Original Research

Validation and Reproducibility of Aortic Pulse Wave Velocity as Assessed With Velocity-Encoded MRI

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Purpose: To validate magnetic resonance imaging (MRI) assessment of aortic pulse wave velocity (PWV_{MRI}) with PWV determined from invasive intra-aortic pressure measurements (PWV_{INV}) and to test the reproducibility of the measurement by MRI.

Materials and Methods: PWV_{MRI} was compared with PWV_{INV} in 18 nonconsecutive patients scheduled for catheterization for suspected coronary artery disease. Reproducibility of PWV_{MRI} was tested in 10 healthy volunteers who underwent repeated measurement of PWV_{MRI} at a single occasion. Velocity-encoded MRI was performed on all participants to assess PWV_{MRI} in the total aorta (Ao_{total}), the proximal aorta (Ao_{prox}), and the distal aorta (Ao_{dist}).

Results: The results are expressed as mean ± SD, Pearson correlation coefficient (PCC), and intraclass correlation (ICC). Good agreement between PWV_{MRI} and PWV_{INV} was found for Ao_{total} (6.5 ± 1.1 m/s vs. 6.1 ± 0.8 m/s; PCC = 0.53), Ao_{prox} (6.5 ± 1.3 m/s vs. 6.2 ± 1.1 m/s; PCC = 0.69), and for Ao_{dist} (6.9 ± 1.1 m/s vs. 6.1 ± 1.0 m/s; PCC = 0.71). Reproducibility of PWV_{MRI} was high for Ao_{total} (4.3 ± 0.5 m/s vs. 4.6 ± 0.7 m/s; ICC = 0.90, $P < 0.01$), Ao_{prox} (4.3 ± 0.9 m/s vs. 4.7 ± 1.0 m/s; ICC = 0.87, $P < 0.01$), and Ao_{dist} (4.3 ± 0.6 m/s vs. 4.4 ± 0.8 m/s; ICC = 0.92, $P < 0.01$).

Conclusion: MRI assessment of aortic pulse wave velocity shows good agreement with invasive pressure measurements and can be determined with high reproducibility.

Key Words: pulse wave velocity; magnetic resonance imaging; aorta; elasticity; coronary artery disease
J. Magn. Reson. Imaging 2009;30:521–526.

THE AORTIC WALL structure undergoes degenerative changes with advancing age, which is associated with a decline of aortic elasticity (1–5). Numerous reports emphasize the importance of aortic pulse wave velocity (PWV) as an indicator of arterial stiffness and as a prognostic indicator for future cardiovascular events (2–12). PWV is defined as the velocity of the systolic wave front propagating through the aorta and is increased when atherosclerotic degeneration of the wall and concomitant reduction of the elastic recoil are present (10).

Intra-arterial pressure measurements provide the most accurate assessment of the aortic PWV (13,14), but this modality requires an invasive procedure and is therefore not suitable for widespread clinical use. Tonometry and ultrasound are established modalities for quantification of global vascular function, but both modalities only provide an estimation of the aortic PWV, due to the limited availability to obtain acoustic windows and the inability to spatially register the distance between the acquisition sites along the length of the aorta (4–6). In addition, as the aortic wall condition may vary along the course of the aorta, regional assessment of aortic PWV is clinically desirable, for which neither technique is suited.

Velocity-encoded (VE) magnetic resonance imaging (MRI) allows accurate assessment of the blood flow velocity with a sufficient temporal and spatial resolution to study the propagation of the aortic systolic flow wave (13–16). The true path length of the pulse wave along the aorta can be directly assessed with MRI, even in the presence of a tortuous course of the aorta, and regional elastic properties of the aorta can be studied, depending on the number of aortic segments studied.

To our knowledge, PWV assessment using MRI has not been validated previously in vivo. The purpose of

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Contract grant sponsor: Netherlands Heart Foundation; Contract grant number: NHS/2006B138.
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Received June 6, 2008; Accepted June 12, 2009.
DOI 10.1002/jmri.21886
Pulished online in Wiley InterScience (www.interscience.wiley.com).

Table 1
Characteristics of Participants

Characteristics	Group 1 (n=18)	Group 2 (n=10)
Male / female	15/3	7/3
Age at MRI (years)*	59 ± 10	29 ± 8
Height (cm)*	174 ± 8	180 ± 10
Weight (kg)*	83 ± 17	80 ± 13
Blood pressure systolic (mmHg) during MRI*	131 ± 19	118 ± 14
Blood pressure diastolic (mmHg) during MRI*	77 ± 12	73 ± 12
Heart rate (beats per minute) during MRI*	66 ± 11	61 ± 8
Smoking (yes / no)	13 / 5	0 / 10
NYHA class II / III / IV	8 / 8 / 2	

Group 1: patients for PWV_{MRI} and PWV_{INV} comparison.
Group 2: healthy subjects for reproducibility of PWV_{MRI}-assessment.
Unless otherwise indicated, data are number of participants and data in parentheses are percentages.
*Data are mean ± standard deviation.
MRI, magnetic resonance imaging; NYHA, New York Heart Association.

the current study was therefore to validate MRI assessment of aortic pulse wave velocity (PWV_{MRI}) with PWV determined from invasive intra-aortic pressure measurements (PWV_{INV}) and to test the reproducibility of PWV_{MRI}.

MATERIALS AND METHODS

Subjects

The local medical ethics committee approved the study and informed consent was obtained from all participants prior to their enrollment in the study. Characteristics of the participant groups are listed in Table 1.

Eighteen nonconsecutive patients (15 male, 3 female; mean ± SD age 59 ± 10 years) with suspected coronary artery disease (group 1)—scheduled to undergo elective coronary angiography on clinical indication—were prospectively included to validate PWV_{MRI} assessment by comparison with PWV_{INV}. The mean interval between cardiac catheterization and MRI was 15 ± 12 days.

Ten healthy nonsmoking volunteers (seven male, three female; mean ± SD age 29 ± 8 years) without signs and symptoms of cardiovascular disease (group 2) were recruited to test the reproducibility in PWV_{MRI} assessment. The volunteers were studied twice (with repositioning of the subjects between the two examinations) using the same MRI protocol.

Exclusion criteria included evidence of aortic valve stenosis (aortic velocity >2.5 m/s on echocardiography), aortic coarctation and/or other forms of congenital heart disease, Marfan syndrome or a family history of Marfan syndrome, and general contraindications to MRI.

VE MRI for PWV_{MRI}

MRI was performed in all participants on a 1.5T MRI scanner with a mean acquisition time of 12 ± 2 minutes (ACS-NT15 Intera, Philips Medical Systems, Best, The Netherlands; software release 11, Pulsar gradient system with amplitude 33 mT/m and 100 mT/m/ms slew rate, 0.33 ms rise time).

PWV_{MRI} was assessed in the proximal aorta (Ao_{prox}) between the ascending and proximal descending aorta, and in the distal aorta (Ao_{dist}) between the proximal descending aorta and the abdominal aorta (Fig. 1A). PWV_{MRI} of the total aorta (Ao_{total}) was assessed using the datasets acquired at the ascending aorta and the abdominal aorta. Imaging sequences were previously described (18). In short, an oblique-sagittal single-slice segmented gradient-echo scout image was obtained to depict the full course of the aorta, with two transverse saturation slabs applied perpendicular to the aorta (at the level of the pulmonary trunk and at the most distal level of the abdominal aorta depicted in the oblique sagittal scout) to indicate the location of the sites for subsequent through-plane VE MRI acquisition (18). One-directional through-plane nonsegmented VE MRI using free breathing with retrospective ECG gating was applied perpendicular to the aorta at the levels of the saturation-slabs in the scout image to assess the aortic flow at the three measurement sites (18). A maximal number of phases reconstructed during one average cardiac cycle resulted in a temporal resolution of 6–10 msec, depending on the heart rate. Arrhythmia rejection was used with an acceptance window of 15% of the set heart rate. A local phase correction filter was used to set velocity values in voxels with low magnitude to zero, in order to suppress background noise.

PWV_{MRI} was calculated as $\Delta x/\Delta t$ (expressed in m/s), where Δx is the aortic path length between the measurement sites and Δt is the transit time between the arrival of the systolic wave front at these sites (Fig. 1B) (14,18,19). The aortic path lengths between the three subsequent measurement sites were manually determined along the centerline of the aorta within the scout image by using the software package MASS (Medis, Leiden, The Netherlands) (Fig. 1A) (18). Aortic velocity maps were analyzed with the analytic software package FLOW (Medis, Leiden, The Netherlands) (18,20). The onset of the systolic wave front was automatically determined using custom-made software from the resulting flow graph by the intersection point of the constant horizontal diastolic flow and upslope of the systolic wave front, modeled by linear regression along the upslope. The regression line was modeled from the flow values between 20% and 80% of the total range.

Invasive Pressure Measurements for PWV_{INV}

In the 18 patients with suspected coronary artery disease (group 1), invasive pressure–time curves and simultaneous ECG recordings were obtained during catheterization immediately after vascular access, to avoid any interference by medication or performed procedures. Pressure measurements were acquired at three sites in the aorta, at similar locations as used for the PWV_{MRI} assessments (Fig. 1A). A 6F JR4 pressure tip catheter (Cordis, Miami Lakes, FL) was introduced through a 6F sheet (Cordis) into either one of the femoral arteries and advanced through the aorta until just distal to the aortic valve, for pressure measurements at

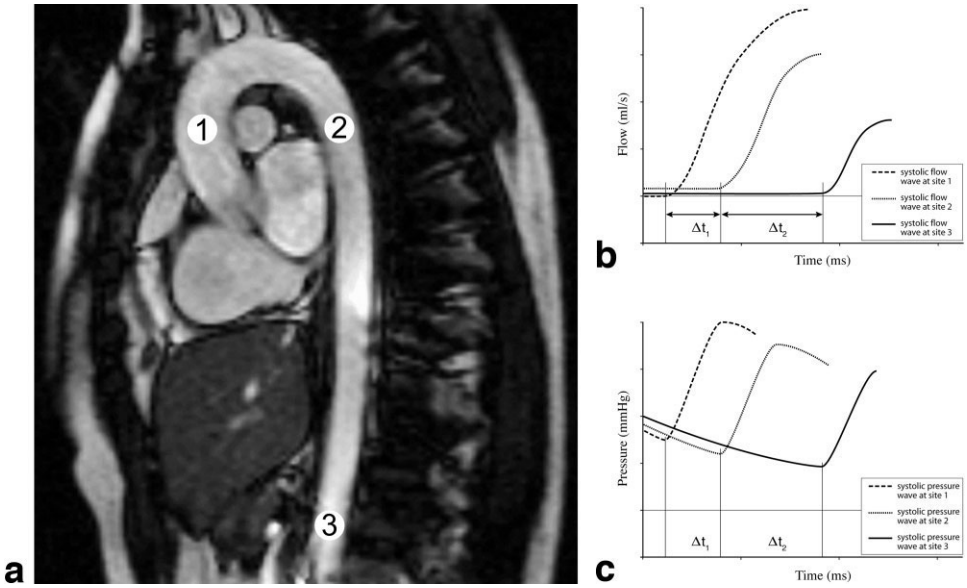

Figure 1. Analysis of pulse wave velocity with MRI and invasive pressure measurements. **a:** An oblique sagittal scout covering the full course of the aorta, indicating the sites for the through-plane velocity-encoded PWV_{MRI} assessments and the invasive pressure measurements for PWV_{INV}: the ascending aorta (1), the proximal descending aorta just distal to the aortic arch (2), and the most distal level of the abdominal aorta depicted in the oblique sagittal scout (3). Determination of the onset of the three systolic flow waves for PWV_{MRI} at the measurement sites are depicted in **b,** while determination of the onset of the three systolic pressure waves for PWV_{INV} at the measurement sites are depicted in **c.** The distance between these sites and the transit time (Δt_1 and Δt_2) between the individual onsets of the systolic flow waves (B,C) determine the PWV.

the level of the ascending aorta. During pullback, pressure waves were recorded at multiple positions, 5.8 cm apart consecutively. After MRI acquisition, the pressure measurements nearest to the MRI measurement sites 2 and 3 were used for determining $PWV_{INV.}$ Pressure–time curves and ECG were recorded with a sampling resolution of 2 kHz during at least 10 cardiac cycles. The pressure–time curves recorded in the ascending and proximal descending aorta were used to calculate the PWV_{INV} of the Ao_{prox}, the pressure–time curves recorded in the proximal descending aorta and the abdominal aorta were used to calculate the PWV_{INV} of the Ao_{dist}, and the pressure–time curves recorded in the ascending and the abdominal aorta were used to calculate the PWV_{INV} of the Ao_{total} (Fig. 1C). PWV_{INV} is similarly expressed by $\Delta x/\Delta t$ as for PWV_{MRI}, although Δt is the transit time between the arrival of the two corresponding systolic pressure wave fronts, relative to the R-wave (Fig. 1C) (19). The onset of the systolic pressure wave front was automatically determined from the timepoint of minimal pressure prior to the upslope of the systolic pressure wave. To minimize variation induced by respiration for assessment of the timepoint of the onset of the systolic pressure wave, 10 consecutive cardiac cycles were analyzed and these timepoints were averaged. Offline analysis of the pressure–time curves was performed using custom-made software.

Statistical Analysis

Statistical analysis was performed using SPSS for Windows (v. 12.0.1; Chicago, IL). All data are presented as mean values ± one standard deviation, unless stated otherwise. Variation between the PWV_{MRI} assessments for validation was studied using the Pearson's correlation coefficient (PCC), while variation between the PWV_{MRI} assessments reproducibility was studied using the two-way mixed intraclass correlation (ICC) for absolute agreement and the coefficients of variation (defined as the standard deviation of the differences between the two series of measurements divided by the mean of both measurements). The approach described by Bland and Altman (21) was followed to study systematic differences. Statistical significance on all tests was indicated by $P < 0.05$.

RESULTS

Results of PWV_{MRI} and PWV_{INV} assessment are listed in Table 2.

Validation of PWV_{MRI}

The mean distance for PWVMRI between site 1 (ascending aorta) and site 2 (proximal descending aorta) was 12.0 ± 1.7 cm; the mean distance between site 2 and site 3 (abdominal aorta) was 25.1 ± 3.0 cm. In Fig. 2A–C, values for PWV_{MRI} assessed in the Ao_{total}, Ao_{prox}, and Ao_{dist} are presented versus PWV_{INV}. In Fig. 2D–F, the differences between PWV_{MRI} and PWV_{INV} are presented using Bland–Altman plots. Good agreement between PWV_{MRI} and PWV_{INV} was found (Ao_{total}: PCC = 0.53; Ao_{prox}: PCC = 0.69; Ao_{dist}: PCC = 0.71) (Fig. 2A). No statistically significant bias was found in the Ao_{total} and the Ao_{prox}, except for the Ao_{dist} (mean differences between PWV_{MRI} and PWV_{INV} in Ao_{total}: 0.4 ± 1.0 m/s, $P = 0.08$; in Ao_{prox}: 0.3 ± 1.0 m/s, $P = 0.16$; in Ao_{dist}: 0.8 ± 0.8 m/s, $P < 0.01$). Coefficient of variation was

Table 2
Results of All Participants

Parameters	Group 1	Group 2:	
		First MRI acquisition	Second MRI acquisition
PWV_{MRI} Ao_{total} (m/s)	6.5 ± 1.1	4.3 ± 0.5	4.6 ± 0.7
PWV_{MRI} Ao_{prox} (m/s)	6.5 ± 1.3	4.3 ± 0.9	4.7 ± 1.0
PWV_{MRI} Ao_{dist} (m/s)	6.9 ± 1.1	4.3 ± 0.6	4.4 ± 0.8
PWV_{INV} Ao_{total} (m/s)	6.1 ± 0.8		
PWV_{INV} Ao_{prox} (m/s)	6.2 ± 1.1		
PWV_{INV} Ao_{dist} (m/s)	6.1 ± 1.0		

Group 1: patients for PWV_{MRI} and PWV_{INV} comparison.
Group 2: healthy subjects for reproducibility of PWV_{MRI}-assessment.
Data are expressed as mean ± standard deviation.
MRI, magnetic resonance imaging; PWV_{MRI}, pulse wave velocity as assessed with magnetic resonance imaging; PWV_{INV} , pulse wave velocity as assessed with invasive pressure measurements; Ao_{total}, total aorta; Ao_{prox}, proximal aorta; Ao_{dist}, distal aorta.

16% in the Ao_{total} (confidence interval [CI] between −2.4 and 1.5), 16% in the Ao_{prox} (CI between −2.3 and 1.6) and 13% in the Ao_{dist} (CI between −2.4 and 0.8). In the Bland–Altman plots a trend is present: for high values of PWV_{INV}, PWV_{MRI} seems to be underestimated as compared to the pressure measurements. This trend occurs for the total aorta, as well as for both segments.

Reproducibility of PWV_{MRI}

Reproducibility of PWV assessment with MRI was examined by repeating the examination on the same day. The mean distance between sites 1 and 2 on the first MRI assessment was 9.4 ± 1.5 cm and on the repeated assessment 9.4 ± 1.3 cm, and neither were statistically significantly different (P = 0.84). The mean distance between sites 2 and 3 was 23.0 ± 3.6 cm and on the repeated assessment 22.3 ± 3.5 cm; these were also not statistically significantly different (P = 0.38). The values for repeated PWV_{MRI} assessment in the Ao_{total}, Ao_{prox} and the Ao_{dist} are presented in Fig. 3A; the differences are presented in Fig. 3B. Reproducibility was high, as PWV_{MRI} in the Ao_{total}, Ao_{prox}, and Ao_{dist} showed good intraclass correlation between the repeated examinations (Ao_{total}: ICC = 0.90, $P < 0.01$; Ao_{prox}: ICC = 0.87, $P < 0.01$; Ao_{dist}: ICC = 0.92, $P < 0.01$), with no statistically significant bias (mean difference Ao_{total}: 0.2 ± 0.4 m/s, P = 0.22; mean difference Ao_{prox}: 0.4 ± 0.6 m/s, P = 0.06; mean difference Ao_{dist}: 0.1 ± 0.4 m/s, P = 0.60). Coefficient of variation was 9% in the Ao_{total} (CI between −0.7 and 1.5), 13% in the Ao_{prox} (CI between −0.7 and 0.8), and 9% in the Ao_{dist} (CI between −0.6 and 0.9).

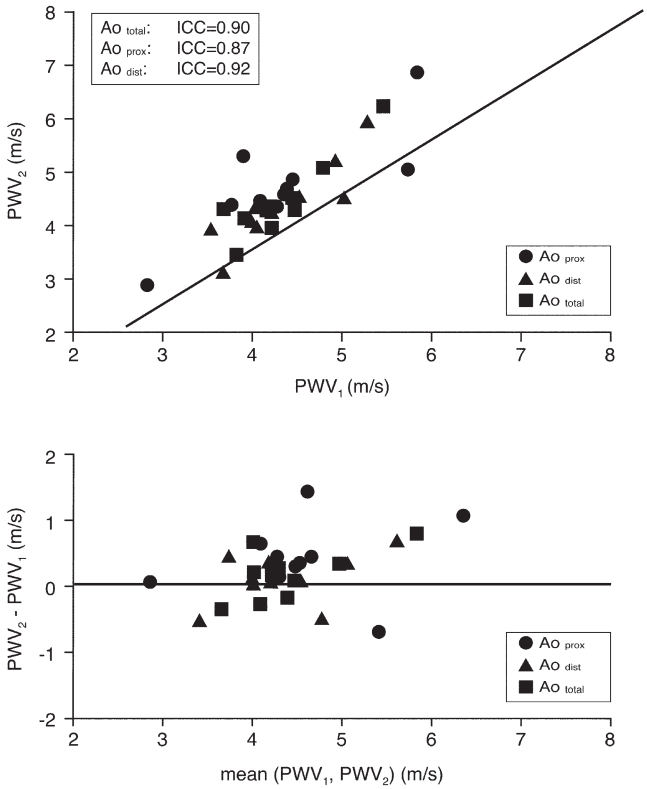

Figure 3. Reproducibility of aortic pulse wave velocity with MRI. **a:** The values for PWV_{MRI} assessment in the proximal, distal, and total aorta for the repeated examination. **b:** The differences using a Bland–Altman plot.

DISCUSSION

The main findings of the current study are: 1) aortic pulse wave velocity as assessed with MRI (PWV_{MRI}) is in good agreement with aortic pulse wave velocity determined from invasive intra-aortic pressure measure-

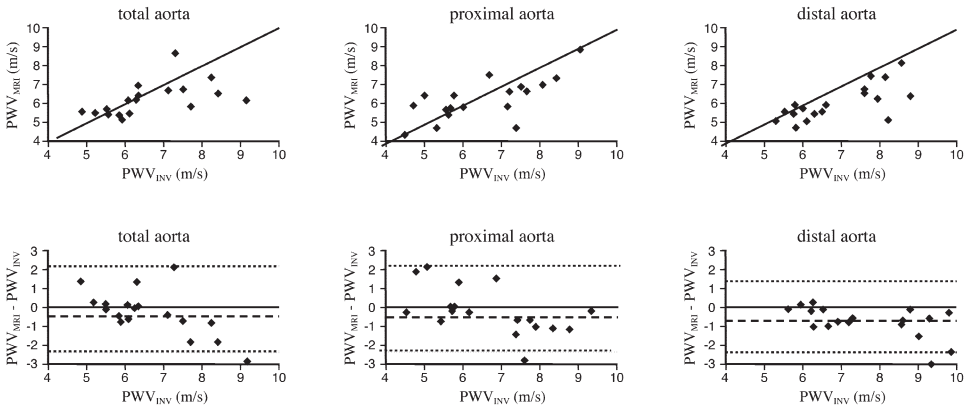

Figure 2. PWV_{MRI} versus PWV_{INV} for the proximal, distal, and total aorta. **a:** Values for PWV_{MRI} assessed in the proximal, distal, and total aorta are shown versus PWV_{INV}. **b:** The differences between PWV_{MRI} and PWV_{INV} are presented using a Bland–Altman plot.

ments (PWV_{INV}); 2) reproducibility is high for PWV_{MRI} assessment of the total aorta, the proximal aorta, and the distal aorta.

Despite numerous reports using MRI to assess the aortic pulse wave velocity (8,10,14,18,19), PWV_{MRI} has not been previously validated in vivo. Bolster et al (14) validated PWV_{MRI} assessment in a flow phantom, showing excellent agreement with PWV_{INV}. However, these modeling conditions do not hold in vivo and limitations should be considered. As the aorta is not a straight tube, the bent shape of the proximal aorta and the multiple branches along the length of the aorta will produce wave reflections that may corrupt pulse wave velocity assessment, affecting both MRI and invasive pressure measurements (16,19). A similar phenomenon occurs in the abdominal aorta, with the abdominal bifurcation producing aortic wave reflections (19). In addition, the number of elastic components of the aorta is known to vary as a function of anatomic position, significantly decreasing from the elastic aortic root to the muscular peripheral vessels (15,22). In this study PWV_{MRI} and PWV_{INV} were acquired 2 weeks apart on average, so physiological variation as part of day-to-day differences in blood pressure, blood flow, and sympathetic tone may have played a role in the found differences (23,24). Also, variation in the heart rate may result in a slight variation in velocity waveforms from cardiac cycle to cardiac cycle, causing errors in the assessed pulse wave velocity (14). Nevertheless, the agreement between PWV_{MRI} and PWV_{INV} was strong in our study, especially for the two measured aortic segments, indicating that PWV_{MRI} is a reliable noninvasive imaging method especially to assess regional aortic PWV. The potential underestimation in PWV_{MRI} due to the underestimation of the measured aortic distance in 2D and not in 3D will increase for longer aortic segments. The curvature of the proximal aorta when compared to the more straight distal aorta is probably a similar potential source of error. Therefore, PWV_{MRI} of the proximal and especially the distal aorta with a shorter aortic path length will probably show less underestimation and better correlation than for the total aorta. Interestingly, PWV_{MRI} of all aortic segments but especially of the distal aorta underestimated the true PWV, as PWV_{MRI} values showed a trend to be lower than the measured PWV_{INV} values.

In this study the onset of the systolic wave front was used to determine the time interval between the subsequent flow and pressure waves. Stevanov et al (19) demonstrated that usage of the onset of the systolic wave front minimizes the disruptive effect of strong wave reflections close to aortic branches, as this feature maintains its identity in the propagating wave. Physiological widening of the aortic waveform and the decrease of the slope of the aortic waveform along the course of the aorta due to wave reflections and damping by the aortic wall will result in artificial prolonging of the time interval between two subsequent acquisition points when the half-heights of the rising systolic flow waveforms or peak-to-peak analysis are used (19).

PWV_{MRI} with repeated examination on the same day showed good agreement in our study, with an acceptable coefficient of variation (between 9% and 13%) and ICC (0.87 or higher). Differences can largely be attributed to physiological variation in PWV (22,23), as all subjects were studied under similar study conditions and our used PWV_{MRI} analysis method was almost operator-independent, with automatic depiction of the onset of systolic waveforms. Given the coefficient of variation between 9% and 13%, a single PWV_{MRI} acquisition may over- or underestimate the representative individual PWV_{MRI} by $\approx$0.5 m/s. As an increase in aortic pulse wave velocity of 1 m/s is associated with a relative risk of all-cause mortality of 1.39 (24), the variation in PWV seems of acceptable relevance in the clinical interpretation of individual results. PWV_{MRI} should therefore preferably be used as an indicative value for clinical purposes, and should be combined with other parameters like elevated blood pressure and MRI-assessed variables such as left ventricular function and left ventricular mass to depict cardiovascular disease (15).

Our study has limitations. PWV_{MRI} assessment is based on cross-sectional data acquisition of the aortic flow, whereas PWV_{INV} data were acquired locally in the aorta, namely, at the tip of the catheter. Another limitation is the difficulty to exactly coregister the acquisition sites for pressure measurements and MRI acquisition, although predefined sites were checked under fluoroscopy guidance. A potential limitation of our used analysis approach for the MRI measurements is related to the used high velocity encoding, as measuring low velocities during the onset of the systolic wave front may become inaccurate due to the increased noise level (25). The precise determination of the onset of the systolic waveform may have been affected, although the high temporal resolution of our used sequence provided a dense set of data points along the course of the resulting flow graph. Depiction of the full course of the aorta with the single-slice scout image may be difficult in the case of advanced stages of atherosclerosis or scoliosis due to elongation and a tortuous course of the aorta. Aortic imaging using 3D MR angiography may be helpful in these cases. PWV_{MRI} and PWV_{INV} were acquired 2 weeks apart on average, so physiological variation as part of day-to-day differences in blood pressure, blood flow, and sympathetic tone may have played a role in the found differences. Further studies are required to assess the value of aortic pulse wave velocity in larger cohorts of patients with vascular disease as well as in patients with different risk profiles.

In conclusion, noninvasive MRI assessment of regional and global aortic pulse wave velocity shows good agreement with the gold-standard as derived by invasive pressure measurements and can be determined with high reproducibility. In the future, evaluation with MRI of shorter aortic segments would allow for even more local identification of aortic vessel wall condition.

ACKNOWLEDGMENTS

No author had any financial interest in the subject matter discussed. No other conflict of interest needs to be disclosed. All authors state that this study complies with the Declaration of Helsinki. The local medical ethics committee approved the study and informed con-

sent was obtained from all participants prior to enrollment in the study.

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