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Influence of the Quantity of Aortic Valve Calcium on the Agreement Between Automated 3-Dimensional Transesophageal Echocardiography and Multidetector Row Computed Tomography for Aortic Annulus Sizing

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> Accurate aortic annulus sizing is key for selection of appropriate transcatheter aortic valve implantation (TAVI) prosthesis size. The present study compared novel automated 3-dimensional (3D) transesophageal echocardiography (TEE) software and multidetector row computed tomography (MDCT) for aortic annulus sizing and investigated the influence of the quantity of aortic valve calcium (AVC) on the selection of TAVI prosthesis size. A total of 83 patients with severe aortic stenosis undergoing TAVI were evaluated. Maximal and minimal aortic annulus diameter, perimeter, and area were measured. AVC was assessed with computed tomography. The low and high AVC burden groups were defined according to the median AVC score. Overall, 3D TEE measurements slightly underestimated the aortic annulus dimensions as compared with MDCT (mean differences between maximum, minimum diameter, perimeter, and area: -1.7 mm, 0.5 mm, -2.7 mm, and -13 mm², respectively). The agreement between 3D TEE and MDCT on aortic annulus dimensions was superior among patients with low AVC burden (<3,025 arbitrary units) compared with patients with high AVC burden (≥3,025 arbitrary units). The interobserver variability was excellent for both methods. 3D TEE and MDCT led to the same prosthesis size selection in 88%, 95%, and 81% of patients in the total population, the low, and the high AVC burden group, respectively. In conclusion, the novel automated 3D TEE imaging software allows accurate and highly reproducible measurements of the aortic annulus dimensions and shows excellent agreement with MDCT to determine the TAVI prosthesis size, particularly in patients with low AVC burden. © 2017 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/). (Am J Cardiol 2018;121:86-93)

Selection of appropriate transcatheter aortic valve implantation (TAVI) prosthesis size, based on accurate measurement of the aortic valve annulus, is crucial to avoid complications.¹ Although the aortic valve annulus is not an anatomic structure, it is defined as the virtual plane bisecting the nadirs of the aortic cusps in their insertion into the aortic wall. Multidetector row computed tomography (MDCT) is currently considered the reference standard to measure the aortic valve annulus. Three-dimensional (3D) transesophageal echocardiography (TEE) permits the acquisition of 3D data along the entire cardiac cycle, allowing for accurate measurements of the aortic annulus without use of nephrotoxic

Methods

This retrospective analysis included patients with severe aortic stenosis who underwent clinically indicated TAVI at Leiden University Medical Center, Leiden, The Netherlands, between July 2015 and March 2017. Patients with preprocedural MDCT data of the aortic valve acquired in systole and 3D TEE data acquired during the procedure with commercially available ultrasound system (E9 or E95 GE-Vingmed, Horten, Norway) were selected. Patients with valvein-valve procedures were excluded.

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agents and risk of radiation. However, aortic valve calcification (AVC) may impact on the measurement accuracy of 3D TEE. This is an important clinical question because TAVI is steadily increasing in lower operative risk populations, and the most appropriate imaging technique should be chosen, considering the accuracy and the potential risks. The present study compared the new automated 3D TEE software with manual MDCT measurements of the aortic annulus dimensions and assessed the agreement between both methods for TAVI prosthesis size selection. In addition, the analysis was stratified based on the AVC burden.



Figure 1. Multidetector row computed tomography of the aortic root. (*A*) Aortic valve calcium (AVC) burden assessment on noncontrast calcium scan. A series of contiguous transverse slices at the level of the aortic root encompassing the aortic valve were analyzed. The AVC score was determined by delineating the calcium of the aortic valve (yellow line in the bottom image) and expressed in arbitrary units (AU). Calcium in the coronary arteries, the mitral valve annulus, and the aortic wall were excluded. (*B*) Multiplanar reconstruction of the aortic valve for measurements of the aortic annulus dimensions. Two orthogonal planes, bisecting the long axis of the left ventricular outflow tract and the ascending aorta, were carefully aligned and a third transverse plane (red line) was moved directly beneath the lowest insertion points of all 3 aortic cusps to obtain the double oblique transverse view of the aortic annulus. Maximum and minimum diameters, perimeter, and aortic annulus area were obtained. The right lower image depicts the 3-dimensional volume rendered reconstruction of the aortic root. (Color version available online.)

Demographic and clinical data were prospectively collected in the departmental electronic clinical files (EPD Vision, Leiden, The Netherlands) and retrospectively analyzed. Baseline transthoracic echocardiographic and procedural TEE data were digitally stored and analyzed off-line with commercially available software (EchoPAC, version 201, GE-Vingmed). MDCT data were stored in institutional picture archiving and communication systems, and were analyzed offline with commercially available software (Vitrea fX 6.7.4, Vital Images, Minnetonka, Minnesota). Aortic valve annulus was defined as the plane bisecting the lowest insertion points of all 3 aortic valve cusps.^{2,3} The agreement between automated 3D TEE software and manual analysis of MDCT data to measure the aortic valve annulus was evaluated within the overall population and divided according to the median value of AVC burden. For this retrospective analysis of clinically acquired data (which were handled anonymously), the institutional review board waived the need for patient's informed consent.

Patients underwent preprocedural MDCT with the volumetric 320-slice MDCT scanner (AquilionOne, Toshiba Medical Systems, Tochigi-ken, Japan) as previously described.^{4,5} Aortic valve morphology (tricuspid/bicuspid) was evaluated from double oblique transverse views of the aortic valve. On noncontrast calcium scans, the AVC was quantified according to the Agatston method,^{6,7} and the calcium score was expressed in arbitrary units (AU) (Figure 1). The aortic annulus size was measured from the systolic images (30% to 35% of R-R interval) using multiplanar reformation planes (Figure 1). Maximum and minimum diameters, perimeter, and planimetered area of the aortic annulus were measured and eccentricity index was calculated.⁸

Periprocedural TEE was performed in all patients with commercially available ultrasound systems (E9 or E95, GE-Vingmed, Horten, Norway). In addition to the standard 2-dimensional TEE views,⁹ 3D datasets of the aortic valve were acquired from mid-esophageal long-axis or short-axis views of the aortic valve. Real-time single-beat 3D full volume images with at least a frame rate of 12 frames per second were acquired. To avoid shadowing of the anterior part of the aortic annulus caused by bulky calcifications of the aortic valve, out-of-plane images of the aortic root were acquired if needed (Figure 2). All images were digitally stored and the 3D aortic valve datasets were analyzed offline with 4D Automated Aortic Valve Quantification (4D Auto AVQ) software (EchoPAC, version 201, GE-Vingmed). The 4D Auto AVQ allowed automated computation of the mid-systolic dimensions of the aortic annulus (maximum and minimum diameter, perimeter, and planimetered area) in 3 steps (Figure 3). In addition, the eccentricity index was calculated.⁸

The TAVI prosthesis size was determined according to the sizing charts for the aortic annulus dimensions provided by the manufacturers. Edwards SAPIEN 3 prosthesis size was decided based on the measurements of the aortic annulus area with the following cut-off values: 338 to 430 mm² for a 23-mm, 430 to 546 mm² for a 26-mm, and 540 to 680 mm² for a 29-mm TAVI prosthesis size. Similarly, the Medtronic CoreValve Evolut prosthesis size was decided based on measurements of aortic annulus perimeter: 56.5 to 62.8 mm for a 23-mm, 62.8 to 72.3 mm for a 26-mm, and 72.3 to 81.7 mm for a 29-mm prosthesis size. Paravalvular leak after valve implantation was classified according to the Valve Academic Research Consortium-2 criteria.¹⁰

Continuous variables are presented as mean \pm standard deviation if normally distributed and as median and interquartile range otherwise. Categorical variables are shown as frequencies and percentages. Patients were divided into 2 groups according to the AVC burden: below and above the median value of AVC obtained on MDCT aortic valve calcium scans. Comparisons between the low and high AVC burden groups



Figure 2. Three-dimensional transesophageal echocardiography acquisition. To avoid shadowing over the aortic annulus caused by calcified aortic cusps, 2 different 3-dimensional (3D) transesophageal echocardiography datasets of the aortic valve are presented side-to-side with 3D long-axis image on the top, 2-dimensional long-axis multiplanar reconstruction image in the middle, and a short-axis multiplanar reconstruction image at the level of aortic annulus in the bottom. In (*panel A*), the aortic valve is parallel to the ultrasound beam and the calcified aortic annulus dimensions. In (*panel B*), the 3D aortic valve dataset was acquired with an oblique angle with respect to the ultrasound beam. The acoustic shadowing caused by the calcium is projected over the sinuses of Valsalva (green arrows), leaving the aortic annulus unaffected and enabling us to measure the aortic annulus dimensions accurately. (Color version available online.)

were performed using independent samples t test, Mann-Whitney U test, Pearson chi-square test or Fischer's exact test, as appropriate. Fischer's exact test was used when the expected value of a categorical variable was <5. The agreement between 3D TEE and MDCT measurements of the aortic annulus dimensions was assessed with Bland and Altman method.¹¹ A single observer analyzed all data and a second observer, blinded to the results of the first observer, remeasured the first 35 3D TEE and MDCT datasets for assessment of interobserver variability with intraclass correlation coefficients. Excellent agreement was defined as an intraclass correlation coefficient >0.8. The agreement between 3D TEE and MDCT to determine the TAVI prosthesis size was assessed with kappa statistics. Excellent agreement was defined by a kappa >0.8. All statistical analyses were performed using IBM SPSS Statistics 23 (IBM, Armonk, New York) and GraphPad Prism 7 (GraphPad Software, San Diego, California).

Results

Of 85 patients with MDCT and 3D TEE data eligible for the analysis, 2 patients were excluded either due to poor 3D TEE image quality or electrocardiogram gating artifacts on MDCT at the level of aortic valve annulus, leaving 83 patients for the final analysis. Demographic, clinical, procedural, echocardiographic, and MDCT characteristics are presented in Table 1. In the overall population, 3D TEE slightly underestimated the aortic annulus maximum diameter, perimeter, and area as compared with MDCT (Table 1, Figure 4). In contrast, 3D TEE yielded slightly larger minimum aortic annulus diameter, leading to smaller eccentricity index compared with MDCT (0.11 vs 0.19, p < 0.001, respectively). There was a very good agreement between 3D TEE and MDCT for the measurement of the aortic annulus dimensions (Figure 4). Furthermore, excellent interobserver agreement was observed for each imaging method in the subset of the first 35 consecutive patients, with MDCT showing only minimally superior reproducibility than 3D TEE (Table 2).

The median AVC burden on calcium scans was 3,025 AU. Patients were divided into low AVC burden (<3,025 AU) and high AVC burden (\geq 3,025 AU). Patients with high AVC burden were more frequently men, had higher transaortic pressure gradients, smaller indexed aortic valve area, and larger aortic annulus dimensions compared with patients with low AVC burden (Table 1). The AVC burden was not associated with



Figure 3. Automated 3-dimensional transesophageal echocardiography analysis of the aortic valve. (*Panel A*) Mid-systolic multiplanar reconstruction of the aortic valve. First, the 2 long-axis orthogonal planes through the aortic valve were aligned, and the transverse plane was moved to the hinge points of the aortic valve cusps. Subsequently, the software automatically delineated the left ventricular outflow tract and the aortic root anatomy, allowing for manual adjustments if needed. (*Panel B*) Once the contouring of the aortic root and aortic annulus (AA) had been approved, the 4D Auto AVQ program automatically computed AA dimensions: average diameter (diameter calculated based on the perimeter), maximum and minimum diameter, perimeter, and area of the aortic annulus. Graphical presentation of the cross-sectional area along the left ventricular outflow tract and the aortic root is shown below.

the incidence of significant paravalvular regurgitation or aortic annulus rupture. The agreement between 3D TEE and MDCT for the measurement of the aortic annulus dimensions was superior among patients with low AVC burden as compared with patients with high AVC burden (Figure 5).

In 73 patients (88%), 3D TEE and MDCT measurements led to the selection of the same TAVI prosthesis size, resulting in excellent agreement in the overall population (kappa = 0.820) (Table 3). When dividing the population according to the AVC burden, the agreement between 3D TEE and MDCT was superior in the low AVC burden group (the same prosthesis size would have been selected in 95% of patients, kappa = 0.926) as compared with the high AVC burden group (agreement in 81% of patients, kappa = 0.709). The agreement between 3D TEE and MDCT to determine the prosthesis size was not influenced by the eccentricity of the aortic annulus; the eccentricity indexes in 73 patients with concordant and 10 patients with discordant prosthesis sizing were 0.19 versus 0.16 (p = 0.336) by MDCT and 0.12 versus 0.10 (p = 0.554) by 3D TEE.

Discussion

The present study demonstrates that novel automated 3D TEE imaging software (4D Auto AVQ) allows reliable as-

sessment of aortic annulus dimensions in patients with severe aortic stenosis undergoing TAVI. Compared with MDCT, 3D TEE measurements slightly underestimated the aortic annulus dimensions, particularly in patients with high AVC burden. Importantly, 3D TEE measurements based on 4D Auto AVQ and MDCT led to the same prosthesis size selection in the majority of the patients. However, the agreement between 3D TEE and MDCT on prosthesis size selection was better among patients with low versus high AVC burden.

Several studies have compared the agreement between 3D TEE and MDCT to measure the aortic annulus dimensions.^{13–15} Ng et al. demonstrated in 53 patients undergoing TAVI that the aortic annulus areas calculated from 3D TEE-derived longaxis diameter, as well as measured by 3D TEE planimetry, were smaller compared with MDCT (4.06 ± 0.79 cm² vs 4.22 ± 0.77 cm² and 4.65 ± 0.82 cm², respectively; p <0.001).¹³ Vaquerizo et al. also showed significant underestimation of 3D TEE-derived aortic annulus dimensions compared with MDCT (mean perimeter: 68.6 ± 5.9 mm vs 75.1 ± 5.7 mm, respectively; p <0.001; mean area: $345.6 \pm 64.5 \text{ mm}^2 \text{ vs}$ $426.9 \pm 68.9 \text{ mm}^2$, respectively; p <0.001).¹⁴ The methodology used to measure the aortic annulus has an important influence on the agreement between MDCT and 3D TEE. Khalique et al. showed that when the aortic annulus was measured on 3D TEE data by using an off-label software that

Table 1

Demographic, clinical, procedural, echocardiographic, multidetector row computed tomography and 3-dimensional transesophageal echocardiography characteristics

Variable	Total population $(N = 83)$	Aortic valve calcium burden		
		Low $(N = 41)$	High $(N = 42)$	P-value
Age (years)	82 [77–86]	80 [75-85]	82 [79–86]	0.092
Men	39 (47%)	12 (29%)	27 (64%)	0.001
Body surface area (m ²)	1.84 ± 0.23	1.81 ± 0.20	1.87 ± 0.25	0.274
Body mass index (kg/m ²)	27.0 ± 4.5	27.1 ± 4.5	26.8 ± 4.6	0.805
Bicuspid aortic valve	2 (2%)	1 (2%)	1 (2%)	0.986
Logistic EuroSCORE (%)	13.1 [9.5–20.8]	13.2 [9.4–20.5]	12.6 [9.6-20.9]	0.884
Transcatheter aortic valve implantation access				0.668
Transfemoral	76 (92%)	37 (90%)	39 (93%)	
Transapical	7 (8%)	4 (10%)	3 (7%)	
Transcatheter aortic valve implantation prosthesis				0.364
Edwards SAPIEN 3	68 (82%)	32 (78%)	36 (86%)	
Medtronic CoreValve Evolut	15 (18%)	9 (22%)	6 (14%)	
More-than-mild paravalvular leak	1 (1%)	0	1 (2%)	1.000
Aortic annulus rupture	1 (1%)	0	1 (2%)	1.000
Echocardiography				
Peak transvalvular gradient (mmHg)	70 ± 24	60 ± 19	79 ± 24	< 0.001
Mean transvalvular gradient (mmHg)	44 ± 16	38 ± 14	51 ± 16	< 0.001
Aortic valve area (cm ²)	0.7 ± 0.2	0.8 ± 0.2	0.7 ± 0.2	0.181
Aortic valve area index (cm ² /m ²)	0.40 ± 0.09	0.42 ± 0.10	0.38 ± 0.08	0.044
Left ventricular stroke volume index (mL/m ²)	36 ± 10	34 ± 10	38 ± 10	0.140
Left ventricular ejection fraction (%)	60 [42–71]	62 [43–70]	59 [40-72]	0.672
Multidetector row computed tomography				
Aortic valve calcium burden (AU)	3025 [1873–3870]	1873 [1198–2520]	3803 [3512–5176]	
Aortic annulus maximum diameter (mm)	27.3 ± 2.9	26.4 ± 3.0	28.0 ± 2.6	0.013
Aortic annulus minimum diameter (mm)	22.1 ± 2.4	21.3 ± 2.0	22.9 ± 2.6	0.003
Aortic annulus perimeter (mm)	78.4 ± 8.3	75.6 ± 7.6	81.2 ± 8.0	0.002
Aortic annulus area (mm ²)	470 ± 95	441 ± 86	498 ± 97	0.006
Eccentricity index	0.19	0.19	0.18	0.620
3-dimensional transesophageal echocardiography				
Aortic annulus maximum diameter (mm)	25.5 ± 2.6	24.9 ± 2.6	26.2 ± 2.5	0.024
Aortic annulus minimum diameter (mm)	22.6 ± 2.5	22.0 ± 2.5	23.2 ± 2.5	0.027
Aortic annulus perimeter (mm)	75.7 ± 7.7	73.7 ± 7.5	77.7 ± 7.5	0.019
Aortic annulus area (mm ²)	458 ± 95	434 ± 90	481 ± 96	0.023
Eccentricity index	0.11	0.11	0.11	0.915

Data are presented as mean ± standard deviation, median [interquartile range] or as number (percentage).

AU = arbitrary units.

permits semiautomated delineation of the aortic annulus in the short-axis view, the underestimation of the aortic annulus size was less than with the manual tracing $(435 \pm 81 \text{ mm}^2 \text{ for})$ semiautomated 3D TEE postprocessing software vs $429 \pm 82 \text{ mm}^2$ for manual measurements vs $442 \pm 79 \text{ mm}^2$ for MDCT).¹⁵ Moreover, the semiautomated 3D TEE planimetry demonstrated better reproducibility of the aortic annulus measurements compared with manual planimetry. Similarly, we found a slight underestimation of the aortic annulus dimension using novel dedicated automated 3D TEE software as compared with MDCT. In addition, MDCT measurements resulted in larger aortic annulus eccentricity indexes compared with 3D TEE. Automated 3D TEE software algorithm may have accounted for a more circular shape of the aortic annulus; however, larger eccentricity indexes compared with MDCT have also been reported previously with manual 3D TEE measurements.13,14

One of the factors that may influence the accuracy of 3D TEE measurements of the aortic annulus is the AVC burden.

Bulky calcification of the aortic valve leaflets and of the aortic root, causing acoustic shadowing over distal aortic annulus, poses a major challenge to accurately delineate the aortic annulus plane on 3D TEE. This may explain the better agreement between 3D TEE and MDCT in patients with low compared with high AVC burden in present study. The deleterious effect of AVC on the definition of the aortic annulus plane can be reduced with appropriate 3D TEE data acquisition as indicated in Figure 2. However, it needs to be stressed that the terms low and high AVC burden groups identify patients in the upper and lower half of the AVC spectrum observed in our population. Both groups of patients had extensively calcified aortic valves as the median AVC score to divide them into 2 groups, 3,025 AU, was well above the suggested cut-off value for severe aortic stenosis proposed by Cueff et al. (1,651 AU) and by Clavel et al. (1,274 AU in women and 2,065 AU in men).^{7,12} The importance of studying the impact of AVC on the accuracy of aortic annulus measurements should be viewed from the perspective of the



Figure 4. Agreement between automated 3-dimensional (3D) transesophageal echocardiography (TEE) software and multidetector row computed tomography (MDCT) for the measurement of the aortic annulus dimensions. Bland-Altman plots, showing overall good agreement between 3D TEE and MDCT on aortic annulus dimension measurements.

Table 2

Inter-observer agreement for automated 3-dimensional transesophageal echocardiography analysis and multidetector row computed tomography for the measurement of the aortic annulus dimensions (N = 35 paired measurements)

	3-dimensional transesophageal echocardiography	Multidetector row computed tomography
Maximum diameter	0.912 (0.826-0.956)	0.962 (0.925-0.981)
Minimum diameter	0.925 (0.852-0.962)	0.950 (0.901-0.975)
Perimeter	0.963 (0.927-0.981)	0.984 (0.969-0.992)
Area	0.966 (0.934-0.983)	0.984 (0.943-0.994)

The intraclass correlation coefficients and the 95% confidence intervals are presented.

anticipated TAVI use in intermediate and eventually lowrisk patients with severe aortic stenosis and in patients with moderate aortic stenosis with concomitant left ventricular systolic dysfunction, where the AVC burden might be lower than in the classical high-risk aortic stenosis population.^{16,17} Our results suggest that in these clinical scenarios, 3D TEE might represent an attractive alternative to MDCT for preoperative TAVI assessment.

The agreement between 3D TEE and MDCT to determine the TAVI prosthesis size has been described before.^{14,15,18} Vaquerizo et al. reported that MDCT and 3D TEE agreed in the prosthesis size in only 44% of patients, if the size was determined by aortic annulus perimeter, and in 38%, if the size was determined by aortic annulus area.¹⁴ On the other hand, Khalique et al. observed excellent agreement between 3D TEE and MDCT valve sizing protocols (based on the aortic annulus area); in 94% of patients, both imaging techniques would have recommended the same prosthesis size.¹⁵ Husser et al. applied the long-axis aortic annulus diameter measurements to determine the TAVI prosthesis size and reported congruent results between 3D TEE and MDCT in 77% of patients (n = 57).¹⁸ Similarly, the present study showed excellent agreement between 3D TEE and MDCT, leading to the same prosthesis size selection in 88% of the patients. When dividing the population according to the AVC burden, the agreement between 3D TEE and MDCT further improved in patients with low AVC burden, as the same prosthesis size was recommended in 95% of patients, whereas high AVC burden had a negative impact, reducing the agreement to 81% of patients. In the majority of patients with high AVC burden and prosthesis-size mismatch, 3D TEE measurements suggested smaller prosthesis size compared with MDCT. Future



Figure 5. Agreement between automated 3-dimensional (3D) transesophageal echocardiography (TEE) software and multidetector row computed tomography (MDCT) for the measurement of the aortic annulus dimensions according to the aortic valve calcium (AVC) burden. Bland-Altman plots, showing better agreement between automated 3D TEE analysis and MDCT on aortic annulus area (A) and perimeter (B) in patients with low AVC burden, as compared with the patients with high AVC burden.

studies are therefore needed to determine whether these patients require different prosthesis sizing recommendations when assessed with 3D TEE.

The study was conducted retrospectively in a single center. The impact of this automated postprocessing software of 3D TEE data on annulus sizing, prosthesis selection, and paravalvular regurgitation rates was not prospectively assessed. No automated MDCT software was used, and the measurements were performed manually. However, the observers measuring MDCT data are highly experienced and have reported good inter- and intraobserver reproducibility.¹⁹ In the view of 3D TEE versus MDCT assessment of aortic annulus dimensions, it needs to be emphasized that MDCT allows for simultaneous peripheral arteries anatomy assessment and the planning of the C-arm projections needed for aortic valve prosthesis deployment.

Disclosures

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Table 3

Agreement between automated 3-dimensional transesophageal echocardiography analysis and multidetector row computed tomography on the selection of transcatheter aortic valve implantation prosthesis size. The agreement is shown for the total population, for the low aortic valve calcium burden group and for the high aortic valve calcium burden group

Total Population $(N = 83)$					
		Prosthesis size according to MDCT (N)			
		23 mm	26 mm	29 mm	
Prosthesis size according to	23 mm	22	7		
3D TEE (N)	26 mm		24	2	
	29 mm		1	27	
	Inter-1	Inter-rater agreement: Kappa = 0.820			
Low aortic valve calcification	(N = 41)				
		Prosthesis size according to MDCT (N)			
		23 mm	26 mm	29 mm	
Prosthesis size according to	23 mm	15	2		
3D TEE (N)	26 mm		11		
	29 mm			13	
	Inter-1	Inter-rater agreement: Kappa = 0.926			
High aortic valve calcification	(N = 42)				
		Prosthesis size according to MDCT (N)			
		23 mm	26 mm	29 mm	
Prosthesis size according to	23 mm	7	5		
3D TEE (N)	26 mm		13	2	

3D = 3-dimensional; MDCT = multidetector row computed tomography; TEE = transesophageal echocardiography.

1

Inter-rater agreement: Kappa = 0.709

14

29 mm

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