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# The Relationship of Age With Regional Aortic Stiffness and Diameter

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**OBJECTIVES** The purpose of this study was to determine the impact of age on regional aortic pulse wave velocity (aPWV).

**BACKGROUND** aPWV is an independent predictor of cardiovascular risk and increases exponentially with age. However, it is unclear whether such changes occur uniformly along the length of the aorta or vary by region.

**METHODS** A total of 162 subjects, aged 18 to 77 years and free of cardiovascular disease and medication, were recruited from the Anglo-Cardiff Collaborative Trial. Cine phase contrast magnetic resonance imaging was performed at 5 aortic levels. Systolic diameter and average blood flow were measured at each level and regional aPWV (regional aPWV measured by cine phase contrast magnetic resonance imaging) determined in 4 aortic segments: the arch (R1), the thoracic-descending aorta (R2), mid-descending aorta (R3), and the abdominal aorta (R4) and across the entire aorta.

**RESULTS** Regional PWV measured by cine phase contrast magnetic resonance imaging values increased from the valve to the bifurcation in the 4 segments (PWV-R1- PWV-R4: 4.6  $\pm$  1.5 m/s, 5.5  $\pm$  2.0 m/s, 5.7  $\pm$  2.3 m/s, 6.1  $\pm$  2.9 m/s, respectively) and did not differ between genders. The greatest age-related difference in stiffness occurred in the abdominal aorta (+0.9 m/s per decade, p < 0.001) followed by the thoracic-descending region (+0.7 m/s, p < 0.001), the mid-descending region (+0.6 m/s, p < 0.001) and aortic arch (+0.4 m/s, p < 0.001). The average systolic diameters decreased moving distally (L1-5: 3.1  $\pm$  0.4 cm, 2.3  $\pm$  0.3 cm, 2.1  $\pm$  0.3 cm, 1.9  $\pm$  0.2 cm, and 1.7  $\pm$  0.2 cm, respectively). The greatest variation in systolic diameter as a function of age occurred in the ascending region (+0.96 mm/decade, p < 0.001). Values of aPWV measured across the entire aorta were strongly correlated with PWV-tonometry (R = 0.71, p < 0.001), although they were significantly lower (mean difference 1.7  $\pm$  1.6 m/s, p < 0.001).

**CONCLUSIONS** The greatest difference in aortic stiffness occurs in the abdominal region, whereas the greatest difference in diameter occurs in the ascending aorta, which may help offset an increase in wall stiffness. (J Am Coll Cardiol Img 2010;3:1247–55) © 2010 by the American College of Cardiology Foundation

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ging is an important determinant of cardiovascular risk and is associated with a number of changes in the structure and function of the cardiovascular system including the large arteries (1). Although the aorta is often thought of as an inert conduit vessel, it plays a vital role in buffering and smoothing the pulsatile nature of blood flow as it travels to the periphery. With age, the aorta stiffens (2), dilates, and becomes tortuous (3), a process known as arteriosclerosis. Such changes lead to an increase in pulse pressure, which places an additional strain on the aorta and limits its buffering capacity. However, the vast majority of data concerning the impact of age on aortic stiffness come from noninvasive measurements of carotid-femoral pulse wave velocity (PWV). Although this is commonly referred to as aortic PWV (aPWV), this ignores the proximal

### ABBREVIATIONS AND ACRONYMS

**aPWV** = aortic pulse wave velocity

aPWV-Total = aortic pulse wave velocity measured across the entire aorta

MRI = magnetic resonance imaging

**PC-MRI** = cine phase contrast magnetic resonance imaging

**PWV** = pulse wave velocity

**PWV-MRI** = regional pulse wave velocity measured by cine phase contrast magnetic resonance imaging Although this is commonly referred to as PWV (aPWV), this ignores the proximal ascending aortic segment. Because the majority of the buffering capacity of the arterial system resides in the proximal aorta, this omission may have important consequences in understanding the impact of age on the aorta. Moreover, given that the aorta changes considerably in structure over its length, identifying the region of the aorta that stiffens most with age may provide valuable insights into the underlying pathology and an anatomic focus for potential therapeutic intervention. Although agerelated differences in regional aortic stiffness have been reported previously, the results are contradictory, reflecting different methodol-

Cine phase contrast magnetic resonance imaging (PC-MRI) provides a validated, noninvasive method for assessing PWV at any location and allows accurate determination of aortic length. Our aim was to determine the relationship between age and regional aPWV measured by PC-MRI, crosssectionally in a large cohort of healthy individuals and to compare PWV of the entire aorta with the more commonly measured carotid-femoral PWV. A priori, we hypothesized that the greatest agerelated difference in regional aortic stiffness would occur in the abdominal region because we previously described the greatest degree of calcium deposition in this area (4).

ogies and small sample sizes.

# METHODS

Subjects. Subjects were recruited from the Cambridge arm of the Anglo-Cardiff Collaborative Trial, which explores the factors influencing arterial stiffness in a community-based investigation. Subjects were free of clinical cardiovascular disease and medication. Approval was obtained from the local research ethics committee, and written informed consent was obtained from all participants.

Hemodynamics. Brachial blood pressure was measured in duplicate in the nondominant arm, according to the British Hypertension Society Guidelines using a validated oscillometric device (HEM-711A-E, Omron Corp., Matsusaka, Japan). Radial artery waveforms were recorded by applanation tonometry (SphygmoCor, AtCor Medical, Sydney, Australia) and a generalized transfer function applied to generate the corresponding central pressure waveform (5). Carotid-femoral PWV was measured using the SphygmoCor (AtCor Medical) (PWVtonometry) device by sequentially recording electrocardiographic gated carotid and femoral artery waveforms as previously described (6). Simultaneous to image acquisition, carotid-femoral PWV was determined using the Vicorder device (PWVcuff) by placing a 5-mm and a 10-mm cuff around the neck and right thigh, respectively. Cuffs were inflated to 60 mm Hg, and the carotid and femoral pressure waveforms were recorded by a volume displacement method (7).

Magnetic resonance imaging (MRI). Images were acquired using a 1.5-T MRI system (Signa HDx, GE Healthcare, Waukesha, Wisconsin). An 8-channel abdominal/pelvic coil was placed over the subject lying supine, and a blood pressure cuff was placed around the left arm for brachial artery pressure measurement. Three plane localizer images were obtained to identify the ascending and descending aorta through to the bifurcation. A multislice, electrocardiographically triggered, black blood fast spin echo sequence was acquired in an oblique sagittal orientation to demonstrate the full length of the aorta. An electrocardiographically gated, segmented k-space, cine phase contrast sequence (PC-MRI) was used with the following parameters: 30° flip angle, 5-mm slice thickness,  $280 \times 280$ -mm field of view, 6.7 repetition time,  $256 \times 256$  matrix, 2 excitations, and 150 cm/s through-plane velocity encoding, with 1 view per segment. The duration of each sequence was approximately 5 min, with a total acquisition time of approximately 30 min. One hundred temporal phases were retrospectively reconstructed with a true temporal resolution of  $2.0 \times 6.7$  ms due to the interleaved positive and negative velocity encoding.

Protocol. After 10 min of supine rest, blood pressure, radial pressure waveforms, and PWVtonometry were recorded. Subjects fasted for 4 h before measurements, and rested for 20 min before entering the MRI scanner. PC-MRI sequences were then performed perpendicular to the aorta at 5 aortic levels: the ascending aorta (L1), located 1 cm distal to the aortic valve; the descending aorta (L2), in line with L1; at the level of the diaphragm (L3); 3 cm above the level of the aortic bifurcation (L5), and midway between L3 and L5 (L4) (Fig. 1). Regional PWV in the MRI (PWV-MRI) was determined in 4 aortic regions: the arch (R1), the thoracic-descending (R2), mid-descending (R3) and the abdominal (R4) aorta (Fig. 1). Brachial blood pressure was measured in the MRI scanner immediately before each sequence, and PWV-cuff measurement was recorded during image acquisition. Data analysis. Power calculations were made assuming a 1 m/s SD in aPWV as per McEniery et al. (2) and 25 subjects per age group, with 6 age groups. This yielded a power of >95% to detect a difference of 0.5 m/s between any 2 groups. Again, assuming a 1 m/s SD in aPWV and 80 subjects per group, we



Figure 1. Sagittal Image of the Aorta From the Aortic Root to the Level of the Bifurcation

L1 through L5 indicate the level of cine phase contrast magnetic resonance imaging image acquisition, and R1 through R4 indicate the region of pulse wave velocity measurement. had a power of 90% to detect a difference of 0.5 m/s between sexes. Data were analyzed offline using CV Flow software (Medis, Leiden, the Netherlands). Aortic contours were automatically detected in each slice location to obtain aortic flow-time curves and aortic areas through the cardiac cycle. Using the average flow, transit time between flow waves was measured at 10% of the pulse height. In the case of a failure of this method ( $\sim$ 5% of cases), an intersecting tangents algorithm was applied. Both algorithms have previously been proven reliable in detecting the foot of the pressure waveform (8), and the accuracy was improved by the high sampling rate used compared to previous studies (9), which was up-sampled to 1 kHz by interpolation with custom software (version 2.6, Python Software Foundation, Wolfeboro Falls, New Hampshire). Aortic diameters were calculated from the aortic areas, and the maximum systolic diameter at each aortic level was used in the analysis. The distance between each aortic level was measured on the black blood images using a curved line along the center of the aorta. Regional differences in aortic stiffness with age were analyzed using a general linear model, adjusting for sex, heart rate, body mass index, high-density lipoprotein cholesterol, and mean arterial pressure. Regional differences in maximum systolic aortic diameter with age were analyzed using analysis of variance. Repeatability of PWV-MRI was assessed across 2 visits, in a subset of 25 subjects. PWV-MRI over the length of the whole aorta (i.e., from L1 to L5 [PWV-Total]) was compared with PWV-tonometry and PWV-cuff measurements as validation using paired Student ttests. Post-hoc analysis was carried out using the Bonferroni method. Values are reported as the mean  $\pm 1$  SD.

# RESULTS

Hemodynamic measurements were performed in 162 subjects. However, 5 subjects were unable to complete the scan due to claustrophobia. The overall subject characteristics of the 157 subjects with valid data are presented in Table 1. The mean age was 49  $\pm$  17 years and ranged from 18 to 77 years. As expected, changes in PWV-tonometry and PWV-Total were significantly higher in older subjects, such that the age-PWV curves for both were best represented by a second-order polynomial (p < 0.001 for both) (Fig. 2). The average regional PWV-MRI increased from R1 to R4 with mean

Table 1. Subject Characteristics							
	Age Group						
Characteristic	20-29 Yrs	30-39 Yrs	40-49 Yrs	50-59 Yrs	60-69 Yrs	70-79 Yrs	
Age, yrs	$24\pm3$	$34\pm3$	$45\pm2$	$57\pm3$	$63\pm3$	$73\pm2$	
Sex, male/female	11/17	11/12	11/16	13/13	14/16	11/12	
Height, m	$1.71 \pm 0.09$	$1.71\pm0.09$	$1.67\pm0.10$	$1.68\pm0.10$	$1.70\pm0.09$	$1.66\pm0.10$	
Weight, kg	67.0 ± 11.9	73.8 ± 10.5	73.0 ± 15.0	$\textbf{73.4} \pm \textbf{13.3}$	$75.2 \pm 13.4$	$69.2 \pm 10.3$	
BMI, kg/m <sup>2</sup>	$23\pm3$	$25\pm3$	$25\pm4$	$26\pm4$	$26 \pm 4$	$25\pm2$	
BSA, m <sup>2</sup>	$1.8\pm0.2$	$1.9\pm0.2$	$1.8\pm0.2$	$1.8\pm0.2$	$1.9\pm0.2$	$1.8\pm0.2$	
HR, beats/min	$63 \pm 10$	62 ± 7	67 ± 9	$67\pm10$	69 ± 12	$69\pm10$	
Supine systolic BP, mm Hg	$115 \pm 12$	121 ± 7	126 ± 16	$120\pm11$	$130\pm18$	$137\pm19$	
Supine diastolic BP, mm Hg	$70\pm8$	77 ± 5	78 ± 9	$75\pm7$	$78\pm8$	$78\pm12$	
Supine MAP, mm Hg	$85\pm8$	92 ± 5	94 ± 11	$90\pm8$	$95\pm10$	$98\pm13$	
Supine central systolic BP, mm Hg	98 ± 10	$103\pm7$	$112 \pm 13$	$107 \pm 12$	$118\pm15$	$125\pm14$	
Total cholesterol, mmol/l	$\textbf{4.3} \pm \textbf{0.9}$	$4.7\pm0.8$	$5.0\pm0.8$	$5.5\pm1.0$	$5.4 \pm 1.0$	$5.7\pm1.1$	
LDL, mmol/l	$\textbf{2.5}\pm\textbf{0.8}$	$2.7\pm0.5$	$2.9\pm0.7$	$3.4\pm0.9$	$3.4\pm0.7$	$3.6\pm0.8$	
HDL, mmol/l	$1.5\pm0.4$	$1.6\pm0.3$	$1.6\pm0.4$	$2.5\pm4.6$	$1.4 \pm 0.3$	$1.5\pm0.5$	
Glucose, mmol/l	$4.1\pm0.6$	$4.2\pm0.7$	$4.4\pm0.7$	4.5 ± 1.1	4.5 ± 1.0	$4.6\pm0.8$	
BMI = body mass index; BP = blood pressure; BSA = body surface area; HDL = high-density lipoprotein; HR = heart rate; LDL = low-density lipoprotein; MAP = mean arterial pressure.							

values of 4.6  $\pm$  1.5 m/s, 5.5  $\pm$  2.0 m/s, 5.7  $\pm$  2.3 m/s, and 6.1  $\pm$  2.9 m/s, respectively (p < 0.001). There were no differences between sexes.

Age-related variation in PWV. The relationship between regional PWV-MRI and age is shown in Figure 3. The greatest difference in aPWV between young and old subjects was observed in the abdominal aorta (PWV-R4: +0.9 m/s per decade, p <0.001) followed by the thoracic-descending region (PWV-R2: +0.7 m/s, p < 0.001) and the middescending region (PWV-R3: +0.6 m/s, p < 0.001), and the least difference in the aortic arch (PWV-R1: +0.4 m/s per decade, p < 0.001). Using R1 as a reference, post hoc analysis indicated a significant difference between regions (p <

0.001). This trend for a significantly greater increase in PWV with advancing age in the abdominal aorta (p = 0.020) was also seen in the raw unadjusted data and when the analysis was restricted to those age 50 years and older.

Age-related variation in aortic diameter. The average systolic diameters decreased moving distally (L1 to L5:  $3.1 \pm 0.4$  cm,  $2.3 \pm 0.3$  cm,  $2.1 \pm 0.3$  cm,  $1.9 \pm 0.2$  cm, and  $1.7 \pm 0.2$  cm, respectively). Average systolic aortic diameters were greater in male than female subjects at all levels (p < 0.01). Values for L1 to L5 were 3.2  $\pm$  0.3 cm, 2.5  $\pm$  0.2 cm, 2.2  $\pm$ 0.3 cm, 2.0  $\pm$  0.2 cm, and 1.8  $\pm$  0.3 cm in male subjects and  $3.1 \pm 0.4$  cm,  $2.3 \pm 0.3$  cm,  $2.0 \pm 0.4$ cm, 1.8  $\pm$  0.2 cm, and 1.8  $\pm$  0.2 cm in female





subjects. However, when adjusted for body surface area, the difference between sexes was eliminated. Systolic diameter at each aortic level correlated positively with age (r = 0.25 to 0.5, p < 0.001 for all levels). The greatest variation in aortic diameter as a function of age occurred in the ascending aorta, L1 (0.96 mm higher per decade), followed by L3 (0.85 mm higher per decade), L2 (0.78 mm higher per decade), L4 (0.64 mm higher per decade), and L5 (0.37 mm higher per decade, p < 0.001 for all levels) (Fig. 4A). Because, theoretically, increasing diameter offsets the effect of higher wall stiffness on PWV, the wall stiffness was calculated using the Moens-Korteweg equation, assuming a constant wall thickness. Although wall thickness does increase with age, this is a very modest change, and this effect in our population was minimized by the inclusion of only healthy individuals. The impact of age on wall stiffness was very similar to that observed for aPWV, with the largest difference in the abdominal aorta and least in the proximal region (data not shown).

Age-related variation in aortic length. The average regional aortic lengths from R1 to R4 were  $108 \pm 21 \text{ mm}$ ,  $116 \pm 19 \text{ mm}$ ,  $79 \pm 13 \text{ mm}$ , and  $79 \pm 13 \text{ mm}$ , respectively. The whole aorta was longer in

older subjects (8 mm/decade, r = 0.36, p < 0.001). This was entirely due to the longer length of the aortic arch (R1) (8 mm longer per decade, p < 0.001), as the other aortic segments remained constant with age (Fig. 4B). This trend remained when aortic length was adjusted for height and for body surface area.

Age-related variation in central blood pressure. As expected, the central systolic blood pressure and central pulse pressure were greater in older subjects (p < 0.001). Additionally, central systolic blood pressure and central pulse pressure were correlated with PWV-Total in all aortic regions (r = 0.3 to 0.2, p < 0.001). Central systolic blood pressure was correlated with aortic diameter at all levels (r = 0.3to 0.2, p < 0.05).

**Repeatability and validation of PWV-MRI.** There was good agreement between repeated values of PWV-MRI (mean difference  $0.1 \pm 2.3$  m/s), and the trends remained consistent across all aortic regions. Values of PWV-Total were strongly correlated and in good agreement with both PWV-tonometry, and PWV-cuff measurements (Fig. 5, Table 2). However, there was an offset between the measurements and overall PWV-Total was significantly lower than both PWV-tonometry and PWV-cuff mea-





other regions.

surement (Table 2). When the data were reanalyzed to exclude the proximal segment of the aorta by calculating PWV-Total measured from L2 to L5, the mean value of PWV-Total was increased and the mean difference between devices was reduced, but remained significant. Moreover, the strong correlation with PWV-tonometry and PWV-cuff measurements remained (Table 2).



(A) Correlation between carotid-femoral pulse wave velocity (PWV) measured with the SphygmoCor device (AtCor Medical) (PWV-tonometry) and aortic PWV across the entire aorta (PWV-Total) (r = 0.71, p < 0.001). (C) Correlation between carotid-femoral PWV measured with the Vicorder system (PWV-cuff) and PWV-Total (r = 0.64, p < 0.001). Corresponding Bland-Altman plots (B and D).

Table 2. Values of PWV and Comparisons of Devices									
Measurement	Mean Value (m/s) ± 2								
PWV-Total (L1–L5)	5.7 ± 1.8								
PWV-Total, arch excluded (L2–L5)	$\textbf{6.3} \pm \textbf{2.7}$								
PWV-Tonometry	$7.3\pm1.8$								
PWV-Cuff	7.1 ± 1.4								
Comparison	Correlation (R Value)	Significance	Mean Difference (m/s)	Significance					
PWV-Total vs. PWV-tonometry	0.71	p < 0.001	1.7 ± 1.6	p < 0.001					
PWV-Total vs. PWV-cuff	0.64	p < 0.001	$1.4\pm1.7$	p < 0.001					
PWV-Total, arch excluded, vs. PWV-tonometry	0.68	p < 0.001	$0.9\pm1.9$	p < 0.001					
PWV-Total, arch excluded, vs. PWV-cuff	0.59	p < 0.001	$0.7\pm2.3$	p < 0.01					
PWV-Total vs. central systolic blood pressure	0.53	p < 0.001							
PWV-Total vs. central pulse pressure	0.53	p < 0.001							
PWV = pulse wave velocity; PWV-cuff = carotid-femoral pulse wave velocity measured by Vicorder; PWV-topometry = carotid-femoral pulse wave velocity									

PWV = pulse wave velocity; PWV-cuff = carotid-femoral pulse wave velocity measured by Vicorder; PWV-tonometry = carotid-femoral pulse wave velocity measured by SphygmoCor (AtCor Medical); PWV-total = aortic pulse wave velocity across the entire aorta measured by magnetic resonance imaging.

### DISCUSSION

The main findings of the current study are that age differentially affects regional aortic stiffness. The greatest age-related difference in regional aPWV was observed in the distal aorta and the least in the aortic arch. Conversely, the greatest difference in systolic diameter and length between old and young subjects was seen in the aortic arch, which may, in part, be compensatory, maintaining capacitance in the face of increased wall stiffness.

aPWV, usually assessed by surface measurements between the carotid and femoral sites increases exponentially with advancing age (2). However, only limited data are available on regional differences within the aorta. O'Rourke et al. (10) reported a greater rate of stiffening in the distal aorta using invasive catheter measurements. In contrast, more recent studies using PC-MRI found that the greatest decrease in aortic distensibility and increase in PWV occurred in proximal aorta (11–13).

In the current study, we used PWV as a measure of vessel stiffness. As expected, the stiffness of the whole aorta was greatest in older subjects, and the impact of age was most marked in those older than 50 years of age, in keeping with previous observations (2,14). In terms of regional stiffness, PWV in the abdominal aorta was 2.4-fold greater in the eighth compared with the third decade of life, but only a 1.9-fold greater in the aortic arch. This trend persisted even when analysis was restricted to subjects older than 50 years of age. Although these data disagree with previous data, our study is the largest MRI-based study to date to explore age-related differences in regional aortic stiffness and encompasses a much wider age range at a higher sampling rate than previous studies. In keeping with previous studies (12,15-17), and contrary to PWV, the greatest age-related differences in aortic diameter and length occurred in the proximal aorta. This dilation may help to offset the wall stiffening by maintaining the capacity of the aorta to store volume during systole. However, in the context of an increased vessel diameter, PWV may underestimate changes in intrinsic wall material stiffness. PWV is directly proportional to the square root of wall thickness and indirectly proportional to the square root of the radius. Therefore, any increase in diameter without a proportional increase in vessel wall thickness will offset an increase in PWV. We therefore determined the effect of aging on estimated wall stiffness calculated from the Moens-Korteweg equation and found a very similar pattern to that observed for PWV, with the largest increase in the abdominal aorta and least in the proximal region.

We found PC-MRI to be repeatable method for determining aPWV, in keeping with the findings of others (12,18,19). Additionally, PWV-Total values were similar to those previously observed (12,20-23) and were closely correlated with values of carotid-femoral PWV. Although PWV-Total was on average lower than both PWV-tonometry and PWV-cuff, this may be explained by 1 or a combination of factors. Surface measurements of carotidfemoral PWV require that path length be determined from anatomic landmarks on the body, which may overestimate the actual arterial path length, increasing the calculated PWV. Additionally, carotid-femoral PWV measurements include segments of the carotid, iliac, and femoral arteries, which are stiffer than the aorta (24,25). Therefore,

the value of carotid-femoral PWV would be higher than that of the aorta itself. Measurements of carotid-femoral PWV also omit the aortic arch (26). Therefore, we examined the impact of excluding this highly elastic region. As might be expected, this reduced the difference and improved the agreement with both PWV-tonometry and PWV-cuff. Because PWV in the proximal segment of the aorta showed the smallest association with an older age, in healthy individuals, ignoring the aortic arch in measuring carotid-femoral PWV may well be of little clinical importance, but the potential impact due to other risk factors needs to be addressed.

One of the main hypotheses explaining aortic stiffening is related to fatigue fracture of the elastin fibers. This is likely to occur in the proximal aorta where these fibers are most prominent. However, it does not explain the greater PWV with advancing age observed in the abdominal aorta, which is made up of a much larger proportion of collagen and smooth muscle fibers (27,28). Stiffening in this distal segment may be caused by localized calcium deposition, which has previously been reported in this region and is strongly correlated with increasing aPWV (4). This may also be of particular significance as abdominal aortic calcium deposits have been linked with the presence of calcified plaques in the coronary arteries (29) and independently predict cardiovascular morbidity and mortality (30). Therefore, targeting therapeutic strategies to the abdominal region of the aorta may be useful in slowing the process of aortic stiffening and have an impact in reducing overall cardiovascular risk.

Study limitations. One limitation to the present study is its cross-sectional design, and further longitudinal studies are desirable to confirm which aortic region truly stiffens most with age. Moreover, given that the study population was composed of healthy individuals, further studies in subjects with underlying disease and increased cardiovascular risk are also desirable to determine the pathophysiological influence on the changes in regional aortic stiffness. In addition, although measurements of regional PWV-MRI were repeatable, the SD of the values was somewhat wide. This in part may be explained by day-to-day variations in confounding factors such as blood pressure and heart rate, which are likely to have been different as measurements were taken across 2 visits on separate days at varying times. Finally, we were unable to calculate distensibility because the PC-MRI sequence that we used was suboptimal to measure diastolic diameter accurately.

Overall, PWV measured with PC-MRI correlates well with carotid-femoral PWV and is repeatable, establishing it as a useful tool for assessing regional aortic stiffening. The largest age-related difference in PWV was seen in the abdominal aorta, whereas the greatest difference in systolic diameter and length occurred in the proximal aorta. The latter may help to offset an increase in wall stiffness and maintain capacitance in this region.

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### REFERENCES

- 1. Lakatta EG, Levy D. Arterial and cardiac aging: major shareholders in cardiovascular disease enterprises: Part I: aging arteries: a "set up" for vascular disease. Circulation 2003; 107:139-46.
- McEniery CM, Yasmin, Hall IR, Qasem A, Wilkinson IB, Cockcroft JR. Normal vascular aging: differential effects on wave reflection and aortic pulse wave velocity: the Anglo-Cardiff Collaborative Trial (ACCT). J Am Coll Cardiol 2005;46:1753–60.
- 3. Nichols WW, O'Rourke MF. McDonald's Blood Flow in Arteries: Theoretical, Experimental and Clini-

cal Principles. 5th ed. London, United Kingdom: Arnold, 2005.

- 4. McEniery CM, McDonnell BJ, So A, et al. Aortic calcification is associated with aortic stiffness and isolated systolic hypertension in healthy individuals. Hypertension 2009;53: 524–31.
- Karamanoglu M, O'Rourke MF, Avolio AP, Kelly RP. An analysis of the relationship between central aortic and peripheral upper limb pressure waves in man. Eur Heart J 1993;14: 160–7.
- Wilkinson IB, Fuchs SA, Jansen IM, et al. Reproducibility of pulse wave velocity and augmentation index measured by pulse wave analysis. J Hypertens 1998;16:2079–84.
- Hickson SS, Butlin M, Broad J, Avolio AP, Wilkinson IB, McEniery CM. Validity and repeatability of the Vicorder apparatus: a comparison with the SphygmoCor device. Hypertens Res 2009;32:1079–85.
- Hermeling E, Reesink KD, Reneman RS, Hoeks AP. Measurement of local pulse wave velocity: effects of signal processing on precision. Ultrasound Med Biol 2007;33:774-81.
- Boonyasirinant T, Rajiah P, Setser RM, et al. Aortic stiffness is increased in hypertrophic cardiomyopathy with myocardial fibrosis: novel insights in vascular function from magnetic resonance imaging. J Am Coll Cardiol 2009;54:255–62.

- O'Rourke MF, Blazek JV, Morreels CL, Jr., Krovetz LJ. Pressure wave transmission along the human aorta. Changes with age and in arterial degenerative disease. Circ Res 1968;23: 567–79.
- 11. Nelson AJ, Worthley SG, Cameron JD, et al. Cardiovascular magnetic resonance-derived aortic distensibility: validation and observed regional differences in the elderly. J Hypertens 2009;27:535–42.
- 12. Rogers WJ, Hu YL, Coast D, et al. Age-associated changes in regional aortic pulse wave velocity. J Am Coll Cardiol 2001;38:1123–9.
- 13. Redheuil A, Yu WC, Wu CO, et al. Reduced ascending aortic strain and distensibility: earliest manifestations of vascular aging in humans. Hypertension 2010;55:319–26.
- 14. Mitchell GF, Parise H, Benjamin EJ, et al. Changes in arterial stiffness and wave reflection with advancing age in healthy men and women: the Framingham Heart Study. Hypertension 2004;43:1239–45.
- 15. Virmani R, Avolio AP, Mergner WJ, et al. Effect of aging on aortic morphology in populations with high and low prevalence of hypertension and atherosclerosis. Comparison between occidental and Chinese communities. Am J Pathol 1991;139:1119–29.
- Hager A, Kaemmerer H, Rapp-Bernhardt U, et al. Diameters of the thoracic aorta throughout life as measured with helical computed tomography. J Thorac Cardiovasc Surg 2002; 123:1060–6.
- 17. Sugawara J, Hayashi K, Yokoi T, Tanaka H. Age-associated elongation

of the ascending aorta in adults. JACC Cardiovasc Imaging 2008;1: 739–48.

- Joly L, Perret-Guillaume C, Kearney-Schwartz A, et al. Pulse wave velocity assessment by external noninvasive devices and phase-contrast magnetic resonance imaging in the obese. Hypertension 2009;54:421–6.
- Grotenhuis HB, Westenberg JJ, Steendijk P, et al. Validation and reproducibility of aortic pulse wave velocity as assessed with velocityencoded MRI. J Magn Reson Imaging 2009;30:521-6.
- 20. Groenink M, de RA, Mulder BJ, Spaan JA, van der Wall EE. Changes in aortic distensibility and pulse wave velocity assessed with magnetic resonance imaging following beta-blocker therapy in the Marfan syndrome. Am J Cardiol 1998;82:203–8.
- Mohiaddin RH, Firmin DN, Longmore DB. Age-related changes of human aortic flow wave velocity measured noninvasively by magnetic resonance imaging. J Appl Physiol 1993;74:492–7.
- 22. Vulliemoz S, Stergiopulos N, Meuli R. Estimation of local aortic elastic properties with MRI. Magn Reson Med 2002;47:649–54.
- 23. Yu HY, Peng HH, Wang JL, Wen CY, Tseng WY. Quantification of the pulse wave velocity of the descending aorta using axial velocity profiles from phase-contrast magnetic resonance imaging. Magn Reson Med 2006;56: 876–83.
- Latham RD, Westerhof N, Sipkema P, Rubal BJ, Reuderink P, Murgo JP. Regional wave travel and reflec-

tions along the human aorta: a study with six simultaneous micromanometric pressures. Circulation 1985; 72:1257–69.

- 25. McDonald DA. Regional pulse-wave velocity in the arterial tree. J Appl Physiol 1968;24:73–8.
- 26. Mitchell GF. Arterial stiffness and wave reflection: biomarkers of cardiovascular risk. Artery Res 2009;3: 56-64.
- 27. Halloran BG, Davis VA, McManus BM, Lynch TG, Baxter BT. Localization of aortic disease is associated with intrinsic differences in aortic structure. J Surg Res 1995;59:17–22.
- Schlatmann TJ, Becker AE. Histologic changes in the normal aging aorta: implications for dissecting aortic aneurysm. Am J Cardiol 1977;39: 13–20.
- Eggen DA, Strong JP, Mcgill HC, Jr. Calcification in the abdominal aorta, relationship to race, sex, and coronary atherosclerosis. Arch Pathol 1964;78: 575–83.
- Wilson PW, Kauppila LI, O'Donnell CJ, et al. Abdominal aortic calcific deposits are an important predictor of vascular morbidity and mortality. Circulation 2001;103:1529–34.

**Key Words:** aging • aortic diameter • cine phase contrast magnetic resonance imaging • regional aortic pulse wave velocity.