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1.1: CAROTID ENDOTHELIAL SHEAR STRESS ASSESSED BY 3T-MRI IS ASSOCIATED WITH AORTIC PULSE WAVE VELOCITY IN HEALTHY VOLUNTEERS

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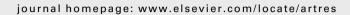
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Oral Presentation Abstracts

1 1

CAROTID ENDOTHELIAL SHEAR STRESS ASSESSED BY 3T-MRI IS ASSOCIATED WITH AORTIC PULSE WAVE VELOCITY IN HEALTHY VOLUNTEERS

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Background: Low endothelial shear stress (ESS) elicits endothelial dysfunction. However, the relationship between ESS and aortic pulse wave velocity (PWV), a validated surrogate marker for cardiovascular disease, is unknown in humans. We developed a 3.0 Tesla magnetic resonance imaging (MRI) protocol to assess associations of ESS and PWV in healthy subjects.

Methods: Common carotid 3 T-MRI measurements were performed in 55 subjects (aged $41\pm15 \rm years$). Axial gradient echo Phase-Contrast images were acquired over 45 phases per heartbeat, using a 5 cm single-element microcoil, with slice thickness 3 mm, non-interpolated pixel size 0.6 x 0.6 mm, velocity encoding 150 cm/s. The mean ESS in the cardiac cycle was calculated: ESS = $\mu\text{-}\text{WSR},~\mu$ is the blood viscosity (3.2 Pa-s), WSR was the slope of the velocities close to the artery wall assessed by second order curve fitting of the velocity profile.

Results: Mean ESS was $0.89(0.23)\text{N/m}^2$, and PWV was 7.21(1.58)m/s. ESS was inversely correlated with PWV (Pearsons' r=-0.40, p=0.01). Multiple linear regression analysis accounting for age, gender and systolic blood pressure revealed that ESS was an independent predictors of the response variable PWV (regression coefficients $[b]=-1.67\,\text{N/m}^2$ per m/s, p=0.04).

Conclusion: Our carotid MRI data show that ESS is an important determinant of arterial stiffness in humans. The data warrant further studies to evaluate use of carotid ESS as a non-invasive tool to understand individual CVD risk and to assess novel drug therapies in cardiovascular disease prevention.

1.2

AUGMENTATION INDEX IS NOT A VALID MEASURE OF WAVE REFLECTION WHEN IT IS NEGATIVE AND THIS DISTORTS THE PRESUMED RELATIONSHIP BETWEEN AGING AND WAVE REFLECTION

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Background: The relationship between aging and wave reflection has been disputed [1, 2]. Augmentation index (AI_x) increases with increasing age, however the validity of AI_x as a measure of wave reflection, particularly when AI_x is negative is unknown.

Methods: Measurements of carotid pressure and flow velocity were made in the carotid artery of 65 healthy normotensive individuals (age

 $21-78\,yr;~43$ male). $Al_x,~wave~reflection~index~(WRI)~and~P_b/P_f~were~calculated.$

Results: Al $_x$ was positively correlated with age (beta (95% CI) = 0.46 (0.19, 0.73); p=0.001). In contrast log WRI and P_b/P_f showed negative associations with age (beta (95% CI) = -0.009 (-0.016, -0.002) p=0.01 and -0.001 (-0.001, -0.000); p=0.001 respectively). Al $_x$ did not correlate with WRI or P_b/P_f , although Al $_x$ and WRI correlated weakly when Al $_x$ was restricted to positive values (rho = 0.35; p=0.03). In contrast log WRI and P_b/P_f were closely correlated (r=0.66; p<0.001). Wave intensity analysis showed that negative augmentation was due to a forward decompression wave in mid systole and was consequently an unreliable indicator of reflected compression waves.

Conclusions: Augmentation index is not a valid measure of wave reflection when it is negative; this is common in younger individuals and distorts the relationship between aging and wave reflection. In healthy normotensive individuals wave reflection in the common carotid artery decreases with increasing age

- [1] Namasivayam et al. Hypertension. 2009; 53: 979-985.
- [2] Vasan. Hypertension. 2008; 51: 33-36

1.3

IS IT TIME TO QUESTION THE VALIDITY OF IMPEDANCE ANALYSIS?

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Although the 3-element Windkessel (Wk) is still a useful analogue of arterial hemodynamics, can the validity of the frequency-domain analysis continue to be assumed? Our alternative time-domain approach holds that measured pressure is the sum of a Wk (P_{Wk}) and an "excess" pressure (P_{excess}).

"Characteristic impedance" (Z_0) is critical. Originally called characteristic resistance by Westerhof, Z_0 was simulated like peripheral resistance in a hydraulic model but recently has been interpreted only in the frequency domain. We have shown that P_{excess} varies linearly with aortic inflow with a slope of Z_0 . Bench-top experiments with canine peak flows and aortic dimensions yielded pressure drops equal to those measured physiologically, and a proximal resistance approximating Z_0 . A bench-top experiment simulating Westerhof's hydraulic circuit demonstrated a P_{WK} waveform.

We calculated the frequency-dependent impedance of measured pressure, P_{Wk} and $P_{\rm excess}$, under the influence of nitroprusside (NP) and methoxamine (Mtx). With NP, there was no impedance minimum and the modulus of $P_{\rm excess}$ was frequency-independent. With Mtx, an impedance minimum was demonstrated but was due entirely to P_{Wk} . Thus, the impedance minimum appears to be due only to the P_{Wk} and may not also be essentially related to wave reflection.

Finally, we used our approach to demonstrate positive and negative wave reflection in the canine aorta. However, if P_{Wk} was not initially subtracted, backward waves appeared first in the ascending aorta and they appeared to be propagated forward (figure).