

Ascending aorta diameters measured by echocardiography using both leading edge-to-leading edge and inner edge-to-inner edge conventions in healthy volunteers

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Aims

Reference ranges of ascending aorta diameters (AAoD) for two-dimensional echocardiography (2DE) using inner edge (IE) convention are lacking, preventing the comparison of AAoD measurements by 2DE with those obtained by other imaging modalities.

Methods and results

We used harmonic imaging 2DE to prospectively study 218 healthy volunteers (56% women, 42 ± 15 years, 18–80 years). Measurements were performed at the level of aortic root (AoR), sinotubular junction (STJ), and proximal tubular portion (TAo, 1 cm from the STJ) using both leading edge (LE) and IE conventions at end-diastole and end-systole. Feasibility of AAoD measurements between end-diastole and end-systole was similar at AoR and STJ levels, but it was significantly different at TAo level (82 vs. 96%, respectively, $P < 0.0001$). Ascending aorta diameters indexed to height were larger in men than in women ($P < 0.0001$). After adjusting for the effect of gender, only age and body surface area (BSA) were independent predictors of AAoD at multivariable analysis. Average end-diastolic AoR, STJ, and TAo diameters measured using IE convention were similar between genders (17 ± 2 , 15 ± 2 , and 15 ± 2 mm/m², respectively). Corresponding AAoD measured using the LE convention were 18 ± 2 , 16 ± 2 , and 17 ± 4 mm/m², respectively. On average, the end-systolic AAoD measured using LE were 2 mm larger than those performed using IE or at end-diastole. Mean aortic wall thickness was 2.4 ± 0.8 mm.

Conclusion

End-diastolic AAoD measured using IE were significantly smaller than those obtained either using LE convention or at end-systole. Gender-specific reference values for AAoD indexed for BSA should be used to identify ascending aorta pathology.

Keywords

Echocardiography • Ascending aorta • Aortic root • Sinotubular junction • Tubular aorta • Reference values • Normal limits • Age • Gender • Body size • Aortic stiffness

Introduction

Accurate and reproducible measurements of ascending aorta diameters (AAoD) are critical to manage patients with native or post-operative aortic valve disease, to diagnose and follow-up patients with ascending aorta dilatation, or to select patients for transcatheter aortic valve implantation.^{1–3}

Two-dimensional echocardiography (2DE) is the most frequently used imaging modality to assess the size of ascending aorta and follow-up patients with diseases of the aorta. Although AAoD with 2DE have been conventionally measured at end-diastole using the leading edge-to-leading edge (LE) convention from parasternal and suprasternal approaches,^{4,5} there is no formal consensus regarding either method or timing of AAoD measurement by 2DE. Moreover,

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recent ACC/AHA guidelines⁵ favour the inner edge-to-inner edge (IE) diameter measurements to increase reproducibility and match to other imaging modalities, such as cardiovascular magnetic resonance (CMR) and multi-detector computerized tomography (MDCT). Since the current 2DE reference values for AAOd have been obtained using only the LE method,^{6,7} it is difficult to implement the IE method for AAOd measurements in the clinical routine of echocardiographic laboratories. Finally, there is no report regarding the actual differences in AAOd induced by the adoption of either of the two methods, and neither any data regarding the normality ranges of aortic wall thickness assessed by 2DE.

Another issue related to AAOd is the timing of the measurements. The latter does not affect only echocardiographic assessment, since also when using other imaging modalities (such as MDCT), the electrocardiographic tracing is rarely available for gating. In previous echocardiographic studies, AAOd measurements have been performed using variable approaches and at different points of the cardiac cycle, most frequently at end-systole.^{8–10} Since there is no study comparing aortic diameters obtained at end-diastole and end-systole, it is currently unclear if the timing of AAOd sizing is clinically relevant and to which extent. Knowledge of these aspects may influence also the practice of other imaging modalities (like MDCT) and improve the comparability of aortic measurements performed by different imaging modalities.

Therefore, we designed this observational, prospective study with the following aims: (i) to obtain reference values of the AAOd using both LE and IE conventions using state-of-the-art echocardiographic equipment in a relatively large population of healthy volunteers with a wide age range; (ii) to study the relationship between AAOd and physiological parameters which likely influence the aorta size (i.e. gender, age, body size, blood pressure); (iii) to compare AAOd measured at end-diastole and end-systole; and (iv) to obtain reference values for aortic wall thickness.

Methods

Study population

Between October 2011 and February 2013, 227 healthy Caucasian volunteers were prospectively recruited in a single tertiary centre among hospital employees, fellows in training, their relatives and people who underwent medical visits for driving or working license and met the inclusion criteria. Prospective criteria for recruitment included: age ≥ 18 years, no history or symptoms of cardiovascular or lung disease, no cardiovascular risk factors (i.e. arterial systemic hypertension, smoking, diabetes, dyslipidaemia), no ongoing or previous cardio- or vaso-active treatment, normal ECG, and physical examination. Risk factors were assessed from the medical files, when available (lipid and glucose levels, history of diabetes, and/or dyslipidaemia), from subject self-reporting (smoking habit, history of blood pressure levels, and metabolic risk factors when otherwise not available), and from physical assessment immediately preceding the echocardiographic examination (blood pressure, weight, and height). Exclusion criteria included: trained athletes, pregnancy, body mass index (BMI) > 30 kg/m², and poor apical acoustic window defined as more than two LV segments not adequately visualized without contrast infusion.

Blood pressure was measured with the patient supine, after 5 min rest and immediately before starting the echo examination. Mean blood

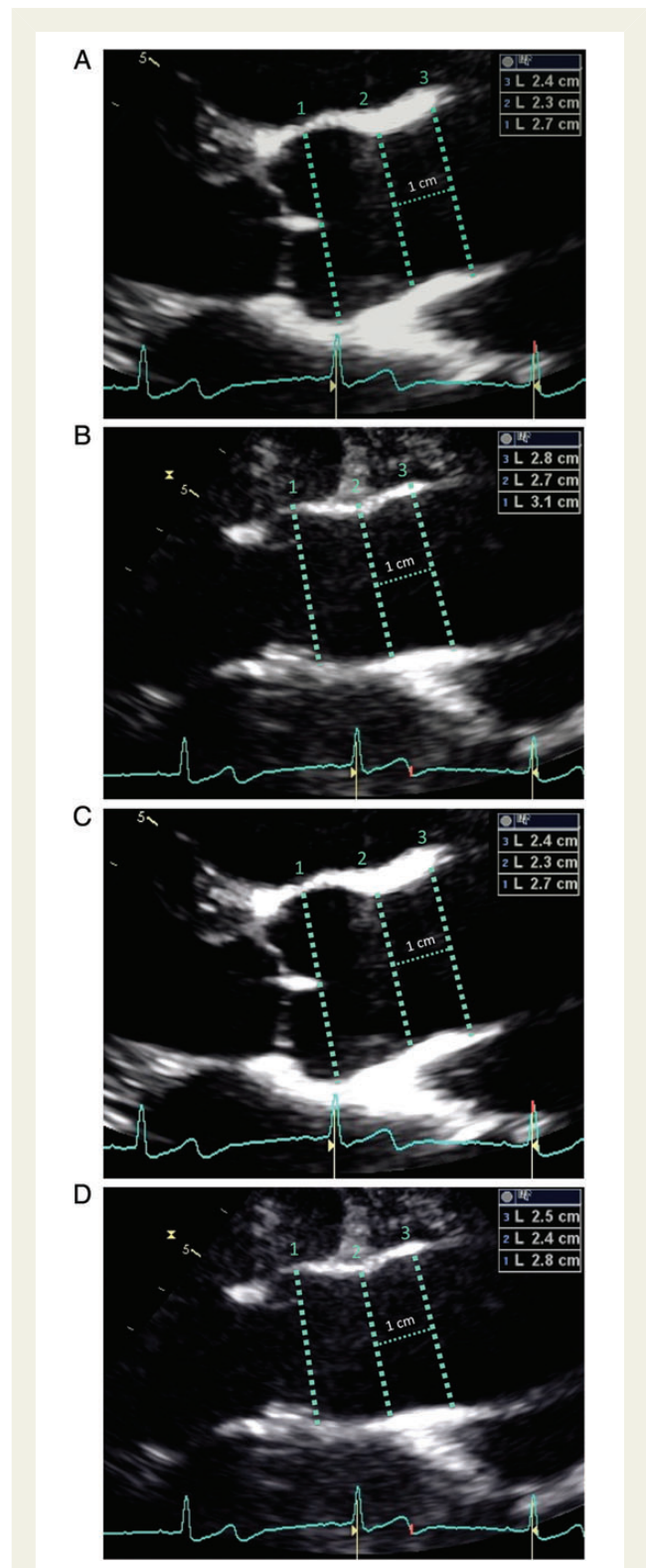


Figure 1 Ascending aorta diameters measured using the leading-edge-to-leading edge convention at end-diastole (A) and end-systole (B), and the inner-edge-to-inner edge convention at end-diastole (C) and end-systole (D).

pressure was calculated as diastolic blood pressure plus one-third of the difference between systolic and diastolic blood pressure. Height and weight were measured using calibrated stadiometer and scale, and body surface area (BSA) was calculated according to the formulas by DuBois and DuBois.¹¹ Body mass index was calculated as weight (kg)/height (m)².

The study was approved by the Ethics Committee of University of Padua (protocol # 2380 P approved on 06 October 2011) and signed informed consent has been obtained in all volunteers before screening for eligibility in the study.

Echocardiographic measurements

Conventional 2D images, optimized for the aortic root (AoR) and ascending aorta, were acquired from the parasternal approach using a commercially available scanner (Vivid E9, GE Healthcare, Horten, Norway) equipped with M5S probe, by three experienced researchers (L.D.B., D.M., and L.P.B.). All patients were examined in the left lateral position using grey-scale second-harmonic 2D imaging technique, with the adjustment of image contrast, focus (at the level of aortic valve), frequency (1.7 MHz transmit frequency and 3.3 MHz receiving frequency), depth (around 10 cm in order magnify the ascending aorta), and sector size for adequate frame rate (70–80 fps) and optimal visualization of aortic wall. Care was taken to acquire images displaying the largest aortic lumen, and acquisition was done during breath hold to minimize translational movements. Aortic root (AoR) at the sinuses of Valsalva, sinotubular junction (STJ), and the tubular (proximal) ascending aorta (TAo, 1 cm from the STJ) diameters were measured at end-diastole and end-systole using both LE(4) and IE(5) conventions (Figure 1). End-diastole was identified according to the peak R wave of the electrocardiographic tracing, while end-systole was assessed on 2DE images and set in the frame right before the beginning of aortic valve closure. All reported values represent the average of at least three measurements on consecutive cardiac cycles. Measurements were indexed to BSA and height, the latter in order to provide reference values applicable for obese patients. Ascending aorta wall thickness was obtained by subtracting the diameter measured using the IE

from the diameter measured using the LE method at the level of the tubular portion.

Statistical analysis

Normal distribution of variables and uniform distribution of subjects per age decade were assessed using the Kolmogorov–Smirnov test. Continuous variables were summarized as mean \pm SD or as median (first, third quartiles) when reporting reference ranges, while scalar variables were reported as percentages. The upper limits of each aortic measurement were defined as the 95th percentile. Differences between values in men and women were assessed using the unpaired *t*-test for normally distributed variables, or the Mann–Whitney *U*-test otherwise. LE and IE measurements, as well as diameters obtained at end-diastole and end-systole obtained from the same subject, were compared using the paired *t*-test. Pearson's correlation was used to analyse the relationships between aortic diameters and demographic and physiological variables such as age, blood pressure, and body size.

Multivariable linear regression analysis after selection of independent demographic variables correlated with AAOd. This was performed for diameters measured using both LE and IE conventions. In each analysis, *R*² was determined to give the proportion of the variability in the AAOd attributable to demographic variables.

In addition, independent associations between aortic diameters were investigated using different set of predictors (only Supplementary data): age, gender, and BSA (model AGBr, ratiometric); age, gender, height, and weight (model AGHWr, ratiometric, or model AGHWa, allometric). The latter models, considering height and weight separately rather than combined in BSA, would avoid the assumptions proper of BSA. In all models, gender was included as a dummy variable, resulting in different constant terms for women and men. Ratiometric scaling approaches divide the variable of interest by a linear combination of body size predictors and adjusting factors (models AGBr and AGHWr), while allometric indexing can be obtained dividing each the measure of interest by each predictor raised to the power of the coefficient of correlation. Since the indexation for height^{1,7}, or the use of allometric indexing did not improve significantly the coefficient of the multivariate models (only

Table 1 Demographics and clinical characteristics of the study population

	All (n = 218)	Women (n = 122)	Men (n = 96)	P-value
Age (years)	44 \pm 15	45 \pm 15	44 \pm 14	0.690
<30 years	44	24	20	
30–39 years	39	20	19	
40–49 years	56	30	26	
50–59 years	34	23	11	
\geq 60 years	45	25	20	
Weight (kg)	68 \pm 11	61 \pm 8	76 \pm 9	<0.001
Height (cm)	170 \pm 9	164 \pm 7	177 \pm 7	<0.001
BMI (kg/m ²)	23 \pm 3	23 \pm 3	24 \pm 3	<0.001
BSA (m ²)	1.78 \pm 0.18	1.66 \pm 0.12	1.93 \pm 0.13	<0.001
Heart rate (bpm)	67 \pm 10	68 \pm 10	67 \pm 11	0.408
SBP (mmHg)	123 \pm 14	118 \pm 14	129 \pm 13	<0.001
DBP (mmHg)	74 \pm 8	71 \pm 8	76 \pm 7	<0.001
MBP (mmHg)	90 \pm 9	87 \pm 9	93 \pm 8	<0.001

Data are expressed as mean \pm standard deviation.

BMI, body mass index; BSA, body surface area; DBP, diastolic blood pressure; MBP, mean blood pressure; SBP, systolic blood pressure.

P-values refer to unpaired Student's *t*-test, women vs. men.

Table 2 Gender-specific reference values for ascending aorta diameters measured using the leading-edge-to-leading-edge or the inner-edge-to-inner-edge conventions at end-diastole

	Women (n = 122)		Men (n = 96)		P-value
	Range	Upper limit	Range	Upper limit	
Leading edge convention					
Aortic root (mm)	30 (27, 32)	35	34 (31, 37)	41	<0.001
Aortic root/BSA (mm/m ²)	18 (17, 19)	22	18 (16, 19)	21	0.133
Aortic root/height (mm/m)	18 (17, 19)	21	19 (18, 21)	24	0.001
Sinotubular junction (mm)	27 (25, 29)	31	31 (29, 33)	37	<0.001
Sinotubular junction/BSA (mm/m ²)	17 (15, 18)	20	16 (15, 17)	19	0.031
Sinotubular junction/height (mm/m)	17 (15, 18)	19	17 (16, 19)	21	0.005
Tubular (mm)	29 (26, 30)	32	31 (28, 34)	36	<0.001
Tubular/BSA (mm/m ²)	17 (16, 18)	20	16 (14, 17)	19	<0.001
Tubular/height (mm/m)	17 (16, 19)	20	17 (16, 19)	22	0.550
Inner edge convention					
Aortic root (mm)	28 (25, 29)	32	31 (29, 34)	38	<0.001
Aortic root/BSA (mm/m ²)	17 (15, 18)	20	16 (15, 18)	19	0.169
Aortic root/height (mm/m)	17 (16, 18)	20	18 (16, 19)	22	0.001
Sinotubular junction (mm)	25 (23, 27)	29	28 (26, 30)	35	<0.001
Sinotubular junction/BSA (mm/m ²)	15 (14, 16)	28	14 (13, 16)	28	0.019
Sinotubular junction/height (mm/m)	15 (14, 16)	18	16 (15, 17)	20	0.014
Tubular (mm)	26 (24, 28)	31	29 (25, 31)	35	<0.001
Tubular/BSA (mm/m ²)	16 (15, 17)	19	15 (13, 16)	18	<0.001
Tubular/height (mm/m)	16 (15, 17)	19	16 (14, 17)	20	0.960
Aortic wall thickness (mm)	2.0 (2.0, 3.0)	3.0	2.0 (2.0, 3.0)	4.0	0.021

Data are expressed as median (first, third quartiles).

Upper limit = 95th percentile of normality.

BSA, body surface area.

P-values refer to unpaired Student's *t*-test or Mann–Whitney *U*-test for independent samples when appropriate.

Table 3 Comparison of ascending aorta diameters measured using leading-edge-to-leading-edge and inner-edge-to-inner-edge conventions at end-diastole

Variable	Leading edge convention		Inner edge convention		P-value
	Range	Upper limit	Range	Upper limit	
Aortic root (mm)	31 (29, 34)	39	29 (27, 31)	37	<0.001
Aortic root/BSA (mm/m ²)	18 (16, 19)	21	16 (15, 18)	20	<0.001
Aortic root/height (mm/m)	19 (17, 20)	23	17 (16, 18)	21	<0.001
Sinotubular junction (mm)	29 (26, 31)	35	26 (24, 28)	32	<0.001
Sinotubular junction/BSA (mm/m ²)	16 (15, 17)	19	15 (14, 16)	18	<0.001
Sinotubular junction/height (mm/m)	17 (16, 18)	20	15 (14, 16)	18	<0.001
Tubular (mm)	29 (27, 32)	36	27 (25, 29)	34	<0.001
Tubular/BSA (mm/m ²)	17 (15, 18)	20	15 (14, 16)	19	<0.001
Tubular/height (mm/m)	17 (16, 19)	21	16 (14, 17)	20	<0.001

Data are expressed as median (first, third quartiles).

Upper limit = 95th percentile of normality.

BSA, body surface area.

P-values refer to paired Student's *t*-test, leading edge VD inner edge conventions.

Supplementary data), we reported our data normalized for BSA as a simple and easy-to-use values.

Interobserver reproducibility for AAOd was analysed in 25 random subjects by two independent blinded observers. Intra-observer reproducibility was analysed in another group of 25 subjects by the same observer performing the same measurements 1 week later. Reproducibility of AAOd was evaluated using intraclass correlation and the coefficient of variation was calculated as the absolute difference between the corresponding pairs of measurements in percent of their mean.

All analyses were performed using SPSS 19.0 (SPSS Inc., Chicago, IL, USA) and MedCalc statistical software version 10.0.1.0. (MedCalc, Mariakerke, Belgium). Differences among variables were considered significant at $P < 0.05$. Upper and lower limits of normality were computed as the mean value plus or minus 2 SDs.

Results

A total of 227 healthy volunteers (125 women, 42 ± 15 years, age range 18–80 years) were enrolled in the study. Nine subjects were excluded from the analysis because of poor parasternal acoustic window. The enrolled volunteers were uniformly distributed across age decades and genders (Table 1). The Kolmogorov–Smirnov test demonstrated uniform distribution across age decade, both for women ($P = 0.759$) and men ($P = 0.653$). Pearson Chi-square did not show significant difference between women and men ($P = 0.663$).

Imaging the ascending aorta at end-systole, rather than at end-diastole, allowed a maximal visualization of its length. Feasibility of AAOd was similar between end-diastole and end-systole at both AoR (98 and 99%) and at STJ (95 and 98%) levels, but it was significantly lower at end-diastole at TAo level (82 vs. 96%, respectively, $P < 0.001$).

Anthropometric characteristics and AAOd of the study population, stratified by gender, are summarized in Table 1. Age and heart rate were similar between men and women. Height, BSA, weight, and BMI were significantly larger in men than in women.

Gender-specific reference values of AAOd measured with LE (top rows) and IE (bottom rows) conventions are summarized in Table 2. All aortic diameters, independently of the adopted measuring convention, were significantly larger in men than in women (Table 2). Indexing diameters by BSA eliminated the significant difference between men and women at the level of the AoR, but not in the other segments, both when applying the IE or the LE methods (Table 2). Conversely, indexing by height resulted in gender-independent diameter of the tubular ascending aorta (Table 2). Finally, aortic wall was thicker in men than in women (Table 2).

Measuring AAOd using the IE convention resulted in significantly smaller values compared with measurements performed using the LE method (Table 3). The differences between AAOd obtained using the two measurement conventions were around 2 mm (Figure 2) accounting for aortic wall thickness, and not significantly different between women and men (Table 2).

All AAOd were found to be significantly related to gender, age, BSA, BMI, height, weight, and systolic blood pressure. Given the higher R^2 at bivariate analysis, BSA was preferred to BMI in multivariate analysis. Table 4 summarizes the results of the multivariate linear regression analyses between AAOd, measured with both LE and IE conventions, with age and anthropometric independent variables. For all the diameters and independently of the convention used,

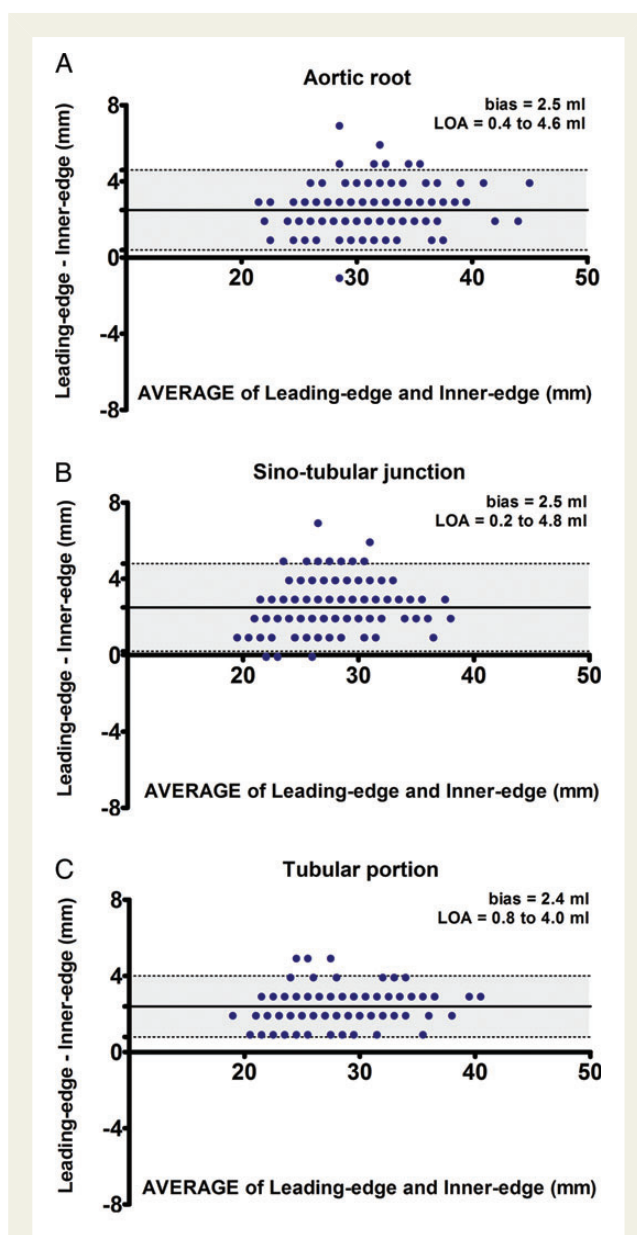


Figure 2 Bland–Altman plots comparing ascending aorta measurements performed using the leading-edge-to-leading-edge (leading-edge) and inner-edge-to-inner-edge (inner-edge) conventions at aortic root (A), sinotubular junction (B), and tubular portion (C) levels, respectively.

the models accounted for approximately half of the observed variance (R^2 ranged between 0.46 and 0.55). Interestingly, BSA and age were significantly associated with all AAOd, while gender was significantly associated with Ao root size. Measurements performed with LE and IE conventions gave similar R^2 for all AAOd (Table 4). Measuring AAOd at end-diastole resulted in significantly smaller values compared with measurements performed at end-systole (Table 5). Aortic root showed a reduced expansion from diastole to systole in comparison with the other aorta segments. Average differences between AAOd obtained at end-diastole and end-systole were around 1 mm (Figure 3).

Table 4 Multiple linear regression analyses of ascending aorta diameters with age and body surface area as independent variables, adjusted for gender

	Root (mm)		STJ (mm)		Asc Ao (mm)	
	β (95% CI)	r^2	β (95% CI)	r^2	β (95% CI)	r^2
Inner edge (BSA)		0.48		0.46		0.51
Constant	8.1 (2.6, 13.5)*		7.1 (2.4, 11.8)*		2.1 (-3.4, 7.5)	
Gender	1.5 (0.3, 2.7)*		0.8 (-0.2, 1.8)		-0.9 (-2.1, 0.3)	
Age (years)	0.11 (0.08, 0.14)*		0.09 (0.07, 0.11)*		0.15 (0.12, 0.18)*	
BSA (m ²)	8.7 (5.5, 11.9)*		8.3 (5.6, 11.1)*		10.5 (7.3, 13.8)*	
Leading edge (BSA)		0.52		0.52		0.55
Constant	7.8 (2.1, 13.6)*		7.4 (2.5, 12.4)*		4.6 (-1.1, 10.3)	
Gender	1.5 (0.2, 2.7)*		1.0 (-0.1, 2.1)		-0.3 (-1.6, 0.9)	
Age (years)	0.13 (0.10, 0.16)*		0.11 (0.08, 0.13)*		0.16 (0.13, 0.19)*	
BSA (m ²)	9.9 (6.5, 13.2)*		9.1 (6.2, 11.9)*		10.0 (6.7, 13.3)*	

Asc, ascending tubular aorta; CI, confidence interval; STJ, sinotubular junction.

* $P < 0.01$ vs. null coefficient.

Table 5 Comparison of aortic diameters measured at end-diastole and end-systole using both leading-edge-to-leading-edge and inner-edge-to-inner-edge conventions

Diameter	Leading-edge-to-leading-edge			Inner-edge-to-inner-edge		
	Diastole	Systole	P-value	Diastole	Systole	P-value
Aortic root (mm)	30 ± 4	32 ± 4	<0.001	29 ± 4	30 ± 4	<0.001
Sinotubular junction (mm)	29 ± 4	30 ± 4	<0.001	26 ± 3	28 ± 3	<0.001
Tubular (mm)	29 ± 4	31 ± 4	<0.001	27 ± 4	29 ± 4	<0.001

Data are expressed as mean ± standard deviation.

P-values refer to paired Student's t-test, diastolic vs. systolic values.

Intra- and interobserver variability of AAoD measurements was similar using either LE and IE convention (Table 6).

Discussion

In the present study, we have used state-of-the-art 2DE to measure AAoD at end-diastole and end-systole using both LE and IE conventions in a relatively large number of healthy volunteers with a wide age range to: (i) find that measuring AAoD using LE convention provides statistically significant larger AAoD than using IE convention; (ii) provide reference values of the AAoD using both LE and IE conventions in order to enhance comparability of AAoD measured with 2DE with other imaging modalities; (iii) confirm that the assessment of AAoD should be based on gender-specific reference values which should take into account patients' age and BSA; (iv) document that AAoD obtained at end-systole are significantly larger than those obtained at end-diastole and the limits of agreement between the two measurements may be as large as 3.8 mm; and (v) provide the reference values for aortic wall thickness.

Aortic dilation is a potential risk factor for the development of life-threatening complications including aneurysm formation, dissection,

and/or rupture.^{11–15} With recent advances in multimodality cardiac imaging, a number of techniques now exist for a noninvasive assessment of aortic disease. Cardiovascular magnetic resonance and MDCT performed with ECG gating are considered the gold standard for the noninvasive assessment of AAoD.⁵ However, CMR is not widely available, is more costly, and cannot be used on patients suffering from claustrophobia and/or implanted devices, and MDCT is limited due to the increased risk of radiation exposure and need for contrast administration. Therefore, 2DE remain the most frequently used imaging technique to screen and follow-up patients with suspected and/or diagnosed ascending aorta disease.

Conventionally, 2DE measurements of AAoD have been obtained from parasternal long-axis view using the LE convention, which includes the thickness of the anterior aortic wall, at end-diastole.^{3,4} The choice of the LE technique was related to the fact that with the quality of 2DE images at the time of the standardization of intracardiac measurements, the tissue–blood interface was a relatively thick, highly gain-dependent line.¹⁶ Therefore, the tissue–blood interface was difficult to identify limiting interobserver and interstudy reproducibility of AAoD measurement. With the axial spatial resolution available with modern echocardiographic machines, the

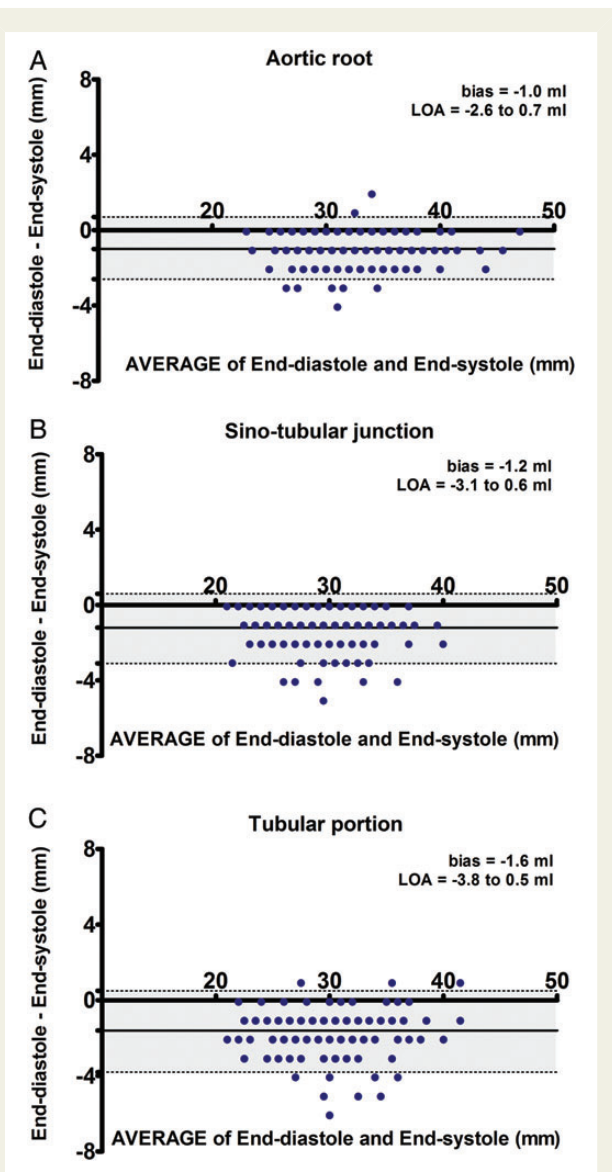


Figure 3 Bland–Altman plots comparing ascending aorta measurements performed using the leading-edge-to-leading-edge at end-diastole and end-systole at aortic root (A), sinotubular junction (B), and tubular portion (C) levels, respectively.

precise identification of tissue–blood interface is no longer an issue and the IE convention could be easily implemented in clinical echocardiography. In addition, both CMR¹⁷ and MDCT¹⁸ measure AAOd using the IE convention, and recent ACC/AHA guidelines⁵ recommend the IE convention to increase reproducibility and intermodality comparison of AAOd measurements. However, there is no echocardiographic study providing the reference values of AAOd obtained using the IE convention, and this represents a major limitation to the introduction of the IE convention in the clinical routine of echocardiographic laboratories. To address this issue, we provided gender-specific reference values and upper limits of normality, using both LE and IE conventions, obtained from a relatively large cohort of healthy volunteers.

As expected, AAOd obtained with the LE convention were significantly larger (from 2 to 4 mm on average) than those measured with the IE convention. Indexed AoR diameters measured in our population were quite similar to those reported by Vasan *et al.*⁷ and Roman *et al.*⁶ in both men and women. Interestingly, AAOd measured with the IE convention in our study population were quite similar to those measured by CT (AoR = 31 ± 4 vs. 32 ± 3 mm in men, and 28 ± 3 vs. 29 ± 2 mm in women, respectively; TAO = 28 ± 4 vs. 28 ± 4 mm in men and 26 ± 3 vs. 28 ± 4 mm in women, respectively).¹⁸ Similarly, AoR measured with IE convention in our study population were comparable with those reported by Burman *et al.*¹⁷ using CMR (31 ± 4 vs. 32 ± 4 in men and 28 ± 3 vs. 28 ± 3 in women, respectively). To date, there is only one report about reference values of 2DE proximal thoracic aorta diameters using the IE convention.¹⁹ However, patients enrolled in that study were not properly normal or healthy subjects since they were retrospectively recruited among those referred for a clinically indicated echocardiographic study. In addition, 70 of them (14%) had mild systemic arterial hypertension. Conversely, in our study, we prospectively enrolled only healthy volunteers who were defined healthy before the echocardiographic study.

Further studies comparing AAOd measured using the different imaging modalities in the same patients are needed to assess the actual intermodality comparability of AAOd obtained with the different measurement conventions.

Two sets of reference values have been provided for each measurement convention used: one set based on gender and BSA, and the other based on gender and height. We chose to provide reference values indexed with two measures of body size because the ideal

Table 6 Intra- and interobserver reproducibility of aortic root and proximal tubular aorta measurements

	Leading-edge-to-leading-edge		Inner-edge-to-inner-edge	
	Intra-class correlation	Coefficient of variation (%)	Intra-class correlation	Coefficient of variation (%)
Intra-observer				
Aortic root	0.96	1 ± 2	0.95	1 ± 1
Tubular ascending aorta	0.89	2 ± 3	0.96	1 ± 1
Inter-observer				
Aortic root	0.88	1 ± 3	0.89	1 ± 3
Tubular ascending aorta	0.80	3 ± 4	0.86	7 ± 5

method for indexing echocardiographic measurements remains to be defined.²⁰ Height is very simple to measure, does not require a calculator to be computed, it has been shown to correlate with aortic annulus, left atrial, and left ventricular diameters (suggesting that cardiac dimensions increase primarily in response to skeletal growth).²¹ In addition, it can be reliably used to index cardiac structure sizes also in obese patients.²²

Differences in TAO measured at end-systole and end-diastole found in our study were quite similar to those reported by Lin et al.¹⁸ who used MDCT to derive age and gender reference values for TAO. Availability of 2DE reference values for AAOd at end-systole is not only useful to improve comparability of AAOd among different imaging modality, but it is also useful during 2DE studies themselves since they will allow the operator to take advantage of the increased visualization of the ascending aorta which is usually obtained in end-systole.

Clinical implications

The results of the present study underscore the fact that AAOd measured using different measurement conventions and/or at different time points during cardiac cycle are not interchangeable. Clinicians who want to use 2DE and/or other imaging modalities (e.g. CMR and MDCT) to monitor patients with dilated ascending aorta should ensure that baseline and follow-up measurements are performed using the same measurement convention and at the same time point of the cardiac cycle. Scientific societies are urged to take initiatives to provide a common standard for AAOd measurement across the different imaging modalities. This will improve the accuracy of the detection of aortic dilation, improve the reliability of serial measurements, and promote comparability of measurements performed using different imaging modalities.

Supplementary material

Supplementary data are available at *European Journal of Echocardiography* online.

Conflict of interest: None declared.

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References

- Vahanian A, Alfieri O, Andreotti F, Antunes MJ, Baron-Esquivias G, Baumgartner H et al. Guidelines on the management of valvular heart disease (version 2012): The Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J* 2012;**33**:2451–96.
- Lancellotti P, Tribouilloy C, Hagendorff A, Moura L, Popescu BA, Agricola E et al. European Association of Echocardiography recommendations for the assessment of valvular regurgitation. Part 1: aortic and pulmonary regurgitation (native valve disease). *Eur J Echocardiogr* 2010;**11**:223–44.
- Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA et al. Recommendations for chamber quantification. *Eur J Echocardiogr* 2006;**7**:79–108.
- Evangelista A, Flachskampf F, Erbel R, Antonini-Canterin F, Vlachopoulos C, Rocchi G et al. Echocardiography in aortic diseases: EAE recommendations for clinical practice. *Eur J Echocardiogr* 2010;**11**:645–8.
- Hiratzka LF, Bakris GL, Beckman JA, Bersin RM, Carr VF, Casey DE Jr et al. Guidelines for the diagnosis and management of patients with thoracic aortic disease. *J Am Coll Cardiol* 2010;**55**:e27–129.
- Roman MJ, Devereux RB, Kramer-Fox R, O'Loughlin J. Two-dimensional echocardiographic aortic root dimensions in normal children and adults. *Am J Card* 1989;**64**:507–12.
- Vasan RS, Larson MG, Benjamin EJ, Levy D. Echocardiographic reference values for aortic root size: the Framingham heart study. *J Am Soc Echocardiogr* 1995;**8**:793–800.
- Albano AJ, Mitchell E, Pape LA. Standardizing the method of measuring by echocardiogram the diameter of the ascending aorta in patients with a bicuspid aortic valve. *Am J Card* 2010;**105**:1000–4.
- Biaggi P, Matthews F, Braun J, Rousson V, Kaufman PA, Jenni R. Gender, age and body surface area are the major determinants of ascending aorta dimensions in subjects with apparently normal echocardiograms. *J Am Soc Echocardiogr* 2009;**22**:720–5.
- Lai WW, Geva T, Shirali GS, Frommelt PC, Humes RA, Brook MM et al. Guidelines and standards for performance of a pediatric echocardiogram: a report from the Task Force of the Pediatric Council of the American Society of Echocardiography. *J Am Soc Echocardiogr* 2006;**19**:1413–30.
- Dubois D, Dubois EF. Clinical calorimetry. A formula to estimate the approximate surface area if height and weight are known. *Arch Int Med* 1916;**17**:863–71.
- Evangelista A, Aguilar R, Cuellar H, Thomas M, Laynez A, Rodriguez-Palomares J et al. Usefulness of real-time three-dimensional transeoesophageal echocardiography in the assessment of chronic aortic dissection. *Eur J Echocardiogr* 2011;**12**:272–7.
- Gott VL, Greene PS, Alejo DE, Cameron DE, Naftel DC, Miller DC et al. Replacement of the aortic root in patients with Marfan's syndrome. *N Engl J Med* 1999;**340**:1307–13.
- Tadros TM, Klein MD, Shapira OM. Ascending aortic dilatation associated with bicuspid aortic valve: pathophysiology, molecular biology, and clinical implications. *Circulation* 2009;**119**:880–90.
- Elefteriades JA, Farkas EA. Thoracic aortic aneurysm clinically pertinent controversies and uncertainties. *J Am Coll Cardiol* 2010;**55**:841–57.
- Schnittger I, Gordon EP, Fitzgerald PJ, Popp RL. Standardized intracardiac measurements of two-dimensional echocardiography. *J Am Coll Cardiol* 1983;**2**:934–8.
- Burman ED, Keegan J, Kilner PJ. Aortic root measurement by cardiovascular magnetic resonance. Specification of planes and lines of measurement and corresponding normal values. *Circ Cardiovasc Imaging* 2008;**1**:104–13.
- Lin FY, Devereux RB, Roman MJ, Meng J, Jow VM, Jacobs A et al. Assessment of the thoracic aorta by multidetector computed tomography: age- and sex-specific reference values in adults without evident cardiovascular disease. *J Cardiovasc Comp Tomogr* 2008;**2**:298–308.
- Mirea O, Maffessanti F, Gripari P, Tamborini G, Muratori M, Fusini L et al. Effects of aging and body size on proximal and ascending aorta and aortic arch: inner edge-to-inner edge reference values in a large adult population by two-dimensional transthoracic echocardiography. *J Am Soc Echocardiogr* 2013;**26**:419–27.
- Sheil MLK, Jenkins O, Sholler GF. Echocardiographic assessment of aortic root dimensions in normal children based on measurements of a new ratio of aortic size independent of growth. *Am J Card* 1995;**75**:711–5.
- Nixdorff SM, Picard MH, Triulzi MO, Thomas JD, Newell J, King ME et al. New perspectives in the assessment of cardiac chamber dimensions during development and adulthood. *J Am Coll Cardiol* 1992;**19**:983–8.
- Zipes DP, Camm AJ, Borggrefe M, Buxton AE, Chaitman B, Fromer M et al. ACC/AHA/ESC 2006 guidelines for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death—executive summary: A report of the American College of Cardiology/American Heart Association Task Force and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Develop Guidelines for Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death) Developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. *Eur Heart J* 2006;**27**:2099–140.