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Assessment of regional aortic stiffness with cardiac magnetic resonance imaging in a healthy Asian population

Eun Kyoung Kim · Sung-A Chang ·
Shin Yi Jang · Yiseul Kim · Sung Mok Kim ·
Jae K. Oh · Yeon Hyeon Choe · Duk-Kyung Kim

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Abstract The aim of this study was to determine the normal values for aortic pulse wave velocity (PWV) and distensibility using cine and phase contrast cardiac magnetic resonance imaging (CMRI) in patients without cardiovascular risk factors. PWV and distensibility are indispensible predictors of global and regional cardiovascular risk. Regional heterogeneity in aortic stiffness plays an important role in the pathogenesis of cardiovascular disease. Contrary to global estimates of aortic PWV that are commonly measured with tonometry, CMRI has emerged as an important method for estimating regional PWV and distensibility. A total of 124 Korean patients, aged 20–79 years and free of cardiovascular risk factors, were categorized by age decade. Using cine and phase contrast sequences, the cross-sectional area for distensibility and average blood flow were measured at four aortic levels: the ascending, upper descending thoracic, lower thoracic and abdominal aorta. Regional PWV was determined in four aortic segments: proximal, descending thoracic, abdominal aorta and across the entire aorta. Distensibility at the four levels of the aorta from the ascending to distal $(4.4 \pm 2.5, 4.0 \pm 1.6, 5.2 \pm 1.9, \text{ and } 3.3 \pm 1.7 \times 10^{-3} \text{ mm/Hg, respectively)}$ was higher in women (P < 0.001) and decreased with age. The regional PWV was highest in the descending thoracic aorta and increased with age. The present study is the first to show the heterogeneity in aortic PWV and distensibility, as well to provide normal values for these parameters using CMRI in an Asian sample.

Keywords Aortic stiffness · Pulse wave velocity · Distensibility · Magnetic resonance imaging

Introduction

Arterial stiffness represents the degree of vessel wall firmness that results from aging-related vascular degeneration or decreased elasticity from pathological conditions. Arterial stiffness is generally accepted as an indispensible predictor of cardiovascular risk [1, 2]. As a large conduit for pulsatile blood

Eun Kyoung Kim, Sung-A Chang: contributed equally to this work.

E. K. Kim \cdot S.-A. Chang \cdot S. Y. Jang \cdot J. K. Oh \cdot D.-K. Kim Division of Cardiology, Department of Medicine, Cardiovascular Imaging Center, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

Y. Kim · S. M. Kim · Y. H. Choe Department of Radiology and Center for Imaging Science, Cardiovascular Imaging Center, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

J. K. Oh Division of Cardiovascular Diseases, Mayo Clinic College of Medicine, Rochester, MN, USA Y. H. Choe (⊠)

Department of Radiology, Cardiac and Vascular Center, Samsung Medical Center, Sungkyunkwan University School of Medicine, #81 Irwon-ro, Gangnam-gu, Seoul 135-710, Republic of Korea e-mail: yhchoe@skku.edu

D.-K. Kim (⊠)

Department of Medicine, Cardiac and Vascular Center, Samsung Medical Center, Sungkyunkwan University School of Medicine, #81 Irwon-ro, Gangnam-gu, Seoul 135-710, Republic of Korea

e-mail: dkkim@skku.edu



flow, a stiffened aorta results in increased blood flow velocity and causes premature reflected waves from the peripheral arteries to the aorta. When systolic blood pressure increases due to the premature reflection of blood pressure, aortic pulse pressure increases, as does cardiovascular morbidity and mortality, including stroke and myocardial infarction [3–5].

Because the aorta changes considerably in structure over its length, stiffness differs across the length of the aorta. Several studies have demonstrated that a stiffened ascending aorta may affect diastolic heart function by increasing the afterload of the left ventricle or through the development of aortic dilatation and dissection in Marfan syndrome (MFS) [6-8]. The risk of dissection and aneurysm in MFS is highly associated with pathology in the proximal ascending aorta [9]. Dilatation and increased stiffness of the thoracic and abdominal aortas predispose patients to aortic aneurysm and rupture [10]. Such biophysical properties of the aorta may be of additional prognostic value for a rtic dilatation, dissection, and rupture in aortic degenerative disease and may contribute to risk stratification in patients at risk for aortic complications [11]. Considering the regional heterogeneity of the aorta, identifying the stiffened region may further our understanding of the pathophysiology of the underlying disease and enhance our ability to predict proper intervention sites.

Aortic distensibility and pulse wave velocity (PWV) are useful parameters for assessing regional aortic stiffness. Distensibility is the ability of the aorta to expand during systole and can be calculated based on relative changes in the cross-sectional area of the vessel. PWV is the propagation speed of the pressure, or the velocity wave along the artery, and can be estimated by measuring the distance and transit times separating two locations [12].

Although applanation tonometry is the most widely established modality for the quantification of vascular function [13–15], it can only provide a global estimate of PWV over the whole aorta. Tonometry uses body surface length and considers neither the proximal ascending aorta, which has a major role in vascular buffering, nor the tortuosity of the vessel. Furthermore, a regional assessment of the aorta is impossible with peripheral PWV.

Recently, cardiac magnetic resonance imaging (CMRI) has emerged as an attractive modality for assessing PWV and distensibility because of its ability to visualize the real aortic length and to identify regional stiffness [16–18]. However, the wider implementation of CMRI in the measurement of aortic stiffness in clinical practice has been hampered by a lack of established norms and by the absence of a standardized calculation system.

The aims of this study were two-fold. First, we sought to determine normal ranges for regional aortic PWV and distensibility in Asians with no cardiovascular risk factors. Second, we evaluated for changes in different demographic groups using cine and phase contrast CMRI.



Study population

We enrolled 124 participants (63 women and 61 men) with the intent to include a minimum of ten participants per age decade between the ages of 20 and 70 years. Recruitment was accomplished through local advertisements. All participants were informed of the study protocol and provided written informed consent. Participants were excluded from the study if their PWV or distensibility measurements were unavailable due to poor MRI, if they had hypertension, diabetes or cardiovascular disease, including an old myocardial infarction, valve disease or congenital heart disease. Baseline brachial blood pressure, height, and weight were recorded in all participants.

Cardiac magnetic resonance imaging

Cardiac magnetic resonance imaging was performed using a 1.5-Tesla scanner (Magnetom Avanto, Syngo MR; Siemens Medical Solutions, Erlangen, Germany). Axial localizer images were used to visualize the position of the ascending and descending aorta. Black blood spine echo sequences were acquired in the oblique sagittal orientation to demonstrate the full length of the aorta. Three plane localizer images were obtained to identify the ascending and descending aorta through the bifurcation. The level of the ascending aorta ended at 4 cm from the upper aortic valve and the upper descending thoracic aorta at the level of the bifurcation of the pulmonary artery. The image plane was perpendicular to the longitudinal axis of the aorta. The lower descending thoracic aorta obtained at the level of the diaphragm and the abdominal aorta was determined just above the iliac bifurcation. After the acquisition of a series of thoracic survey images that were used for planning purposes, four consecutive velocity-encoded MRI acquisitions were performed with breath-hold and retrospective gating. The maximal encoding velocity was 200 cm/s and the temporal resolution was 30-40 frames/beat. The total acquisition time for these sequences was approximately 20 min. Cine imaging was also performed at the same levels as those for the MRI to measure aortic stiffness. Before and after scanning each aortic level, non-invasive blood pressure monitoring at the brachial artery was performed and the average measurement used for calculations of regional aortic distensibility.

MR imaging analysis

Analyses of the MRIs were performed using commercial software (Argus version 4.02; Siemens Medical Systems, Germany) by experienced observers blinded to patient



information. From the velocity-encoded MRIs, aortic contours were automatically detected and manually adjusted in each slice area throughout the cardiac cycle. The transit time between the flow curves of each region of the aorta was determined from the midpoint of the systolic up-slope on the flow versus time curve [19]. The up-slopes were identified by drawing a line from the points of 40-60 % maximum velocity on the waveform. The distance between each aortic level was measured on black blood images using a curved line along the center of the aorta. Based on these data, the regional PWV was calculated as the ratio of the distance between levels and the time differences between the arrivals of the pulse wave at each level. Consequently, the PWV of the entire aorta was determined, in addition to the PWV of each of the three segments of the aorta.

To measure regional distensibility, the systolic and diastolic cross-sectional areas were measured by manual contouring of the aorta through the cardiac cycle on the cine image. Distensibility (D) at the four regions was calculated as the mean of the following equation:

 $D = (Amax - Amin)/\{Amin \times (Pmax - Pmin)\}(mm/Hg)$, where Amax is the maximal (systolic) aortic area, Amin is the minimal (diastolic) aortic area, Pmax is the systolic blood pressure, and Pmin is the diastolic blood pressure.

Statistical analysis

All statistical analyses were performed using the PASW version 17.0 statistical analysis software (SPSS Inc., Chicago, IL, USA). Participant characteristics at baseline are provided as means with standard deviations for continuous variables and percentages for discrete variables. Mean

PWV and distensibility values were compared with parametric (paired t tests) and nonparametric (Wilcoxon) tests when appropriate. The relationships between age and the various aortic parameters were studied using linear regression models. Observer agreement was quantified using concordance correlation coefficients. The threshold for statistical significance was P < 0.05.

Results

Participant characteristics, including hemodynamic measurements, are presented in Table 1. The mean age was 43 ± 13 years and ranged from 20 to 69 years. Although height decreased moderately with age, the trends for sex, weight, heart rate and blood pressure were not significantly different across age groups.

Normal values for distensibility

Normal values for regional aortic distensibility as measured by CMRI are presented in Table 2. Distensibility differed significantly by region of the aorta. In most age decades, the maximum aortic distensibility was noted at the lower descending thoracic aorta and the minimal distensibility at the abdominal aorta. The average regional distensibilities from the ascending to the distal aorta were 4.5 ± 2.5 , 4.0 ± 1.6 , 5.2 ± 1.9 , and $3.3 \pm 1.7 \times 10^{-3}$ mm/Hg (P < 0.0001).

Distensibility was significantly higher in females for all levels of the aorta (P < 0.05 for all levels). Aortic distensibility demonstrated a significant inverse linear correlation

Table 1 Participant characteristics at baseline

	20-29 years (n = 26)	30-39 years (n = 28)	40-49 years (n = 24)	50–59 years (n = 25)	60–69 years (n = 21)
Age, years	25.5 ± 2.3	35.7 ± 3.1	42.9 ± 2.9	53.2 ± 2.6	62.6 ± 2.4
Male, n (%)	12 (46.2)	16 (57.1)	11 (45.8)	12 (48.0)	10 (47.6)
Female, n (%)	14 (53.8)	12 (42.9)	13 (54.2)	13 (52.0)	11 (52.4)
Height (cm)	171.1 ± 8.9	168.0 ± 8.2	166.9 ± 7.2	163.2 ± 8.0	160.1 ± 8.0
Weight (kg)	63.1 ± 11.7	64.3 ± 13.0	63.6 ± 9.8	63.3 ± 9.0	60.7 ± 8.3
BMI (kg/m ²)	21.4 ± 2.2	22.6 ± 3.3	22.8 ± 3.1	23.7 ± 3.1	23.6 ± 2.2
BSA (m ²)	1.7 ± 0.2	1.7 ± 0.2	1.7 ± 0.1	1.7 ± 0.1	1.6 ± 0.2
SBP (mm/Hg)	115.2 ± 12.1	116.4 ± 15.0	119.2 ± 13.1	127.1 ± 14.6	126.6 ± 14.8
DBP (mm/Hg)	70.0 ± 6.6	71.5 ± 11.9	73.4 ± 11.4	79.2 ± 8.2	77.2 ± 8.3
Pulse pressure (mm/Hg)	45.7 ± 8.1	44.9 ± 7.0	45.8 ± 6.7	47.8 ± 8.1	49.6 ± 8.0
Mean BP (mm/Hg)	92.4 ± 8.8	93.9 ± 13.1	96.3 ± 11.8	103.1 ± 11.1	102.3 ± 11.2
Heart rate (beats/min)	70.0 ± 11.6	70.0 ± 8.9	68.4 ± 8.8	67.6 ± 12.0	68.7 ± 10.1

BMI body mass index, BSA body surface area, BP blood pressure, SBP systolic blood pressure, DBP diastolic blood pressure



Table 2 Normal values for regional aortic distensibility

Distensibility (10 ⁻³ mm/Hg)	Male (n = 61)	Female (n = 63)	P
D1			
20-29 years	5.60 ± 1.45	7.94 ± 3.43	< 0.0001
30-39 years	3.56 ± 1.39	6.46 ± 3.04	
40-49 years	3.53 ± 1.50	5.29 ± 1.24	
50-59 years	3.23 ± 1.62	3.64 ± 1.09	
60-69 years	2.09 ± 1.33	2.68 ± 1.02	
D2			
20-29 years	4.19 ± 0.93	5.96 ± 1.42	< 0.0001
30-39 years	3.80 ± 1.26	5.54 ± 1.89	
40-49 years	3.33 ± 0.57	4.19 ± 1.17	
50-59 years	2.88 ± 1.13	3.73 ± 1.28	
60-69 years	2.26 ± 0.88	3.07 ± 0.91	
D3			
20-29 years	5.77 ± 0.94	7.66 ± 1.67	0.0040
30-39 years	4.94 ± 1.69	6.60 ± 1.15	
40-49 years	4.97 ± 1.59	5.88 ± 1.25	
50-59 years	4.04 ± 1.96	3.96 ± 1.22	
60-69 years	3.19 ± 1.31	3.75 ± 1.41	
D4			
20-29 years	3.36 ± 1.30	5.72 ± 1.38	< 0.0001
30-39 years	2.77 ± 0.84	5.04 ± 1.80	
40-49 years	2.94 ± 0.83	3.55 ± 1.31	
50-59 years	2.33 ± 1.33	2.54 ± 1.04	
60–69 years	1.48 ± 0.67	2.15 ± 1.25	

DI distensibility of the ascending aorta at the level of bifurcation of the pulmonary artery; D2 distensibility of the upper descending thoracic aorta at the level of bifurcation of the pulmonary artery; D3 distensibility of the lower descending thoracic aorta at the level of the diaphragm; D4 distensibility of the abdominal aorta just above the iliac bifurcation

with aging (r = 0.69–0.72, P < 0.0001 for all levels). The trends according to age and sex remained consistent across all aortic regions. Interestingly, the discrepancy in distensibility between sexes diminished after 50 years of age for all levels of the aorta (Fig. 1). The normal range and the

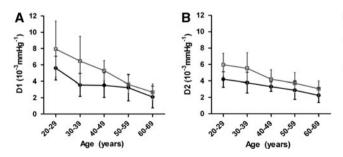


Fig. 1 a Relationships between age, sex and regional aortic distensibility of the ascending aorta at the level of the bifurcation of the pulmonary artery. **b** The upper descending thoracic aorta at the level

best fit between age and distensibility accounting for sex differences are shown in Fig. 2 and Table 3.

Normal values for PWV

Normal values for PWV as measured by CMRI and the regional heterogeneity are presented in Table 4 and Fig. 3. The PWV of the aorta increased with age and changes in PWV were significantly greater in older participants, which was well represented by a second-order polynomial (PWV-total = $5.27-0.08 \times age+0.005 \times age^2$, $R^2=0.55$, P<0.001). There were no significant differences in PWV values between sexes.

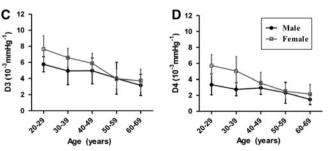
The average regional PWV was greatest in the lower descending thoracic segment (PWV-Region 1 to PWV-Region 3: 5.9 ± 3.6 , 7.4 ± 4.5 , 5.5 ± 2.6 m/s). The greatest difference in PWV according to age was observed at the proximal segment, including the ascending, arch and upper descending thoracic aorta (r = 0.63, P < 0.001). The PWV of the proximal segment correlated with PWV-total throughout the whole aorta (r = 0.81, P < 0.001). Age-related changes in abdominal aortic PWV were the smallest of all regions of the aorta.

In accordance with the theory proposed by Bramwell and Hill [20], the entire aortic PWV was inversely correlated with distensibility at all levels of the aorta (r = -0.519 to -0.673, all P < 0.001) (Fig. 4).

Good correlations for inter-observer variability were obtained for both PWV and distensibility. The reliability of aortic distensibility and PWV estimates between the three observers were excellent [concordance correlation coefficient; 0.96 (0.87–0.99) for D1, 0.92 (0.78–0.97) for D2, 0.88 (0.71–0.95) for D3, 0.90 (0.80–0.98) for D4 and 0.94 (0.78–0.99) for PWV-total].

Discussion

Measurements of aortic stiffness using CMRI facilitate the demonstration of regional heterogeneity of the aorta [21].



of the bifurcation of the pulmonary artery. ${\bf c}$ The lower descending thoracic aorta at the level of the diaphragm. ${\bf d}$ The abdominal aorta just above the iliac bifurcation



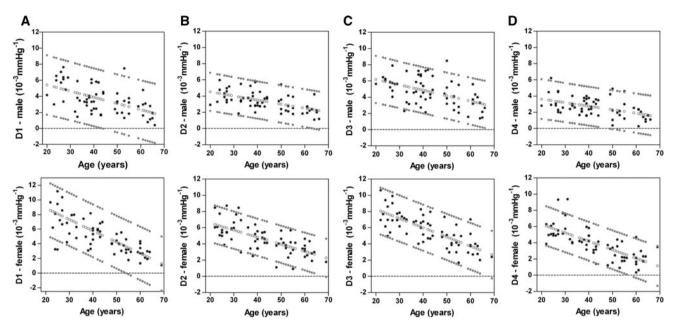


Fig. 2 Normal ranges for aortic distensibility according to age and sex were expressed using regression equations and 95 % confidence intervals for each region of the aorta. **a** Distensibility of the ascending aorta at the level of bifurcation of the pulmonary artery.

b Distensibility of the upper descending thoracic aorta at the level of bifurcation of the pulmonary artery. **c** Distensibility of the lower descending thoracic aorta at the level of diaphragm. **d** Distensibility of the abdominal aorta just above the iliac bifurcation

Identifying the stiffest regions provides valuable insight into any underlying pathology and may help focus therapy or choose a more efficacious therapy. While values for PWV and distensibility as measures of regional aortic stiffness using CMRI have been reported, their use has been limited because reliable reference values are lacking. One significant contribution of the current study is the establishment of normal values for distensibility and PWV for different regions of the aorta by CMRI analysis. Our results demonstrate that aortic distensibility decreases and PWV increases with aging. Considering that age differentially affects regional aortic stiffness, normal values are presented as an age and region-specific range.

The proximal portions of the ascending arch, and the upper descending thoracic aorta demonstrated the greatest differences in PWV between young and old adults. The PWV of the proximal aorta was slowest among all regions until 50 years, whereas adults older than 50 had a rapidly increasing PWV. The PWV highest values were observed in adults older than 60. These changes correlated strongly with PWV-total across the aorta. The proximal aorta, which is a key component in afterload, provides a buffer against pulsatile blood flow from the heart. These findings support the hypothesis that a main cause of left ventricular diastolic dysfunction in the elderly is an increase in proximal aortic stiffness [22, 23]. In accordance with previous studies, the lower descending thoracic aorta at the level of diaphragm was the most distensible and its upper segment showed the highest PWV [24]. Elevated distensibility of the abdominal aorta is a known marker for rapid growth and a future requirement for operative repair in patients with abdominal aortic aneurysms [25, 26]. Our finding that the normal abdominal aorta has the lowest distensibility and exhibits less significant age-related PWV changes may provide a useful parameter for monitoring abdominal aortic

Table 3 Regression equations for regional aortic distensibility according to age and sex

	Equations	\mathbb{R}^2	P
D1		0.51	0.0023
Male	Distensibility = $6.96 - 0.08 \times age$		
Female	Distensibility = $11.96 - 0.16 \times age$		
D2		0.49	0.0206
Male	Distensibility = $5.52 - 0.05 \times age$		
Female	Distensibility = $8.31 - 0.09 \times age$		
D3		0.47	0.0180
Male	Distensibility = $7.52 - 0.06 \times age$		
Female	Distensibility = $10.55 - 0.11 \times age$		
D4		0.52	0.0003
Male	Distensibility = $4.50 - 0.04 \times age$		
Female	Distensibility = $8.38 - 0.10 \times age$		

D1 distensibility of the ascending aorta at the level of bifurcation of the pulmonary artery; D2 distensibility of the upper descending thoracic aorta at the level of bifurcation of the pulmonary artery; D3 distensibility of the lower descending thoracic aorta at the level of diaphragm; D4 distensibility of the abdominal aorta just above the iliac bifurcation



Table 4 Normal values for aortic pulse wave velocity as measured by cardiac MRI

	Mean ± SD	Median (5th–95th percentile)
PWV-Region 1 (m/s)		
20-29 years	3.7 ± 0.8	3.7 (3.4-4.0)
30-39 years	3.8 ± 3.2	3.8 (3.5-6.0)
40-49 years	4.4 ± 1.5	4.3 (3.7–5.0)
50-59 years	6.3 ± 2.2	5.6 (5.4–7.2)
60-69 years	9.9 ± 5.5	9.0 (7.4–12.4)
PWV-Region 2 (m/s)		
20-29 years	4.8 ± 1.3	4.8 (4.3–5.3)
30-39 years	6.9 ± 3.4	6.2 (5.5-8.2)
40-49 years	7.7 ± 5.3	5.9 (5.4–9.9)
50-59 years	9.4 ± 5.8	8.1 (7.1–11.8)
60-69 years	8.6 ± 4.4	7.9 (6.6–10.6)
PWV-Region 3 (m/s)		
20-29 years	4.7 ± 1.2	4.4 (4.3–5.2)
30-39 years	5.6 ± 4.7	4.8 (3.8–7.5)
40-49 years	5.3 ± 1.5	4.9 (4.7–5.9)
50-59 years	5.5 ± 1.2	5.4 (5.0-6.0)
60-69 years	6.2 ± 1.6	5.8 (5.4-6.9)
PWV-total (m/s)		
20-29 years	4.2 ± 0.6	4.2 (4.0–4.5)
30-39 years	4.7 ± 0.8	4.5 (4.4–5.0)
40-49 years	4.9 ± 0.8	4.9 (4.6–5.3)
50-59 years	6.0 ± 0.9	5.8 (5.6-6.4)
60-69 years	6.9 ± 1.6	6.5 (6.2–7.7)

PWV-Region 1 Regional PWV from the ascending to the upper descending thoracic aorta, PWV-Region 2 Regional PWV from the upper descending thoracic to the lower descending thoracic aorta, PWV-Region 3 Regional PWV from the lower descending thoracic aorta to the abdominal aorta, PWV-total PWV of the entire aorta from the ascending aorta to the bifurcation

aneurysms and optimizing indications for and timing of treatment.

In contrast to previous studies [27, 28], the regional aortic PWV did not increase from proximal to distal along

the aorta. This may have been because our study did not involve distal muscular arteries, such as the iliac or femoral arteries, and, therefore, our study should be interpreted cautiously given that prior studies have demonstrated a regional increase in PWV along the aorta. Furthermore, because the increase in PWV in the proximal aorta was significantly greater than in other regions of the aorta in older adults, the difference in average regional PWV between the proximal and distal aorta was relatively small.

In contrast to the PWV values in this study, our analysis revealed that aortic distensibility differs between sexes. Although regional aortic distensibility was higher in women, such differences were lower in adults older than 50 years of age. One possible explanation is that differences in sex hormones between sexes may affect vessel wall elasticity, and that elasticity may diminish with decreasing levels of female hormones after menopause.

Recent studies have shown that MRI techniques enable in vivo examination of aortic stiffness in different ways [12, 16, 17, 29, 30]. MRI is considered the most appropriate technique to directly and noninvasively measure intra-aortic path length and is thought to be free from operator bias. Aortic distensibility can also be measured through cine imaging. However, the clinical implementation of CMRI in evaluating aortic stiffness has been delayed by an absence of standardized and unified methodology. In this study, the parameters for aortic stiffness were assessed automatically and noninvasively using CMRI. Velocity-encoded sequencing and black blood imaging were used to measure PWV and phase contrast cine imaging was used to assess distensibility. Automatic segmentation of the aorta enabled measurements of both local distensibility and regional PWV.

Although measurement of aortic stiffness by CMRI is more costly and less frequently available than applanation tonometry in clinical practice, CMRI is useful in the regional assessment of vascular aging and pathological changes in the aorta.

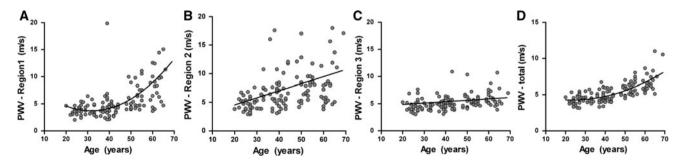


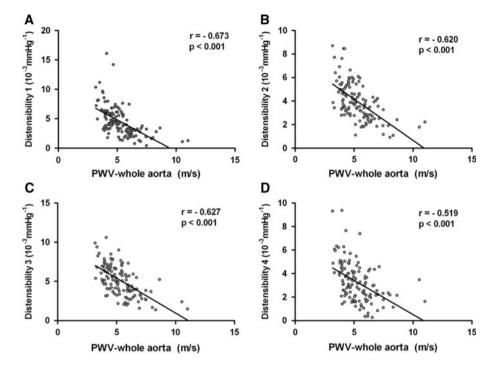
Fig. 3 The relationship between age and regional aortic pulse wave velocity (PWV). a PWV from the ascending to the upper descending thoracic aorta. b PWV from the upper descending thoracic to the

lower descending thoracic aorta. c PWV from the lower descending thoracic to the abdominal aorta. d PWV across the entire aorta from the ascending aorta to the bifurcation



Fig. 4 Correlation between the total aortic PWV and distensibility. a Distensibility of the ascending aorta at the level of bifurcation of the pulmonary artery. b Distensibility of the upper descending thoracic aorta at the level of the bifurcation of the pulmonary artery. c Distensibility of the lower descending thoracic aorta at the

- level of diaphragm.
- d Distensibility of the abdominal aorta just above the iliac bifurcation



Themainlimitation of our study was the small sample size. We demonstrated a normal trend for PWV and distensibility of the aorta, but did not show the reference standard values for aortic stiffness. Additionally, we were unable to simultaneously measureaorticstiffnessbyaninvasivecathetermethod, which is consideredthegoldstandardformeasurementofaorticpressure and flow time. The study sample was composed of healthy individuals, thus future studies in patients with underlying diseases andcardiovascularriskfactorsaredesirableinordertodetermine the pathophysiological influence of such factors on regional aortic stiffness.

Conclusion

Measurements of distensibility and PWV using CMRI enable regional assessments of aortic stiffness. The establishment of normal values for regional stiffness of the aorta is essential if CMRI is to be applied clinically in the assessment of vascular pathology. We defined normal distributions for distensibility and PWV according to a gean da orticlocation, making it possible to identify patients at higher risk according to age and sex. This study is the first to determine normal values for PWV and distensibility using CMRI in a healthy Asian sample without cardiovascularrisk factors.

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Conflict of interest Author Eun Kyoung Kim, Sung-A Chang, Shin Yi Jang, Yiseul Kim, Sung Mok Kim, Jae K. Oh, Yeon Hyeon Choe, Duk-Kyung Kim declare that they have no conflict of interest.

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