Comparison of local against regional elastic properties of the vessel wall in a murine atherosclerosis model by PWV measurements

Alexander Gotschy[1,2], Volker Herold[1], Elisabeth Bauer[2], Gunthard Lykowsky[3], Christian Schrodt[2], Eberhard Rommel[1], Peter M. Jakob[1], and Wolfgang R. Bauer[1]
[1]*Department of Experimental Physics 5, University of Würzburg, Würzburg, Germany,* [2]*Department of Internal Medicine I, University of Würzburg, Würzburg, Germany,* [3]*Research Center Magnetic Resonance Bavaria (MRB), Würzburg, Germany*

Introduction

Increased aortic stiffness is known to be associated with atherosclerosis and has a predictive value for cardiovascular mortality. Furthermore it could be shown in an animal study that the local Pulse Wave Velocity (PWV), as an indicator for the elasticity of the vessel wall, increases before morphological changes of the vessel become detectable [1]. However, to our knowledge, it has never been investigated whether the augmentation of vascular stiffness is equally distributed over the vessel or if it differs from one section to the other. In this study we investigated the relation of the regional PWV, measured over the whole length of the descending aorta, to the local PWV measured in the upper abdominal aorta. Both parameters were determined by MR-microscopy at 17.6 T in ApoE-/- and control mice. Thereby we found that local and regional PWV show a good agreement regarding the mean PWV value of each group. However both parameters were hardly correlated in the individual mice in the ApoE-/- group, whereas the control group showed a good correlation. This may indicate that the vascular stiffening accompanying atherogenesis shows a high variation along the vessel.

Methods

MR-experiments were performed on an experimental 17.6 T small animal MR spectrometer with a max. gradient strength of 1000 mT/m. As receiver coil, we used two home build bird cage resonators with an inner diameter of 20 mm for mice of less than 24.0 g bodyweight and 25 mm for mice over 24.0 g bodyweight.

Regional PWV: Regional PWV was determined by a multisite transit time (TT) method [2]. This method detects the time point of the first systolic flow acceleration at 20 – 30 sites along the vessel. Therefore a 2D-CINE data set with axial velocity encoding along the direction of the blood flow was acquired. The slices were positioned in a way that the flow direction in the descending aorta was parallel to the frequency encoding direction. To guarantee only little variation of the heart rate for the duration of a measurement, the total measurement time had to be minimized. This was achieved by using only a one dimensional flow encoding scheme.

Local PWV: Under the assumption of a reflectionless waveform in the early systolic flow pulse, the local PWV can be approximated by PWV=dQ/dA (Q(t): volume flow through the vessel; A(t): cross sectional area of the vessel) with the date of a single slice [3]. For the measurement of the time course of the parameters Q and A, a high resolution PC-Cine-FLASH sequence was performed perpendicular to the arterial vessel with through plane flow encoding (TE = 1.7 ms; TR = 5 ms; slice thickness = 1 mm; frames per heart cycle: 40). By the use of an interlaced acquisition mode, a temporal resolution of 1 ms could be achieved.

Animal model: Local and regional PWV were determined in eight C57Bl/6 mice and eight ApoE-/- mice at the age of 18 weeks. The ApoE-/- group was fed a high cholesterol diet starting at the age of 4 weeks, whereas the control group was on chow for the duration of the study. For the measurements mice were anaesthetized with 1.5 – 2.0 vol.% isoflurane inhalation, while the gradient cooling unit was used to maintain the body temperature at 37°C. All experimental procedures were in accordance with institutional guidelines and were approved by an external ethics committee.

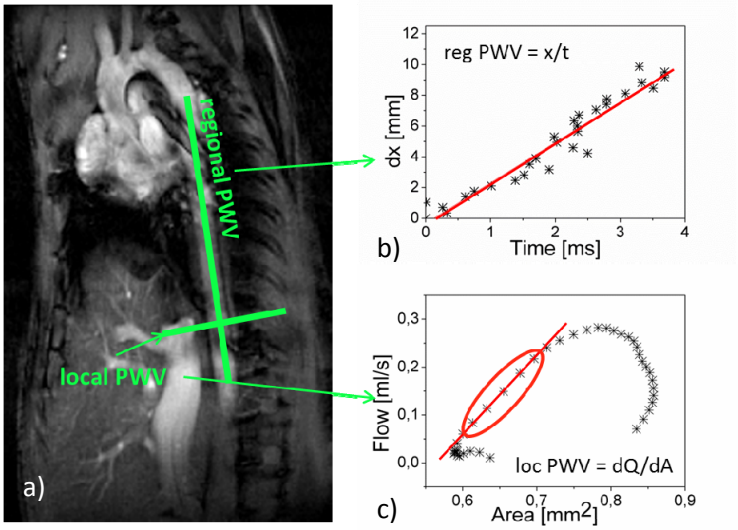

Fig. 1: a) shows the anatomical sites of regional and local PWV determination. Exemplary datasets for the evaluation of regional **(b)** and local **(c)** PWV are depicted.

Results

In the control group the local PWV (2.2 ± 0.2) m/s is in a good agreement with the regional PWV (2.1 ± 0.2) m/s. Fig. 2a shows the correlation plot of local vs. regional PWV of the control group. For a linear regression, the correlation coefficient (r) is 0.81 and the regression coefficient is 0.97. For the ApoE -/- group the means of local (2.9 ± 0.2) m/s and regional PWV (2.7 ± 0.2) m/s show no significant difference. But regional and local PWV values in the individual mice show no correlation (Fig. 2b, r = -0.14, regression coefficient = -0.17).

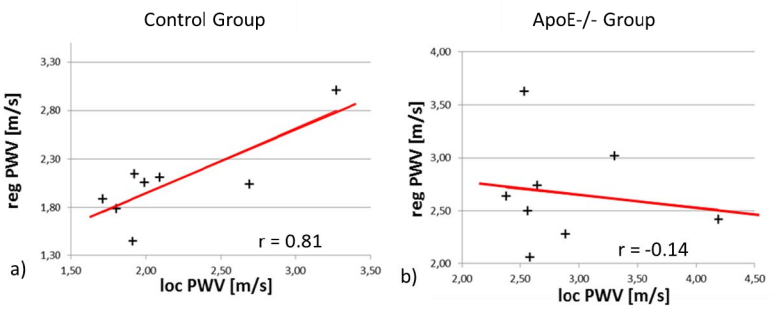

Fig. 2: Correlation plot of individual PWV values obtained with the multisite TT-method and the QA-method for the control group **(a)** and the ApoE-/- group **(b)**.

Conclusion

Although local and regional PWV show a good correlation in the control group, there seems to be no correlation between both values in the atherosclerotic ApoE-/- mouse group. This indicates that vascular stiffening caused by early atherosclerosis may be very unequally distributed over the length of a vessel. Due to the small sample size this conclusion is associated with some uncertainty. However the results stress the need for further investigation of the interrelation between atherosclerosis and the elastic properties of the vessel.

References

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