



Intermodality variation of aortic dimensions: How, where and when to measure the ascending aorta

Lidia R. Bons^{a,1}, Anthonie L. Duijnhouwer^{b,1}, Sara Boccalini^{c,1}, Allard T. van den Hoven^{a,1}, Maureen J. van der Vlugt^{b,1}, Raluca G. Chelu^{c,1}, Jackie S. McGhie^{a,1}, Isabella Kardys^{a,1}, Annemien E. van den Bosch^{a,1}, Hans-Marc J. Siebelink^{d,1}, Koen Nieman^{c,e,1}, Alexander Hirsch^{a,c,1}, Craig S. Broberg^{f,1}, Ricardo P.J. Budde^{a,c,1}, Jolien W. Roos-Hesselink^{a,*,1}

^a Department of Cardiology, Erasmus Medical Center, Rotterdam, the Netherlands

^b Department of Cardiology, Radboud University Medical Center, Nijmegen, the Netherlands

^c Department of Radiology and Nuclear Medicine, Erasmus Medical Center, Rotterdam, the Netherlands

^d Department of Cardiology, Leiden University Medical Center, Leiden, the Netherlands

^e Departments of Cardiovascular medicine and Radiology, Stanford University School of Medicine, Stanford, CA, USA

^f Knight Cardiovascular Institute, Oregon Health & Science University, Portland, OR, USA

ARTICLE INFO

Article history:

Received 23 May 2018

Received in revised form 14 August 2018

Accepted 22 August 2018

Available online 24 August 2018

Keywords:

Aortic pathology

Echocardiography

Computed tomography

Magnetic resonance imaging

ABSTRACT

Background: No established reference-standard technique is available for ascending aortic diameter measurements. The aim of this study was to determine agreement between modalities and techniques.

Methods: In patients with aortic pathology transthoracic echocardiography, computed tomography angiography (CTA) and magnetic resonance angiography (MRA) were performed. Aortic diameters were measured at the sinus of Valsalva (SoV), sinotubular junction (STJ) and tubular ascending aorta (TAA) during mid-systole and end-diastole. In echocardiography both the inner edge-to-inner edge (I-I edge) and leading edge-to-leading edge (L-L edge) methods were applied, and the length of the aortic annulus to the most cranial visible part of the ascending aorta was measured. In CTA and MRA the I-I method was used.

Results: Fifty patients with bicuspid aortic valve (36 ± 13 years, 26% female) and 50 Turner patients (35 ± 13 years) were included. Comparison of all aortic measurements showed a mean difference of 5.4 ± 2.7 mm for the SoV, 5.1 ± 2.0 mm for the STJ and 4.8 ± 2.1 mm for the TAA. The maximum difference was 18 mm. The best agreement was found between echocardiography L-L edge and CTA during mid-systole. CTA and MRA showed good agreement. A mean difference of 1.5 ± 1.3 mm and 1.8 ± 1.5 mm was demonstrated at the level of the STJ and TAA comparing mid-systolic with end-diastolic diameters. The visible length of the aorta increased on average 5.3 ± 5.1 mm during mid-systole.

Conclusions: MRA and CTA showed best agreement with L-L edge method by echocardiography. In individual patients large differences in ascending aortic diameter were demonstrated, warranting measurement standardization. The use of CTA or MRA is advised at least once.

© 2018 Elsevier B.V. All rights reserved.

1. Introduction

Progressive dilation of the ascending aorta is an important risk factor for aortic dissection and rupture [1], which is associated with significant morbidity and mortality. The estimated incidence of thoracic aortic enlargement (including ascending aortic aneurysm) is 10.4 cases per 100,000 person-years [2,3]. This figure varies in part

by non-standardized definitions of how the aorta should be measured or what constitutes an abnormal diameter. The more widespread application of multiple imaging modalities in a given patient adds to the variations seen in clinical practice. Three imaging modalities are currently in use for measuring the ascending aorta: transthoracic two-dimensional echocardiography (2DE), computed tomography (CT) and magnetic resonance imaging (MRI) [4]. Each modality has its strengths and weaknesses [5]. Recently, guidelines specifically focused on the ascending aorta have been published. The American College of Cardiology Foundation (ACCF)/American Heart Association (AHA) guidelines [6] recommend measuring the outer edge-to-outer edge (O-O) edge of the vessel wall for CT or MRI derived diameters, but the inner edge-to-inner edge (I-I) for 2DE. In contrast, the

* Corresponding author at: Room Ba 583a, 's Gravendijkwal 230, 3015 CE Rotterdam, the Netherlands.

E-mail address: j.roos@erasmusmc.nl (J.W. Roos-Hesselink).

¹ This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

American Society of Echocardiography (ASE) and the European Association of Cardiovascular Imaging (EACVI) guidelines for 2DE suggest that the leading edge-to-leading edge (L-L edge) convention at end-diastole should be used [7,8]. Finally, the 2010 ASE pediatric guidelines [9] pose that by 2DE the I-I measurement, during systole is preferred. Just as guidelines are inconsistent [10,11] so is clinical practice. By CT, the I-I method is most frequently used when contrast is given since the wall itself is hardly visible [12,13], while the O-O method is used in non-contrast enhanced scans [14,15]. In contrast, most physicians using 2DE prefer the L-L edge method [16,17]. Also in the general population, age, gender and BSA have impact on aortic diameters as discussed by Vríz et al. [18]. Furthermore, since the aortic root is not circular, there is debate of whether to report cusp-to-commissure or cusp-to-cusp measurements for sinus of Valsalva measurements. Despite attempts at congruency, the ASE/EACVI concluded that there was insufficient data to favor one standard [7]. Some studies have compared reported measurements, though currently there are no studies comparing all three imaging modalities performed in the same patient on the same day. The aim of this study was to determine agreement between modalities and techniques and provide guidance on the optimal approach to measure the ascending aorta. The following measurements were compared: [1] ascending aortic measurements on echocardiography, CTA and MRA, [2] cusp-to-cusp and cusp-to-commissure diameter at the level of the sinus of Valsalva on CTA and [3] aortic measurement during diastole and systole.

2. Methods

2.1. Study population

The study population consisted of adult patients with a bicuspid aortic valve (BAV) and/or Turner syndrome who had been included in a prospective cohort study to elucidate the etiologies and pathogenic mechanisms leading to BAV/aneurysm formation and unravel risk factors for disease progression [19]. For research purposes the patients were scheduled for 2DE, CTA and magnetic resonance angiography (MRA) on the same day. Therefore, the data of this cohort made it possible to directly compare 2DE, CTA and MRA measurements of the ascending aortic diameter. Patients visited our tertiary center between October 2014 and March 2016. The inclusion criteria for BAV patients were age ≥ 18 year and one of the following: [1] aortic stenosis (gradient >2.5 m/s), [2] aortic regurgitation (at least moderate) or [3] ascending aortic dilation ≥ 40 mm and/or aortic size index >2.1 cm/m². All three types of a bicuspid aortic valve according to the Sievers classification were included. This classification is based on the number of raphe, which is a fused area between two cusps. Bicuspid aortic valves with no raphe are called type 0, valves with one raphe type 1 and valves with two raphe type 2. Turner patients needed to have a genetically confirmed 45,X or 45,X/46,XX mosaic karyotype. Patients with contra-indication to CTA, MRA or contrast agents were excluded. Renal function was checked in all patients. Patients with no MRA due to claustrophobia or technical problems remained in the study, but patients who did not receive either 2DE or CTA were excluded. Patients without MRA were included, because some of our research questions do not require information about MRA measurements. Patients also underwent physical examination. Hypertension was defined as current use of antihypertensive medication. The study complied with the Declaration of Helsinki and was approved by the medical ethical committee of the Erasmus Medical Center (MEC14-225). Written informed consent was provided by all patients.

2.2. Transthoracic two-dimensional echocardiography (2DE)

Standard 2DE was performed by one of two experienced sonographers. All studies were acquired using harmonic imaging on an iE33 or EPIQ7 ultrasound system (Philips Medical Systems, Best, the Netherlands) equipped with an $\times 5-1$ matrix-array transducer (composed of 3040 elements operating at 1–5 MHz). The aorta was measured from either the standard parasternal long axis view or from a more cranial intercostal window to improve visualization of the ascending aorta [6]. Aortic stenosis was defined based on peak aortic velocity and aortic regurgitation was evaluated according to the EAE/ASE guidelines [20].

2.3. Computed tomography angiography (CTA)

A retrospectively ECG-gated spiral CTA was performed using a dual-source CT system (Somatom Force or Somatom Definition Flash, Siemens Healthineers, Forchheim, Germany). In order to image the ventricles, aortic valve and aorta, the scan range was set from the aortic arch to the inferior border of the heart. Dose modulated ECG-pulsing was employed with nominal tube current during the 0 to 40% window of the R-R interval, and tube current reduced to 20% of the nominal output for the remainder to reduce the radiation dose. In total 20 different reconstructions with a 1.5-mm slice thickness and 1.0-

mm overlap were made in each patient at each 5% of the R-R interval. Reference tube current was set at 150 mAs per rotation. Automatic kV selection was used. The table speed was adapted to the heart rate. No beta blockers were administered prior to the scan. A 65 ml bolus of iodinated contrast material (Iodixanol 320, Visipaque, GE, Health Care, Cork, Ireland) was administered through an antecubital vein followed by a 40 ml 70/30% saline/contrast medium bolus, both at 5 ml/s. Image acquisition was started using bolus tracking in the ascending aorta.

2.4. Magnetic resonance angiography (MRA)

Image acquisition was performed using a 1.5 T scanner (Discovery MR450, GE Medical Systems, Milwaukee, WI, USA) using a 32-channel phased-array cardiac surface coil. For aortic imaging an angiography sequence was used. First a test bolus of 1 ml gadobutrol (Gadovist, Bayer Schering Pharma, Leverkusen, Germany) followed by 20 ml of saline flush, was injected to identify the individual scan delay time to the maximum enhancement of contrast in the descending aorta. Second, non-ECG-gated MRA images were acquired in coronal orientation after injection of a double dose of 7 ml gadobutrol (0.05–0.18 mmol/kg) followed by 20 ml of saline flush, both with an injection rate of 2.5 ml/s. Typical scan parameters were: FOV 460 mm (phase 90%), matrix size 320 \times 192, slice thickness 2.0 mm, flip angle 17°, NEX 0.75, bandwidth 83.3 kHz, TR 3.1 ms, TE 1.09 ms.

2.5. Measurements of the ascending aorta

Analyses of the 2DE, CTA and MRA images were performed by experienced investigators blinded to the results of the other imaging modalities. Images were analyzed offline with the use of dedicated software: Xcelera (version R4.1, Philips Medical Systems, the Netherlands) for 2DE and Syngo.Via (Version VB10B, Siemens, Germany) for CTA and MRA. For CTA and MRA maximal aortic diameters were measured from reconstructed short-axis images generated with double-oblique multiplanar reformation [21].

To compare the diameter between the three modalities the aorta was measured at three predefined levels for all three imaging techniques: sinus of Valsalva (SoV), sinotubular junction (STJ) and tubular ascending aorta (TAA, 1 cm cranial of the sinotubular junction), as indicated in Fig. 1A. When referring to the widest diameter at any level of the ascending aorta, we used 'ascending aorta'. Both the L-L edge and I-I edge methods were applied in 2DE (Fig. 1B). For CTA and MRA only the I-I edge method was applied, because the vessel wall is difficult to distinguish on contrast-enhanced images in the absence of atherosclerotic disease. For this reason, measurements with the O-O edge method were not possible for CTA and MRA. Calcified plaques were included in the diameter measurement. Measurements were made at both end-diastole and mid-systole for 2DE and CTA according to the guidelines [7,8] (Fig. 1C). The MRA was acquired without ECG-synchronization. The measurements on MRA were compared with both the end-diastolic and mid-systolic measurement on CTA. End-diastole was defined as the moment before opening of the aortic valve and ranged between 75% and 100% of the R-R interval on CTA. Mid-systole was defined as the phase exactly halfway between opening and successive closure of the aortic valve and ranged between 15% and 35% of the R-R interval on CTA. The maximal length of the aorta that was visualized with 2DE (defined as the length from the aortic annulus to the most cranial part of the ascending aorta which was visible) was measured during mid-systole and end-diastole (Fig. 1A).

For CTA and MRA three cusp-to-commissure distances were measured at the level of the SoV (widest plane) when patients had a tricuspid aortic valve or bicuspid aortic valve type 1 or 2 according to the Sievers classification [22]. In CTA the diameter was also measured with the cusp-to-cusp method according to Goldstein et al. [7] (Fig. 1D). For bicuspid aortic valves type 0 this was measured in two directions (maximum diameter and diameter perpendicular to the maximum diameter). At the level of the sinus of Valsalva the largest measurements on CTA and MRA was compared to echocardiography. Detailed information about separate analysis of the three cusp-to-cusp measurements (tricuspid or bicuspid type 1 or 2 valves) and measurements in two directions (bicuspid type 0 valves) can be found in the supplemental material. Using this protocol, the aorta was measured with seven different methods across all modalities at each of three levels (supplemental table 1). The absolute value of the maximum difference between these seven measurements at each level (maximum difference) was calculated for each patient. Inter- and intra-observer agreement was assessed by repeated analyses of a randomly selected sample of 25 subjects.

2.6. Statistical analysis

Categorical variables are presented as frequencies with percentages. Comparison of categorical variables was done using the Chi-square test and in case of an expected count <5 in one of the cells of the crosstable the Fisher's exact test was used. All continuous variables are presented as mean with standard deviation when normally distributed, and in case of non-normal distribution, medians with interquartile ranges are provided. Data distribution was checked using histograms. Comparison of normally distributed continuous variables was done using the Student's t-test or, in case of a skewed distribution, the Mann-Whitney test. Comparison of normally distributed continuous variables between two imaging modalities or techniques in one patient was done using the paired student's t-test or, in case of a skewed distribution, the Wilcoxon one-sample test. Pearson correlation coefficient and linear regression analysis was applied for associations. Mean differences between imaging modalities or techniques were determined by Bland-Altman plots, and the limits of agreement calculated using the mean and standard deviation of

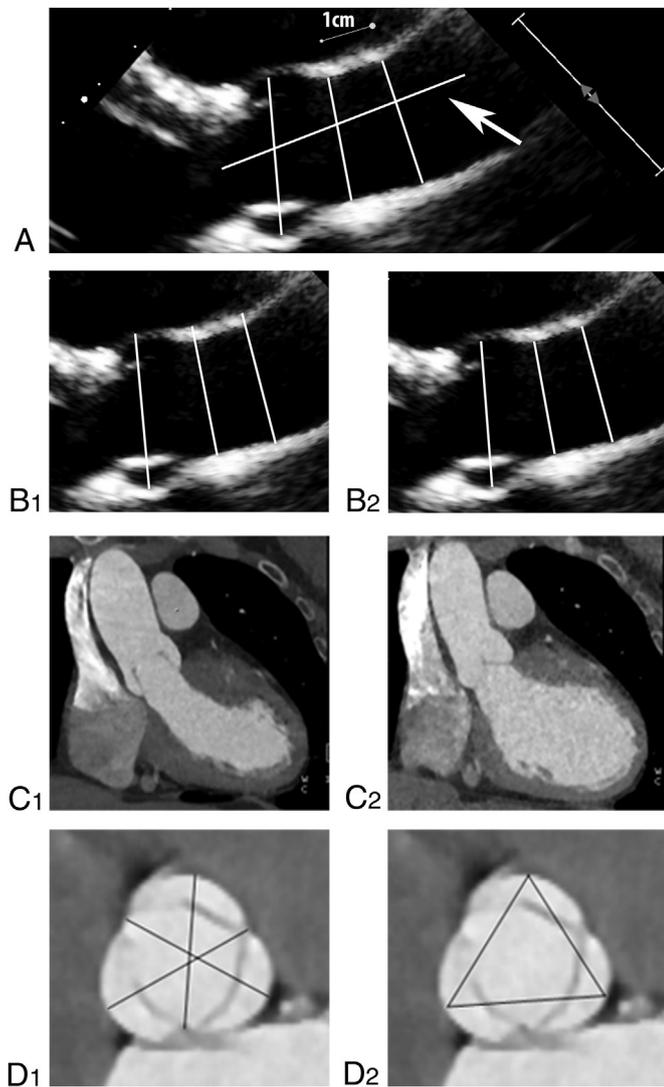


Fig. 1. Measurements of the aortic root and ascending aorta. Aortic diameters were measured at three predefined levels: the Sinus of Valsalva, the sinotubular junction and the ascending aorta (A), with use of the leading edge-to-leading edge (B1) and inner edge-to-inner edge (B2) methods in echocardiography and during mid-systole (C1) and end-diastole (C2) in both echocardiography and CTA. Also the length of the aorta (arrow in A) was measured by 2DE. At the level of the sinus of Valsalva both the cusp-to-commissure diameter (D1) and the cusp-to-cusp diameter (D2) were measured by CTA.

the difference. To assess intra- and inter observer variability the intraclass correlation coefficient (ICC) was calculated. The IBM SPSS® statistics 21.0 software was used for data analysis. Two-sided *p* values of <0.05 were considered statistically significant.

3. Results

3.1. Study population

In total 100 subjects were included: 50 subjects with BAV (age 36 ± 13 years; 26% female) and 50 subjects with Turner syndrome (age 35 ± 13 years, 100% female, 24% BAV). Nineteen patients had BAV type 0, 36 patients BAV type 1 and 7 patients BAV type 2. Renal function was normal in all. MRA was not performed in 12 subjects due to claustrophobia ($n = 4$), technical problems ($n = 4$), contra-indications ($n = 2$) and logistic reasons ($n = 2$). In 26 subjects (26%) the investigations were not performed on the same day. In these subjects the median time between investigations was 7 (IQR 6.5–22.8) days, mostly due to technical or practical issues. The mean total dose length product was

362.2 ± 196.4 mGy * cm. Table 1 shows the baseline patient characteristics of the total study population and separately for the three groups: BAV subjects, Turner subjects without BAV and Turner subjects with BAV.

3.2. Comparison of aortic diameters among different imaging modalities

All absolute measurements of the aorta with 2DE, CTA and MRA are shown in Supplemental Tables 2 and 3. Comparison between MRA and CTA showed a Pearson correlation coefficient of 0.84–0.95 at the level of the SoV and >0.96 at the levels of the STJ and TAA (Table 2 and Supplemental Table 4).

When comparing 2DE with CTA, the L-L edge method showed best agreement with CTA compared to the I-I edge method at the level of the STJ and TAA in both end-diastole and mid-systole (Table 2 and supplemental Fig. 1). The smallest difference between 2DE and CTA was found at the STJ in mid-systole with the L-L edge method ($r = 0.96$, mean difference 0.1 ± 1.8 mm). At the level of the SoV the I-I edge method underestimated the diameter compared to the cusp-to-commissure method in CTA (supplemental Figs. 2 and 3 and Supplemental Table 5). In the majority of cases, lower Pearson correlation coefficients and higher mean differences were found at the level of the SoV.

3.3. Comparison between cusp-to-commissure and cusp-to-cusp diameter

Between the cusp-to-commissure and the cusp-to-cusp diameter measured on CTA no significant difference was found (mean difference 0.0 ± 1.5 mm, $p = 1.00$). The maximum difference between these two methods in one patient was 4 mm.

3.4. Comparison between end-diastole and mid-systole

Mid-systolic aortic diameters were significantly larger than end-diastolic diameters at nearly all levels (Supplemental Table 6). Comparison of mid-systolic and end-diastolic aortic diameters demonstrated mean differences from 0.7 ± 2.3 mm up to 1.8 ± 1.5 mm. The standard deviations of mid-systole and end-diastole did not differ significantly at all levels by both 2DE and CTA (Levene's test $p > 0.05$). The aortic length by 2DE was significantly longer during mid-systole (51.1 ± 13.8 mm) compared to end-diastole (45.8 ± 13.2 mm) with a mean difference of 5.3 ± 5.1 mm ($p < 0.001$).

3.5. Maximum single-subject difference between all aortic measurements

Distribution of differences by aortic level are displayed in Fig. 2. The maximum difference was 5.4 ± 2.7 mm for the SoV (maximum 18 mm), 5.1 ± 2.0 mm for the STJ (maximum 11 mm) and 4.8 ± 2.1 mm for the TAA (maximum 11 mm). The maximum difference is a result from both inter-modality differences as from differences between modalities, but was most often explained by the differences between measurements on 2DE (29%) or between 2DE and CTA (38%, Supplemental Fig. 4). Maximum difference showed a moderate positive correlation with the absolute diameter at each level (Supplemental Fig. 5), specifically SoV ($r = 0.42$, $p \leq 0.001$), STJ ($r = 0.41$, $p \leq 0.001$) and TAA ($r = 0.45$, $p \leq 0.001$). Patients with BAV showed a larger maximum difference (SoV $p = 0.001$, STJ $p < 0.001$, TAA $p < 0.001$). After adjustment for aortic diameter, this correlation remained significant for the STJ ($\beta = 0.87$, $p = 0.042$) and TAA ($\beta = 0.95$, $p = 0.027$). Patients in which investigations were performed on different days ($n = 26$), did not show a larger maximum difference compared to the patients who received all investigations on the same day.

Table 1
Baseline characteristics.

	All (n = 100)	Bicuspid aortic valve without Turner syndrome (n = 50)	Turner syndrome (n = 50)		p-Value BAV and TS vs BAV without TS	p-Value TS and BAV vs TS without BAV
			Tricuspid aortic valve (n = 38)	Bicuspid aortic valve (n = 12)		
Age (y)	35 ± 13	35 ± 13	35 ± 13	36 ± 13	0.882	0.892
Gender, female	63 (63%)	13 (26%)	38 (100%)	12 (100%)	<0.001 [†]	–
Height (cm)	169 ± 16	181 ± 12	157 ± 9	154 ± 7	<0.001	0.330
Weight (kg)	72 ± 17	78 ± 15	69 ± 18	61 ± 11	<0.001	0.131
Systolic blood pressure (mm Hg)	124 ± 16	124 ± 15	124 ± 18	126 ± 16	0.685	0.719
Diastolic blood pressure (mm Hg)	80 ± 11	80 ± 10	80 ± 12	83 ± 14	0.319	0.449
Hypertension	16 (16%)	8 (16%)	7 (18%)	1 (8%)	0.675 [†]	0.661 [†]
Coarctation	13 (13%)	9 (18%)	0 (0%)	4 (33%)	0.256 [†]	0.002 [†]
Aortic dilatation (>40 mm and/or ASI > 2.1 cm/cm ²)	47 (47%)	33 (66%)	7 (18%)	7 (58%)	0.618	0.023 [†]
Aortic stenosis (echo V _{max} > 2.5 m/s)	29 (29%)	28 (56%)	0 (0%)	1 (8%)	0.003 [†]	0.240 [†]
Aortic regurgitation (moderate or severe)	17 (17%)	16 (32%)	0 (0%)	1 (8%)	0.153 [†]	0.240 [†]
Echocardiography	100 (100%)	50 (100%)	38 (100%)	12 (100%)	–	–
Computed tomography angiography ^a	100 (100%)	50 (100%)	38 (100%)	12 (100%)	–	–
Diameter sinus of Valsalva (mm)	35 ± 6	39 ± 6	31 ± 3	34 ± 5	0.005	0.140
Diameter sinotubular junction (mm)	31 ± 6	34 ± 6	27 ± 3	29 ± 6	0.016	0.233
Diameter ascending aorta (mm)	33 ± 7	37 ± 7	29 ± 4	31 ± 6	0.004	0.244
Magnetic resonance angiography	88 (88%)	44 (88%)	33 (87%)	11 (92%)	1.000 [†]	1.000 [†]

Data are expressed as mean ± SD or number (percentage). ASI = aortic size index (aortic diameter divided by BSA), TS = Turner syndrome, V_{max} = maximum velocity.

^a Aortic measurements during systole and with the inner-to-inner edge method.

[†] Fisher's exact test.

3.6. Intra- and interobserver variability

Intra- and interobserver variability for 2DE, CTA and MRA are shown in supplemental tables 7 and 8. There was good agreement for most measurements. Agreement was least optimal at the SoV.

4. Discussion

Our study compared measurements of three aortic levels using three imaging modalities (CTA, MRA and 2DE), different edge detections and different cardiac phases. Our goals were to determine agreement and provide guidance on the optimal approach to measure the ascending aorta. We included two groups of patients giving a wide spectrum of aortic dimensions and leaflet configurations. The findings are important for all patients with confirmed or suspected aortic pathology.

Although overall agreement was very good, the maximum difference between two measurements in any given subject was high. Despite measurements performed by experienced investigators, we showed differences up to 18 mm at the SoV, 11 mm at the STJ and 11 mm at the TAA. Given the guideline thresholds for the definition of aortic dilation (>40 mm) and indications for preventive surgery (>55 mm) [6,23], measured differences of this range are too large to be of use in clinical practice. Intra- and interobserver variability were good to excellent, so these differences are probably related to the differences in technique and not to differences in individual measurements. Larger maximum differences were found in larger aortas, and most often between the different measurements on 2DE or between 2DE and CTA. Also patients with BAV show larger maximum differences. Since the root is generally well-imaged on all standard 2DE, one would assume that there would be better agreement at this level. Yet lower Pearson correlation coefficients and higher mean differences were observed at the SoV relative to higher up the aorta, suggesting that for patients with dilation at this level CTA or MRA may be preferable for accurate follow-up.

Our data also showed that the L-L edge method by 2DE corresponds best with the I-I edge method by CTA and MRA. Although it seems logical to use the same method for comparison between modalities, it appears that the L-L edge method is preferable for 2DE. This supports current clinical practice, since most physicians who use 2DE already

apply the L-L edge method and current reference values are based on this method [16,17].

An advantage of the current study is that in most subjects imaging with all three modalities was performed on the same day, meaning any variation due to loading conditions should be controlled. In addition, the twenty-six patients who received the investigations on different days, did not show larger maximum differences. Although our data does not contain information about physiological conditions, such as heart rate or blood pressure, we assume this will probably not have affected our results. However, we have to admit that our MRA protocol was not completely optimal. Despite this limited MRA sequences, we found excellent agreement between CTA and MRA, as others have similarly reported [24,29]. Also intermodality comparisons between echocardiography and CTA/MRA are previously published using studies in varying aortic patient groups, with some findings that are congruent with our own. By 2DE for example, better agreement with CTA has been shown using L-L techniques rather than I-I [24–30]. Several studies show echo dimensions to be smaller than either MRI or CTA [31,32] including our previous study [28]. Consistency with other publications adds credibility to the findings overall.

Based on these results, several recommendations can be made to maximize intermodality agreement. Our findings support the necessity of using the same imaging modality and technique in an individual patient to accurately compare serial measurements. CTA or MRA should be performed at least once in addition to 2DE for optimal imaging of the aorta. In patients with good agreement 2DE may be used for serial follow-up. We found no difference between the cusp-to-commissure and cusp-to-cusp methods in CTA. Although another study [26] found a slightly larger diameter of 1.3 mm when using the cusp-to-cusp method, there is currently not enough evidence for the use of one technique over another. Preferably the same technique should be used every time.

Our study is the first to assess the length of aorta visible during 2DE. Echocardiographic images showed on average a 5.3 mm longer segment of the aorta during mid-systole compared to end-diastole. This could be an additional reason to measure the aorta during systole. Guidelines generally advise end-diastolic measures because of the greater reproducibility (blood pressure is most stable and distension is more plateaued), but this is not confirmed in our and other studies [25,33]. In addition, physicians prefer to use the largest diameter of the aorta in their decision making. For this reason, the higher values found during mid-systole

Table 2
Agreement between echocardiography, CTA and MRA.

		Lower limit-upper limit of agreement (mm)								
Mean difference ± standard deviation (mm)			Echo L-L Diastole	Echo L-L Systole	Echo I-I Diastole	Echo I-I Systole	CTA I-I Diastole	CTA I-I Systole	MRA I-I	
	EchoL-LDiastole	SoV			-3.4-1.4	1.1-4.2	-0.6-4.1	-6.6-5.9	-7.6-4.6	-7.1-5.3
		STJ			-4.5-1.8	1.1-4.7	-2.0-4.9	-3.2-3.8	-5.0-2.6	-5.3-3.5
		AA			-4.6-2.3	1.2-4.1	2.6-5.3	-3.1-4.8	-5.7-3.5	-4.9-4.9
	EchoL-LSystole	SoV	-1.0 ± 1.2		0.9-6.3	1.1-4.3	-5.8-7.0	-6.7-5.8	-6.2-6.4	
		STJ	-1.3 ± 1.6		0.9-7.6	1.1-4.5	-2.1-5.3	-3.4-3.7	-3.9-4.6	
		AA	-1.2 ± 1.8		0.1-7.5	1.2-3.9	-2.3-6.2	-3.8-4.0	-3.4-5.7	
	EchoL-IDiastole	SoV	2.7 ± 0.8	3.6 ± 1.4		-3.3-1.4	-9.3-3.2	-10.4-2.1	-9.7-2.6	
		STJ	2.9 ± 0.9	4.3 ± 1.7		-4.6-1.7	-6.3-1.2	-8.3-0.0	-8.4-7.0	
		AA	2.7 ± 0.7	3.8 ± 1.9		-5.3-2.7	-5.8-2.2	-8.5-1.0	-7.9-2.5	
EchoL-ISystole	SoV	1.8 ± 1.2	2.7 ± 0.8	-0.9 ± 1.2		-8.4-4.1	-9.5-3.0	-8.9-3.5		
	STJ	1.5 ± 1.8	2.8 ± 0.9	-1.4 ± 1.6		-5.1-2.7	-6.5-1.1	-7.0-2.1		
	AA	1.4 ± 2.0	2.5 ± 0.7	-1.3 ± 2.0		-5.0-3.9	-6.6-1.7	-6.2-3.4		
CTAI-IDiastole	SoV	-0.3 ± 3.2	0.6 ± 3.2	-3.0 ± 3.2	-2.1 ± 3.2		-4.0-1.8	-4.2-3.0		
	STJ	0.3 ± 1.8	1.6 ± 1.9	-2.6 ± 1.9	-1.2 ± 2.0		-4.0-1.1	-4.8-2.3		
	AA	0.9 ± 2.0	2.0 ± 2.2	-1.8 ± 2.0	-0.6 ± 2.3		-4.6-1.1	-4.3-2.7		
CTAI-ISystole	SoV	-1.5 ± 3.1	-0.5 ± 3.2	-4.1 ± 3.2	-3.2 ± 3.2	-1.1 ± 1.5		-3.0-4.1		
	STJ	-1.2 ± 2.0	0.1 ± 1.8	-4.1 ± 2.1	-2.7 ± 1.9	-1.5 ± 1.3		-3.0-3.7		
	AA	-1.1 ± 2.3	0.1 ± 2.0	-3.8 ± 2.4	-2.4 ± 2.1	-1.8 ± 1.5		-2.2-4.4		
MRAI-I	SoV	-0.9 ± 3.2	0.8 ± 3.2	-3.6 ± 3.1	-2.7 ± 3.2	-0.6 ± 1.8	0.6 ± 1.8			
	STJ	-0.9 ± 2.3	0.3 ± 2.2	-3.8 ± 2.3	-2.5 ± 2.3	-1.3 ± 1.8	0.3 ± 1.7			
	AA	-0.0 ± 2.5	1.1 ± 2.3	-2.8 ± 2.7	-1.4 ± 2.4	-0.8 ± 1.8	1.1 ± 1.7			

Mean difference ± standard deviation (colored boxes) and lower limit-upper limit of agreement (non-colored boxes) for comparison between different measurements at the level of the sinus of Valsalva (SoV) sinotubular junction (STJ) and the ascending aorta (AA). Green: mean difference < 1.0 mm. Orange: mean difference 1.0–2.0 mm. Red: mean difference ≥ 2.0 mm.

shown in our together with one other study [34], could be an additional reason to choose systole. Yet since natural history studies have largely been based on 2DE measurements in diastole, some have argued that changing conventions would adversely impact clinical management.

A limitation of our study was the inclusion of both bicuspid and tricuspid valve subjects. Because in some bicuspid aortic valves it was not possible to measure three cusp-to-commissure distances, we also analyzed this group separately at the level of the SoV. This resulted in a small number of subjects for analysis. We did not include healthy participant, which could have made the results even more generalizable. Because we used the protocols of a previous developed cohort study, the imaging modalities showed some limitations, such as the reduced tube current during the last 60% of the R-R interval. Also, the slice thickness of CTA was 1.5 mm, which is slightly thicker than recommended by guidelines [7]. Our MRA protocol was non-ECG-gated, which caused some blurring and limited comparisons to averaged diastole/systole measurements from CTA. Others have shown sharper edge detection and favorable variation for steady-state free precession imaging without contrast [35,36] than the methods we were able to use here. Despite these potential limitations there was good agreement between CTA and MRA. Also the large maximum single-subject difference was not caused by the limited MRA sequences.

In conclusion, our study supports the L-L edge method by 2DE to provide the best agreement with the I-I edge method by CTA or MRA. This is also recommended by the ASE/EACVI guidelines [7,8]. CTA or MRA should be performed at least once and follow-up measurements of the aorta should be done at the same level, during the same cardiac phase and using the same technique and modality.

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ijcard.2018.08.067>.

Funding

This study was supported by the Dutch Heart Foundation (contract grant number: 2013T093). Dr. Broberg was supported by a grant from the National Heart, Lung, and Blood Institute in the United States (1R34HL115032-01A1).

Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

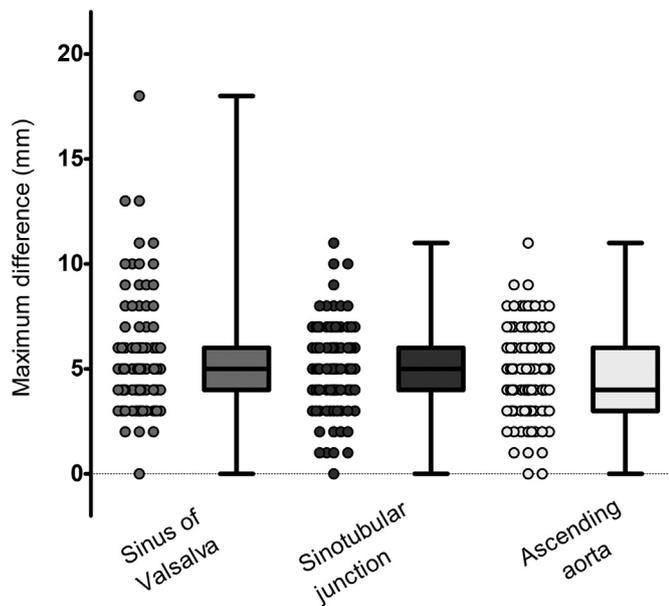


Fig. 2. Distribution of maximum differences found between the seven measurements. The maximum difference are plotted for the three different levels: sinus of Valsalva, the sinotubular junction and the ascending aorta.

Acknowledgements

None.

References

- [1] R.R. Davies, L.J. Goldstein, M.A. Coady, et al., Yearly rupture or dissection rates for thoracic aortic aneurysms: simple prediction based on size, *Ann. Thorac. Surg.* 73 (2002) 17–27 (discussion 27–8).
- [2] W.D. Clouse, J.W. Hallett Jr., H.V. Schaff, M.M. Gayari, D.M. Ilstrup, L.J. Melton 3rd., Improved prognosis of thoracic aortic aneurysms: a population-based study, *JAMA* 280 (1998) 1926–1929.
- [3] C. Olsson, S. Thelin, E. Stahle, A. Ekblom, F. Granath, Thoracic aortic aneurysm and dissection: increasing prevalence and improved outcomes reported in a nationwide population-based study of more than 14,000 cases from 1987 to 2002, *Circulation* 114 (2006) 2611–2618.
- [4] M. Cantinotti, R. Giordano, A. Clemente, et al., Strengths and limitations of current adult nomograms for the aorta obtained by noninvasive cardiovascular imaging, *Echocardiography* 33 (2016) 1046–1068.
- [5] F.P. Mongeon, F. Marcotte, D.G. Terrone, Multimodality noninvasive imaging of thoracic aortic aneurysms: time to standardize? *Can. J. Cardiol.* 32 (2016) 48–59.
- [6] L.F. Hiratzka, G.L. Bakris, J.A. Beckman, et al., ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guidelines for the diagnosis and management of patients with Thoracic Aortic Disease: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Thoracic Surgeons, and Society for Vascular Medicine, *Circulation* 121 (2010) e266–e369.
- [7] S.A. Goldstein, A. Evangelista, S. Abbara, et al., Multimodality imaging of diseases of the thoracic aorta in adults: from the American Society of Echocardiography and the European Association of Cardiovascular Imaging: endorsed by the Society of Cardiovascular Computed Tomography and Society for Cardiovascular Magnetic Resonance, *J. Am. Soc. Echocardiogr.* 28 (2015) 119–182.
- [8] R.M. Lang, L.P. Badano, V. Mor-Avi, et al., Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging, *J. Am. Soc. Echocardiogr.* 28 (2015) 1–39 (e14).
- [9] L. Lopez, S.D. Colan, P.C. Frommelt, et al., Recommendations for quantification methods during the performance of a pediatric echocardiogram: a report from the Pediatric Measurements Writing Group of the American Society of Echocardiography Pediatric and Congenital Heart Disease Council, *J. Am. Soc. Echocardiogr.* 23 (2010) 465–495 (quiz 576–7).
- [10] M.K. Son, S.A. Chang, J.H. Kwak, et al., Comparative measurement of aortic root by transthoracic echocardiography in normal Korean population based on two different guidelines, *Cardiovasc. Ultrasound* 11 (2013) 28.
- [11] E. Bossone, E. Yuriditsky, S. Desale, F. Ferrara, O. Vriz, F.M. Asch, Normal values and differences in ascending aortic diameter in a healthy population of adults as measured by the pediatric versus adult American Society of echocardiography guidelines, *J. Am. Soc. Echocardiogr.* 29 (2016) 166–172.
- [12] A. Hager, H. Kaemmerer, U. Rapp-Bernhardt, et al., Diameters of the thoracic aorta throughout life as measured with helical computed tomography, *J. Thorac. Cardiovasc. Surg.* 123 (2002) 1060–1066.
- [13] S.S. Mao, N. Ahmadi, B. Shah, et al., Normal thoracic aorta diameter on cardiac computed tomography in healthy asymptomatic adults: impact of age and gender, *Acad. Radiol.* 15 (2008) 827–834.
- [14] H. Kalsch, N. Lehmann, S. Mohlenkamp, et al., Body-surface adjusted aortic reference diameters for improved identification of patients with thoracic aortic aneurysms: results from the population-based Heinz Nixdorf recall study, *Int. J. Cardiol.* 163 (2013) 72–78.
- [15] A. Wolak, H. Gansar, L.E. Thomson, et al., Aortic size assessment by noncontrast cardiac computed tomography: normal limits by age, gender, and body surface area, *JACC Cardiovasc. Imaging* 1 (2008) 200–209.
- [16] P. Biaggi, F. Matthews, J. Braun, V. Rousson, P.A. Kaufmann, R. Jenni, Gender, age, and body surface area are the major determinants of ascending aorta dimensions in subjects with apparently normal echocardiograms, *J. Am. Soc. Echocardiogr.* 22 (2009) 720–725.
- [17] R.B. Devereux, G. de Simone, D.K. Arnett, et al., Normal limits in relation to age, body size and gender of two-dimensional echocardiographic aortic root dimensions in persons ≥ 15 years of age, *Am. J. Cardiol.* 110 (2012) 1189–1194.
- [18] O. Vriz, V. Aboyans, A. D'Andrea, et al., Normal values of aortic root dimensions in healthy adults, *Am. J. Cardiol.* 114 (2014) 921–927.
- [19] A.T. van den Hoven, J.S. Mc-Ghie, R.G. Chelu, et al., Transthoracic 3D echocardiographic left heart chamber quantification in patients with bicuspid aortic valve disease, *Int. J. Card. Imaging* 33 (2017) 1895–1903.
- [20] P. Lancellotti, C. Tribouilloy, A. Hagendorff, et al., Recommendations for the echocardiographic assessment of native valvular regurgitation: an executive summary from the European Association of Cardiovascular Imaging, *Eur. Heart J. Cardiovasc. Imaging* 14 (2013) 611–644.
- [21] N. Rudarakanchana, C.D. Bicknell, N.J. Cheshire, et al., Variation in maximum diameter measurements of descending thoracic aortic aneurysms using unformatted planes versus images corrected to aortic centerline, *Eur. J. Vasc. Endovasc. Surg.* 47 (2014) 19–26.
- [22] H.H. Sievers, C. Schmidtke, A classification system for the bicuspid aortic valve from 304 surgical specimens, *J. Thorac. Cardiovasc. Surg.* 133 (2007) 1226–1233.
- [23] R. Erbel, V. Aboyans, C. Boileau, et al., 2014 ESC guidelines on the diagnosis and treatment of aortic diseases: document covering acute and chronic aortic diseases of the thoracic and abdominal aorta of the adult. The Task Force for the Diagnosis and Treatment of Aortic Diseases of the European Society of Cardiology (ESC), *Eur. Heart J.* 35 (2014) 2873–2926.
- [24] B.P. Paelinck, P.L. Van Herck, I. Rodrigus, et al., Comparison of magnetic resonance imaging of aortic valve stenosis and aortic root to multimodality imaging for selection of transcatheter aortic valve implantation candidates, *Am. J. Cardiol.* 108 (2011) 92–98.
- [25] J.Y. Park, T.A. Foley, C.R. Bonnicksen, et al., Transthoracic echocardiography versus computed tomography for ascending aortic measurements in patients with bicuspid aortic valve, *J. Am. Soc. Echocardiogr.* 30 (2017) 625–635.
- [26] J.F. Rodriguez-Palmares, G. Teixido-Tura, V. Galuppo, et al., Multimodality assessment of ascending aortic diameters: comparison of different measurement methods, *J. Am. Soc. Echocardiogr.* 29 (2016) 819–826 (e4).
- [27] J.F. Tsang, M. Lytwyn, A. Farag, et al., Multimodality imaging of aortic dimensions: comparison of transthoracic echocardiography with multidetector row computed tomography, *Echocardiography* 29 (2012) 735–741.
- [28] D. van der Linde, A. Rossi, S.C. Yap, et al., Ascending aortic diameters in congenital aortic stenosis: cardiac magnetic resonance versus transthoracic echocardiography, *Echocardiography* 30 (2013) 497–504.
- [29] D. Leone, F. Tosello, R. Faletti, et al., Accuracy of transthoracic echocardiography in the assessment of proximal aortic diameter in hypertensive patients: comparison with cardiac magnetic resonance, *J. Hypertens.* 35 (2017) 1626–1634.
- [30] G. Tamborini, C.A. Galli, A. Maltagliati, et al., Comparison of feasibility and accuracy of transthoracic echocardiography versus computed tomography in patients with known ascending aortic aneurysm, *Am. J. Cardiol.* 98 (2006) 966–969.
- [31] A. Nejatian, J. Yu, T. Geva, M.T. White, A. Prakash, Aortic measurements in patients with aortopathy are larger and more reproducible by cardiac magnetic resonance compared with echocardiography, *Pediatr. Cardiol.* 36 (2015) 1761–1773.
- [32] S.F. Tsai, M. Trivedi, C.J. Daniels, Comparing imaging modalities for screening aortic complications in patients with bicuspid aortic valve, *Congenit. Heart Dis.* 7 (2012) 372–377.
- [33] L.M. de Heer, R.P. Budde, W.P. Mali, A.M. de Vos, L.A. van Herwerden, J. Kluin, Aortic root dimension changes during systole and diastole: evaluation with ECG-gated multi-detector row computed tomography, *Int. J. Card. Imaging* 27 (2011) 1195–1204.
- [34] D. Muraru, F. Maffessanti, G. Kocabay, et al., Ascending aorta diameters measured by echocardiography using both leading edge-to-leading edge and inner edge-to-inner edge conventions in healthy volunteers, *Eur. Heart J. Cardiovasc. Imaging* 15 (2014) 415–422.
- [35] S. Veldhoen, C. Behzadi, T. Derlin, et al., Exact monitoring of aortic diameters in Marfan patients without gadolinium contrast: intraindividual comparison of 2D SSFP imaging with 3D CE-MRA and echocardiography, *Eur. Radiol.* 25 (2015) 872–882.
- [36] F. von Knobelsdorff-Brenkenhoff, H. Gruettner, R.F. Trauzeddel, A. Greiser, J. Schulz-Menger, Comparison of native high-resolution 3D and contrast-enhanced MR angiography for assessing the thoracic aorta, *Eur. Heart J. Cardiovasc. Imaging* 15 (2014) 651–658.