachial blood pressure (BD, mmHg), brachial-ankle pulse wave velocity (baPWV, cm/s) and the augmentation index (Aix, %) by using tonometry, volume-plethysmography and Doppler ultrasonography before and after 20 weeks of treatment with valsartan (40 to 160 mg/day). Statistical significance was assessed by t-test or two-way ANOVA of the dose responses curves.

Results: After 20 weeks of treatment with valsartan, baPWV and Aix were reduced: mean delta systolic BP 12 ± 1.6 mmHg ($P = 0.02$ vs. baseline), diastolic BP 5.1 ± 1.8 mmHg ($P < 0.0001$ vs. baseline), mean BP 7.5 ± 2.7 mmHg ($P = 0.003$ vs. baseline), baPWV 2.4 ± 0.03 cm/s ($P = 0.02$ vs. baseline), Aix $23 \pm 8\%$ ($P = 0.002$ vs. baseline). Delta baPWV was significantly higher in the group of female patients with the MS (F/M: 2.9 ± 0.02 cm/s vs. 2.1 ± 0.05 cm/s, $P = 0.003$).

Conclusion: AT₁ receptor antagonism reduced the arterial stiffness in hypertensive patients with MS, and may provide new therapeutic strategies for cardiovascular risk reduction.

P.072

THE DIFFERENTIATION IN THE CONTRIBUTION OF VASCULAR AND CEREBRAL SEGMENTS TO BRS

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Background: The baroreflex pathway is composed of vascular and cerebral segments, which are individually affected by variations in blood pressure. Baroreceptor sensitivity (BRS) is conventionally derived from spectral relationship between changes in peripheral blood pressure and heart-rate (R-R), and recently from carotid artery (CA) diameter and R-R, within the spectral frequency band of 0.05-0.15 Hz.

Objective: To discriminate the contribution of distinct segments to the overall BRS value calculated, in response to blood pressure variations induced by posture changes.

Methods: The common CA was visualised in B/M-mode with an ultrasound system. Processing of received signal resulted in beat to beat changes in diameter characteristics as a function of time, over 10min. To reveal the segmental response to local changes in transmural pressure, the BRS mean amplitudes were computed for 20 young subjects in supine and upright-seated postures.

Results: Correlation analysis revealed variation in the transfer function of the cerebral segment, has a dominant contribution to the overall BRS value. Paired t-test revealed that the pressure-based BRS value is significantly lower in sitting than supine position ($p < 0.01$), while the strain-based BRS value did not change.

Conclusions: Shifting to an upright posture results in a lower CA transmural pressure, causing a larger change in diameter for a given blood pressure stimulus, thus enhancing the pressure-based BRS. The arterial pressure to CA diameter transfer function has the largest contribution to the change in the pressure-based BRS value, in response to the variation in pressure by posture.

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INTEGRATED ARTERIAL SYSTEM ANALYSIS IN A POPULATION OF HEALTHY MIDDLE-AGED MEN AND WOMEN: AUGMENTATION INDEX VERSUS WAVE REFLECTION INDICES

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Background: Age-induced alterations in arterial impedance and wave reflection contribute to elevated systolic and pulse pressure. Surrogate indices such as the augmentation index (Aix), suggest increased susceptibility for wave reflection in women.

Methods and Results: Carotid pressure and central flow waveforms were acquired non-invasively in 2132 apparently healthy subjects (1093 F/1039 M), aged between 35 and 55 at inclusion (a subgroup of the 'Asklepios' population). Input impedance, reflection coefficient $|r_1|$ and the ratio of backward-to-forward pressure amplitude, P_b/P_f , both direct measures of wave reflection, were derived. Aix was assessed using (automated) identification of characteristic points on the pressure waveform, and the effective length of the arterial tree, L_{eff} , was calculated from the timing of the reflected wave and pulse wave velocity. In addition, we calculated Aix^* and L_{eff}^* where information from pressure and flow was used to obtain the timing of the reflected wave (through wave separation analysis). Both $|r_1|$ (from 0.4143 ± 0.0033 at age 38 to 0.4618 ± 0.0048 at 54; mean \pm SEM) and P_b/P_f (0.4491 ± 0.0033 to 0.5038 ± 0.0044) increased with age ($P < 0.001$) without gender differences. Aix also increased with age, but was persistently higher in women ($P < 0.001$), while L_{eff} spuriously increased with age. Interestingly, while still increasing with age, there was virtually no gender difference in Aix^* and L_{eff}^* demonstrated the anticipated shift of reflection sites towards the heart.

Conclusion: With ageing, wave reflection increases to a similar degree in middle-aged healthy men and women. Analysis of wave reflection, using a modified Aix^* , appears to yield more consistent results than conventional Aix.

P.074

VASCULAR STRUCTURAL AND FUNCTIONAL CHANGES IN PATIENTS WITH HEART FAILURE

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Purpose: Heart failure (HF) is increasing in prevalence and a common cause of morbidity and mortality. We evaluated vascular structure and function in patients with HF.

Methods: Forearm flow-mediated dilatation (FMD) was used as a measure of endothelial nitric oxide (NO)-dependent vasodilation, and brachial artery dilation in response to sublingual glyceryl trinitrate (GTN 25 µg) was used to assess endothelial-independent dilation. Carotid intima media thickness (IMT) and pulse wave velocity (PWV), an index of arterial stiffness, was assessed using the Sphygmocor® system. All data were expressed as mean±SEM. $P < 0.05$ (two tailed) was taken as indicating statistical significance.

Results: We studied 20 patients with HF (IHD-14 & DCM-6) and 24 controls of similar age and sex. Patients were studied on usual medication. FMD was impaired in patients with HF compared to controls ($4.4 \pm 0.6\%$ vs. $6.6 \pm 0.6\%$, $p = 0.025$), whereas GTN-induced dilatation was similar to controls ($10.9 \pm 0.9\%$ vs. $11.1 \pm 1.4\%$). IMT was higher in HF patients (1.19 ± 0.09 mm vs. 0.83 ± 0.04 mm, $p = 0.0008$), and PWV was greater in patients with HF (10.7 ± 1.1 m/s vs. 8.5 ± 0.4 m/s, $p = 0.048$). In subgroup analysis of the HF subjects, IMT was elevated specifically in the patients with IHD (1.16 ± 0.03 mm vs. 0.80 ± 0.04 mm in controls, $p < 0.01$) but not in those with DCM (0.96 ± 0.11 mm vs. 0.81 ± 0.05 mm in controls, $p > 0.05$); furthermore, the patients with IHD had higher PWV (11.5 ± 1.3 m/s vs. 8.9 ± 0.3 m/s in controls, $p < 0.01$), whereas those with DCM did not (8.1 ± 0.6 m/s vs. 8.9 ± 0.3 m/s in controls, $p > 0.05$). FMD impairment was similar in IHD and DCM subjects.

Conclusions: Patients with HF have endothelial dysfunction as well as elevated arterial stiffness and increased IMT, and that the latter two changes are seen specifically in patients whose HF is secondary to IHD.

P.075

PREDICTORS OF LARGE ARTERIAL STIFFENING AND WAVE REFLECTIONS IN DIABETES: THE EFFECTS OF AUTONOMIC NEUROPATHY AND ERECTILE DYSFUNCTION

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Background and Aim: Premature arterial stiffening (AS) may contribute to macrovascular complications in diabetes. Cardiovascular autonomic neuropathy (CAN) and erectile dysfunction (ED) are also associated with adverse cardiovascular outcomes. The aim of this observational study was to investigate the relationships between CAN, ED and AS in men with diabetes.

Methods: Thirty male subjects with diabetes (type 1 and 2) (age range 39-74 yrs) but without overt cardiovascular disease were studied. AS and wave reflections were assessed by measuring pulse wave velocity (PWV) (carotid-femoral [cf] and carotid-radial [cr]) and augmentation index (AIX) (Sphygmocor). Cardiovascular autonomic function was assessed by measures of blood pressure and heart rate variability during continuous ECG recording following standard postural and breathing manoeuvres. Erectile function was evaluated using the validated International Index of Erectile Function IIEF-5 questionnaire.

Results: (Mean±SD); Comparing subjects with CAN (n=16) versus subjects without CAN (n=14), cfPWV was higher (10.8 ± 2.8 m/s vs 8.9 ± 1.5 m/s, $p < 0.05$) despite no differences in age, brachial blood pressure, erectile function, crPWV or AIX. Comparing subjects with severe ED (n=17) versus normal erectile function (n=13) there were no differences in arterial function despite higher systolic and diastolic blood pressure in subjects with severe ED. Multiple regression analysis ($R^2 = 0.83$, $p < 0.01$) identified CAN (autonomic score) ($\beta = 0.66$, $p = 0.01$) and ED (IIEF score) ($\beta = -0.62$, $p = 0.014$) as independent predictors of cfPWV but not of crPWV or AIX.

Conclusion: Both CAN and ED are independently associated with increased aortic stiffness in diabetes. CAN appears the stronger predictor and may exert a pathophysiological role in the process of aortic stiffening.

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VENTRICULAR-ARTERIAL COUPLING IN A RAT MODEL OF REDUCED ARTERIAL COMPLIANCE

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Rodent models of isolated systolic hypertension (ISH) are rare. One exception is the vitamin D and nicotine (VDN) model, in which arterial calcification raises arterial stiffness and vascular impedance. Complete analysis of the effect of VDN on ventricular-arterial interaction is lacking. Wistar rats were treated with VDN (VDN group, n=9) and a control untreated group (CTRL, n=10) was included. At sacrifice, invasive indexes of cardiac function were obtained using a conductance catheter. Aortic pressure and flow were measured to derive impedance and ventricular-arterial interaction. VDN caused significant increases in systolic (138 ± 6 mmHg vs. 116 ± 13 mmHg) and pulse pressure (42 ± 10 mmHg vs. 26 ± 4 mmHg). Arterial compliance decreased (0.12 ± 0.08 ml/mmHg vs. 0.21 ± 0.04 ml/mmHg CTRL) and pulse

wave velocity increased significantly (8.8 ± 2.5 m/s vs. 5.1 ± 2.0 m/s CTRL). Elastic modulus rose in the VDN group. Preload recruitable stroke work and end-systolic elastance were both elevated in the VDN group thus decreasing the ratio of arterial elastance over end-systolic elastance (0.94 ± 0.30 vs. 1.57 ± 0.60 CTRL). Wave reflection was augmented in the VDN group, expressed by the increase in the wave reflection coefficient (0.63 ± 0.06 vs. 0.52 ± 0.05 CTRL), as well as the amplitude of the reflected pressure wave (13.3 ± 3.1 mmHg vs. 8.4 ± 1.0 mmHg CTRL). VDN lead to development of ISH and provoked alterations in cardiac function, arterial impedance, arterial function, and ventricular-arterial interaction, which in many aspects are similar to effects of an aged and stiffened arterial tree. The VDN model may be a useful model to study the patho-physiological effects of increased arterial stiffness.

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ARTERIAL WALL REMODELING USING A CONSTITUENT-BASED MODEL

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Earlier studies in experimental hypertension have shown that acute hypertension leads to wall remodelling, which, in general, aims in restoring mean wall stress to control levels. This postulate has not been yet thoroughly studied, mainly because precise knowledge of stresses acting on each wall constituent and in all parts of the wall is still a difficult task. This requires a constituent-based modelling and analysis of the arterial wall. The three-dimensional biomechanical behavior of the vascular wall is best described by means of strain energy functions, which allow for the analysis of stresses over a wide range of deformations. The Zulliger et al. model developed by our group uses a strain energy function, which accounts for the constituents and structural properties of the wall (i.e., collagen, elastin and vascular smooth muscle as well as a statistical description for collagen engagement). The Zulliger et al. model was subsequently challenged by the work of Roy et al., which showed that significant residual stresses are released when the arterial wall is decellularized, suggesting an in-series arrangement of the VSM with elastin. The in-series elastin would be in tension, whereas the in-parallel elastin would be in compression. Upon VSM disruption, the in-series elastin cannot bear tension anymore and thus the compressed elastin expands relieving the additional residual strains. Treatment with Cytochalasin D partially destroys stress fibres and disengages the VSM cytoskeleton, leading to further release of residual stresses and to a more compliant wall, all being consistent with the model of Roy et al.

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REFERENCE VALUES IN WHITE EUROPEANS FOR THE ARTERIAL PULSE WAVE RECORDED BY MEANS OF THE SPHYGMOCOR DEVICE

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Aim: Measurement of blood pressure together with applanation tonometry at the radial artery allows the reproducible assessment of various indexes of arterial stiffness, including the peripheral (PPp) and central (PPc) pulse pressures and the peripheral (Alp) and central (Alp) augmentation indexes. We defined preliminary diagnostic thresholds, using the distributional characteristics of these haemodynamic measurements in a reference population.

Methods: We randomly recruited 870 subjects from 3 European populations. PPp was the average difference between systolic and diastolic BP measured five times. For measurement of PPc, Alp and Alc, we used the SphygmoCor device. We selected subjects without hypertension, diabetes, dyslipidemia or previous and concomitant cardiovascular disease.

Results: Study population included 228 men and 306 women (mean age 34.9 years). All haemodynamic measurements were curvilinearly related to age and Alp and Alc were lower in men than in women. In men at age 40, the upper 95% prediction bands of the relations of the haemodynamic measurements with age approximated to 60 mmHg for PPp, 40 mmHg for PPc, 90% for Alp, and 30% for Alc. For PPc, Alp and Alc, these thresholds must be adjusted for age, leading to more lower and higher thresholds at younger and older age, respectively. In addition, in women of any age, the Alp and Alc thresholds must be increased by 10% and 7%, respectively.

Conclusion: Pending validation in prospective outcome studies, distributional characteristics of arterial stiffness indexes in a reference population can be used to generate operational thresholds for use in clinical practice.