Catheterization and Cardiovascular Interventions 81:148–159 (2013)

VALVULAR AND STRUCTURAL HEART DISEASES

Original Studies

Objective Quantification of Aortic Valvular Structures by Cardiac Computed Tomography Angiography in Patients Considered for Transcatheter Aortic Valve Implantation

Grigorios Korosoglou,[1*] MD, Gitsios Gitsioudis,[1] MD, Irina Waechter-Stehle,[2] PhD, Juergen Weese,[2] PhD, Ulrike Krumsdorf,[1] MD, Emmanuel Chorianopoulos,[1] MD, Waldemar Hosch,[3] MD, Hans-Ulrich Kauczor,[3] MD, Hugo A. Katus,[1] MD, and Raffi Bekeredjian,[1] MD

Purpose: To test the ability of a model-based segmentation of the aortic root for consistent assessment of aortic valve structures in patients considered for transcatheter aortic valve implantation (TAVI) who underwent 256-slice cardiac computed tomography (CT). Methods: Consecutive patients (n = 49) with symptomatic severe aortic stenosis considered for TAVI and patients without aortic stenosis (n = 17) underwent cardiac CT. Images were evaluated by two independent observers who measured the diameter of the aortic annulus and its distance to both coronary ostia (1) manually and (2) software-assisted. All acquired measures were compared with each other and to (3) fully automatic quantification. Results: High correlations were observed for 3D measures of the aortic annulus conducted on multiple oblique planes (r = 0.87 and 0.84 between observers and model-based measures, and r = 0.81 between observers). Reproducibility was further improved by software-assisted versus manual assessment for all the acquired variables (r = 0.98 versus 0.81 for annulus diameter, r = 0.94 versus 0.85 for distance to the left coronary ostium, P < 0.01 for both). Thus, using software-assisted measurements very low limits of agreement were observed for the annulus diameter (95%CI of −1.2 to 0.6 mm) and within very low time-spent (0.6 ± 0.1 min for software-assisted versus 1.6 ± 0.3 min per patient for manual assessment, P < 0.001). Assessment of the aortic annulus using the 3D model-based instead of manual 2D-coronal measurements would have modified the implantation strategy in 12 of 49 patients (25%) with aortic stenosis. Four of 12 patients with potentially modified implantation strategy yielded postprocedural moderate paravalvular regurgitation, which may have been avoided by implantation of a larger prosthesis, as suggested by automatic 3D measures. Conclusion: Our study highlights the usefulness of software-assisted preprocedural assessment of the aortic annulus in patients considered for TAVI. © 2012 Wiley Periodicals, Inc.

[1]University of Heidelberg, Department of Cardiology, Heidelberg, Germany
[2]Philips Research Aachen, Germany
[3]University of Heidelberg, Department of Radiology, Heidelberg, Germany

Additional Supporting Information may be found in the online version of this article.

Conflict of interest: I.W and J.W are employees of Philips Research. All other authors had full control of the inclusion of any data or information that might have presented a conflict of interest for the authors who are employees of Philips Research.

*Correspondence to: Grigorios Korosoglou, MD, Department of Cardiology, University Hospital Heidelberg, Heidelberg, Germany.
E-mail: grigorios.korosoglou@med.uni-heidelberg.de

Received 27 July 2011; Revision accepted 14 November 2011

DOI 10.1002/ccd.23486
Published online 19 December 2012 in Wiley Online Library (wileyonlinelibrary.com)

Key words: aortic annulus; transcatheter aortic valve implantation (TAVI); cardiac computed tomography; model-based segmentation; quantitative analysis

INTRODUCTION

Transcatheter aortic valve implantation (TAVI) is increasingly used in patients with symptomatic severe aortic stenosis who are considered at high risk for cardiac surgery [1–3]. In contrast to surgery however, where sizing is performed under direct visualization, preprocedural imaging is essential before TAVI. Hereby, prosthesis sizing and positioning are essential to avoid peri-procedural complications as for e.g., occlusion of the coronary ostia [4], paravalvular regurgitation or dislocation of the valve into the aorta or the left ventricle [5,6]

The aortic annulus is anatomically defined as a virtual ring with three anatomical anchors at the nadir of each aortic leaflet. Contrast aortography and echocardiography have been previously proposed for the assessment of aortic valve structures [4,7]. However, the complex 3D-geometry and the crown-like and additionally elliptical shape of the aortic annulus may limit the accuracy of 2D-measures, which may not transect the full diameter but tangent cuts across the aortic root [8]. Technical developments with cardiac computed tomography angiography (CTA) have recently enabled ECG-gated imaging of the heart with high temporal and isotropic submillimeter spatial resolution [9]. In this regard, cardiac CTA has emerged as a valuable noninvasive tool for the assessment of aortic valve structures in patients considered for TAVI in recent clinical trials [10–12]. However, objective approaches for the quantitative estimation of aortic valve structures are still lacking.

We recently introduced a model-based segmentation software for the automatic extraction of aortic valve anatomy from CTA images [13]. The aim of our study was to test the ability of this method for consistent and reproducible measurements of aortic valve structures in patients considered for TAVI and in control subjects without aortic stenosis who underwent 256-slice CTA (Brilliance iCT, Philips Healthcare). Measures on CT images were assessed by two experienced independent observers (1) manually, (2) software-assisted by the same 2 observers, and (3) fully automatically using the model-based approach. The degree of agreement between visual, software-assisted and automatic measures was evaluated.

METHODS

Patient Population

From October 2009 to April 2010 consecutive patients ($n = 49$) with symptomatic severe aortic stenosis diagnosed by echocardiography and cardiac catheterization and considered for TAVI underwent cardiac CT. In addition, 17 randomly selected patients without aortic valve stenosis who underwent clinically indicated CT for suspected or known coronary artery disease within the same time period served as a "control" group. Patients with nonsinus rhythm, unstable angina, elevated serum creatinine (>2.0 mg/dl), or other contraindications to the administration of contrast agent were excluded. All procedures complied with the Declaration of Helsinki, were approved by our local ethic committee and all patients gave written informed consent.

256-Slice CT Scanning Technique

All scans were performed using a 256-slice Brilliance iCT scanner (Philips Healthcare) that features a gantry rotation time of 270 ms, resulting in a temporal resolution of 36–135 ms, depending on the heart rate of the patient and the performance of multisegment reconstruction algorithms, and an isotropic submillimeter spatial resolution.

For cardiac CT angiography a bolus of 80 ml of contrast agent (Ultravist 370, Bayer Schering Pharma) was injected intravenously using an antecubital i.v.-line (18GA, BD Venflon TM Pro Safetly). The contrast agent was injected at a flow of 5 ml/sec followed by a saline flush (50 ml at a flow of 5 ml/sec). The scan started automatically using a bolus tracking with a region of interest placed in the descending aorta and a threshold of 110 Hounsfield Units (HU). The entire volume of the heart was acquired during one breath-hold in 4–7 sec with simultaneous ECG recording. The detector collimation was $2 \times 128 \times 0.625$ mm^3, with 256 overlapping slices of 0.625 mm thickness and dynamic z-focal spot.

The CT study protocol included the intravenous administration of incremental doses of 2.5 mg of metoprolol (range, 2.5–25.0 mg), (Lopresor®, Novartis, Pharma GmbH) and sublingual glyceryl nitrate in control subjects. No premedication was given in patients with severe aortic stenosis. The tube voltage was 120 kV and the gantry rotation time was 0.27 sec. In all patients retrospective CT was performed using dose modulation (with a pulsing window at 75% and a tube current of 800–1,050 mAs (depending on patient habitus). For control subjects who underwent prospective CT and a current of 200 mAs was applied. For assessment of aortic valvular structures diastolic images (75% of the cardiac cycle) were used both in patients with aortic stenosis and in control subjects.

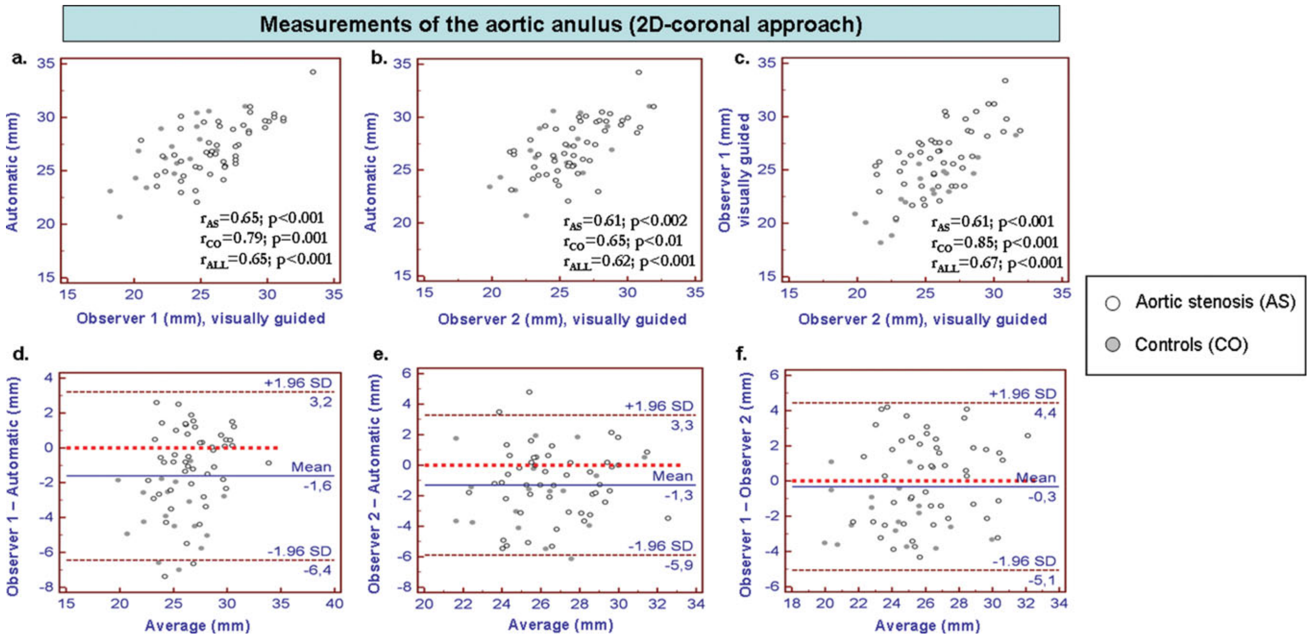

Fig. 1. **Moderate agreement was noticed between observers and model-based measures for $D_{\text{annulus coronal}}$ (a–c), while a trend for underestimation of ~1–2 mm was detected for manual versus fully automatic assessment of $D_{\text{annulus coronal}}$ (d–f). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]**

CT Image Analysis

CT data sets were anonymized and were analyzed in a random order using commercially available software (Philips Extended Brilliance Workspace 4.0).

Diameter Assessment of the Aortic Root and Its Distance to the Coronary Ostia

Standard coronal and sagittal views were used for the initial orientation of the aortic valve. Multiple oblique cuts through the aortic root were then obtained by aligning three perpendicular analysis windows (axial, oblique sagittal and oblique coronal), so that the most caudal attachments of all three aortic valve leaflets could be simultaneously depicted in one multiple oblique image (as shown in the Supporting Information Fig. 1). Subsequently, the following diameters and distances were assessed by two independent observers with at least 10 years experience in cardiovascular imaging (R.B. and G.K.):

1 The diameter of the aortic annulus using two-dimensional coronal images ($D_{\text{annulus coronal}}$).
2 The shortest diameter of the aortic annulus on multiple oblique planes defined by the base (i.e., most caudal attachments) of the native leaflets ($D_{\text{annulus short}}$).
3 The longest diameter of the aortic annulus on the same multiple oblique plane ($D_{\text{annulus long}}$).
4 The distance between the annulus and the left coronary ostium ($D_{\text{left ostium}}$).
5 The distance between the annulus and the right coronary ostium ($D_{\text{right ostium}}$).

Hereby it should be noted that the oblique sagittal plane approximates the parasternal long-axis view on echocardiography, which usually provides the smallest annulus, while the oblique coronal plane approximates the postero-anterior view on contrast aortography (interventionalist's view), providing the largest annulus diameter [11,14] (Supporting Information Fig. 1).

Model-Based Measurements

The software used in our study is based on the Philips general segmentation framework [15]. Further modifications were performed with this software for measuring distances and diameters of aortic valve structures (I.W and J.W) [13]. Details on the mathematic algorithms used for the model-based segmentation are provided elsewhere [13,15]. Briefly, a generic model of the aortic valve structures, in which anatomical landmarks are encoded, is matched to the CT images. Anatomical landmarks are placed on the basal ring of the aortic annulus, taking into account its complex anatomical crown line and elliptical shape. Hereby, the annulus plane is calculated out of a 3D-volume data set, by joining the most caudal basal attachments of the aortic valve leaflets.

1 Automatic Measures. To assess the short and long annulus diameter ($D_{\text{annulus short}}$ and $D_{\text{annulus long}}$) the mesh is cut by the respective plane, and an ellipse is fitted to the vertices of the resultant contours using direct least square fitting. The annulus diameter in the coronal images ($D_{\text{annulus coronal}}$) is determined by intersecting the ellipse with a coronal plane and by selecting the coronal image with the largest diameter. To localize the coronary ostia, a search region is encoded in the model and the ostium is identified using a pattern matching technique. For calculation of $D_{\text{left ostium}}$ and $D_{\text{right ostium}}$, their distance to the lowest point of the annulus plane is computed.

2 Interactive measures: For software-assisted measurements, observers are able to adjust the annulus plane by manually shifting the plane towards the aortic bulbus or the outflow tract. Furthermore, the position of both coronary ostia can be manually defined by clicking at the desired location.

Cardiac Catheterization

All patients underwent invasive cardiac evaluation, including coronary angiography and hemodynamic assessment of the severity of the aortic stenosis using simultaneous left and right heart catheterization. Simultaneous peak-to-peak and mean transvalvular gradients were routinely determined after transseptal puncture or retrograde crossing of the aortic valve. The aortic valve area (AVA) was calculated using the Gorlin formula [16]. In addition, selective angiography of the left and right coronary artery was performed according to the angiographic guidelines.

TABLE I. Demographic, Clinical, Hemodynamic, and Laboratory Parameters

Parameters	Controls	Severe aortic stenosis
	Demographics	
No of subjects	$n = 17$	$n = 49$
Age (years)	65 ± 12	78 ± 17*
Male sex	8 (47%)	29 (59%)
	Atherogenic risk factors	
Arterial hypertension	11 (65%)	43 (88%)
Hypercholesterolemia	10 (59%)	26 (53%)
Diabetes mellitus	2 (12%)	19 (39%)*
Smoker	4 (24%)	10 (20%)
Family history for CAD	6 (35%)	11 (22%)
	Computed tomography angiography data	
Heart rate during CTA	61 ± 7	72 ± 6*
Coronary artery disease (>50% stenosis)	6 (35%)	43 (88%)*
Single-vessel coronary artery disease	3 (18%)	24 (50%)*
Multi-vessel coronary artery disease	3 (18%)	19 (39%)
	Aortic stenosis assessment by cardiac catheterization	
Peak-to-peak gradient (mmHg)	n.a.	62 ± 27
Mean gradient (mmHg)	n.a.	41 ± 17
Aortic valve area (cm^2)	n.a.	0.7 ± 0.2
	Laboratory findings	
Serum creatinine (mg/dl)	0.8 ± 1.0	1.2 ± 0.6*
NT-proBNP serum levels (pg/ml)	n.a.	3173 ± 2994

Data presented as number of patients or as mean ± standard deviation; n.a, not applicable; NT-proBNP, N-terminal brain natriuretic peptide.
*$P < 0.05$ between patients with severe aortic stenosis and subjects without aortic stenosis which served as controls.

Peri-Procedural Complications and Follow-Up Data

In patients who underwent TAVI echocardiographic examinations were routinely performed in order to assess the presence of postprocedural paravalvular aortic regurgitation (semiquantitative grading of I–III° for mild, moderate, or severe regurgitation). Furthermore, peri-procedural complications and clinical events at one month of follow-up (death, nonfatal myocardial infarction and all cause-mortality) were documented.

Statistical Analysis

Statistical analysis was performed using commercially available software MedCalc9.3 (MedCalc software, Mariakerke, Belgium). Continuous variables were expressed as mean ± standard deviation and categorical variables as proportions. To compare diameter and distance measures performed automatically, manually, or software-assisted, repeated-measures ANOVA with Bonferroni correction for multiple comparisons were used. All tests were two-tailed. Linear regression was used to compare diameter and distance measures performed fully automatically, manually, or software-assisted (by observer 1 and 2). Bland-Altman statistics [17] were performed to determine whether there was any systematic bias in either measurement approach. Furthermore, comparison of correlation coefficients was assessed using z-statistics. Differences were considered significant at $P < 0.05$.

RESULTS

Demographic Parameters

In all patients, CTA was performed without adverse events. Clinical, hemodynamic and demographic data in patients with severe aortic stenosis and in control subjects are summarized in Table I.

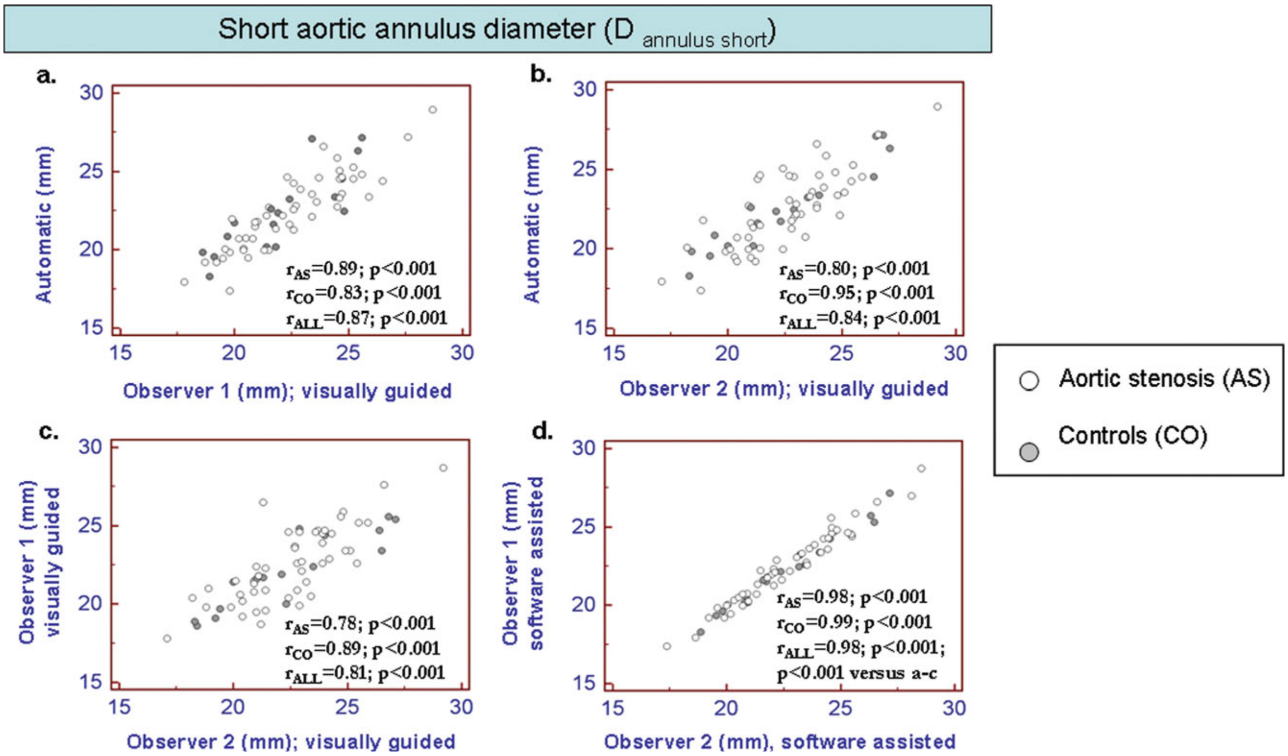

Fig. 2. **Using multiple oblique planes good agreement was noticed between observers and model-based measures for $D_{\text{annulus short}}$ (a–c). Software-assisted estimation $D_{\text{annulus short}}$ exhibited an excellent correlation between observers (d). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]**

2D-Coronal Diameters by Cardiac CT

A moderate agreement ($r = 0.62$ and 0.65 between observers and model-based measures, and $r = 0.67$ between observers) was noticed for $D_{\text{annulus coronal}}$ (Fig. 1a–c), while a trend for underestimation of ~1–2 mm was observed for manual versus fully automatic assessment of $D_{\text{annulus coronal}}$ on Bland-Altman plots (Fig. 1d–f).

3D-Multiple Oblique Diameters by Cardiac CT

With multiple oblique measures at the most caudal attachments of all three aortic valve leaflets a higher degree of agreement ($r = 0.87$ and 0.84 between observers and model-based measures, and $r = 0.81$ between observers for $D_{\text{annulus short}}$; $P < 0.05$ for all compared to 2D-measures) could be achieved (Fig. 2a–c). Furthermore, software-assisted assessment $D_{\text{annulus short}}$ exhibited an excellent correlation between observers ($r = 0.98$, $P < 0.001$ versus manual assessment in Fig. 2d). In contrast to coronal measures no trend for over- or underestimation of $D_{\text{annulus short}}$ was present between observers and model-based measures (Fig. 3a–c). Using software-assisted measurements for $D_{\text{annulus short}}$ extremely low limits of agreement (95%CI of −1.2 to 0.6 mm) were observed (Fig. 3d). Similar results were acquired for $D_{\text{annulus long}}$ (Supporting Information Figs. 2 and 3).

Distances to the Coronary Ostia by Cardiac CT

For assessment of $D_{\text{left ostium}}$ correlation coefficients of $r = 0.81$ and 0.80 were acquired between observers and fully automatic measures and of $r = 0.85$ between observers (Fig. 4a–c). Again software-assisted assessment of $D_{\text{left ostium}}$ also significantly improved the agreement between observers ($r = 0.94$ in Fig. 4d); while no trend for over- or underestimation was noted (Fig. 5). Similar results were acquired for $D_{\text{right ostium}}$ (Supporting Information Figs. 4 and 5).

The mean values for all five acquired variables and corresponding correlation coefficients between observers to each other and with automatic measures are summarized in Tables II and III. A representative example of a patient with severe aortic stenosis and the corresponding diameters and distances assessed by model-based segmentation of the aortic root are presented in Figure 6.

Follow-up Data and Implantation Strategy Based on CT Measures

Of 42 patients who underwent TAVI, 10 developed high-grade AV block requiring a permanent

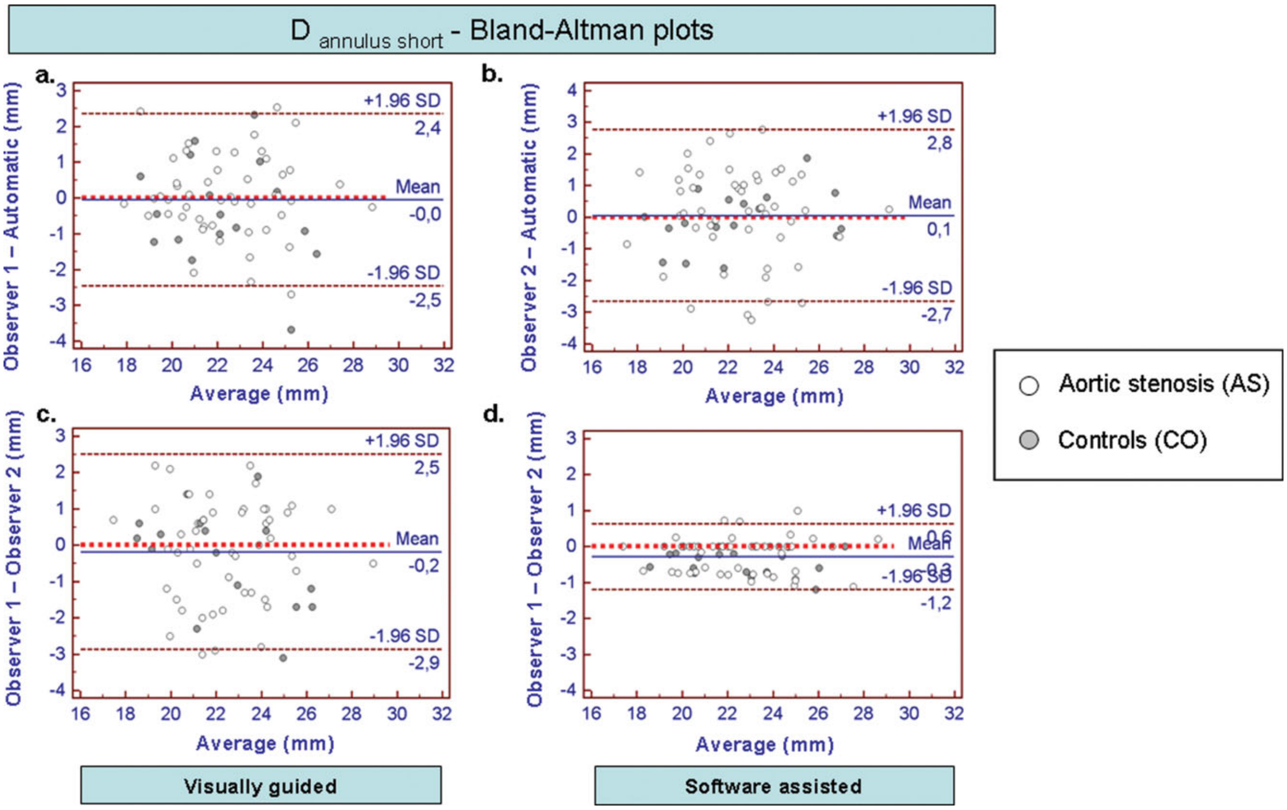

Fig. 3. No trend for over- or underestimation of $D_{\text{annulus short}}$ was present between observers and model-based measures (a–c). Using software-assisted measurements for $D_{\text{annulus short}}$ extremely low limits of agreement (95%CI of −1.2 to 0.6 mm) were observed (d). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

pacemaker, 7 showed moderate post-procedural paravalvular regurgitation, and 4 had peripheral complications. Occlusions of coronary arteries and valve dislocations were not observed. At 1 month of follow-up 5 (12%) patients died (4 due to sepsis and 1 due to fulminant pulmonary embolism).

Of 49 patients screened by cardiac CT and based on the *manual assessment of 2D-coronal annulus diameter*, 6 received the Edwards Sapien XT valve (26 mm), 15 the CoreValve system (26 mm), and 21 received the CoreValve system (29mm), while the 7 remaining were deemed as ineligible for TAVI due to annulus diameter >27 mm (Fig. 7a).

If prothesis sizing had been assessed by the automatically model-based mean of $D_{\text{annulus short}}$ and $D_{\text{annulus long}}$ instead of 2D-coronal manual measures however, the implantation strategy would have been modified in 12 of 49 (25%) cases (blue dots, see Fig. 7b for details). Hereby, postprocedural moderate paravalvular regurgitation was observed in 33% (4 of 12) patients with potentially modified versus 8% (3 of 37) patients with nonmodified implantation strategy (Fig. 7c). In 4 of 12 patients with moderate paravalvular regurgitation and potentially modified implantation strategy, automatic 3D measures suggested the implantation of a larger prosthesis ($n = 3$) or deemed patients as noneligible for TAVI ($n = 1$). Similar results were obtained for software-assisted measures of $D_{\text{annulus short}}$ and $D_{\text{annulus long}}$ (Fig. 7d).

Time-Spent

All variables could be assessed within a time-spent of 0.6 ± 0.1 min versus 1.6 ± 0.3 min per patient ($P < 0.001$) using software-assisted versus manual assessment.

DISCUSSION

The results of our study demonstrate for the first time in the current literature the ability of a model-based segmentation algorithm to consistently quantify the diameter of the aortic annulus and its distance to the coronary ostia on CT images. The agreement of automatic measures derived from the proposed model with manual assessment was high for measures conducted on multiple oblique planes, while a lower correlation accompanied by systematic overestimation of the annulus diameter was observed using 2D-coronal

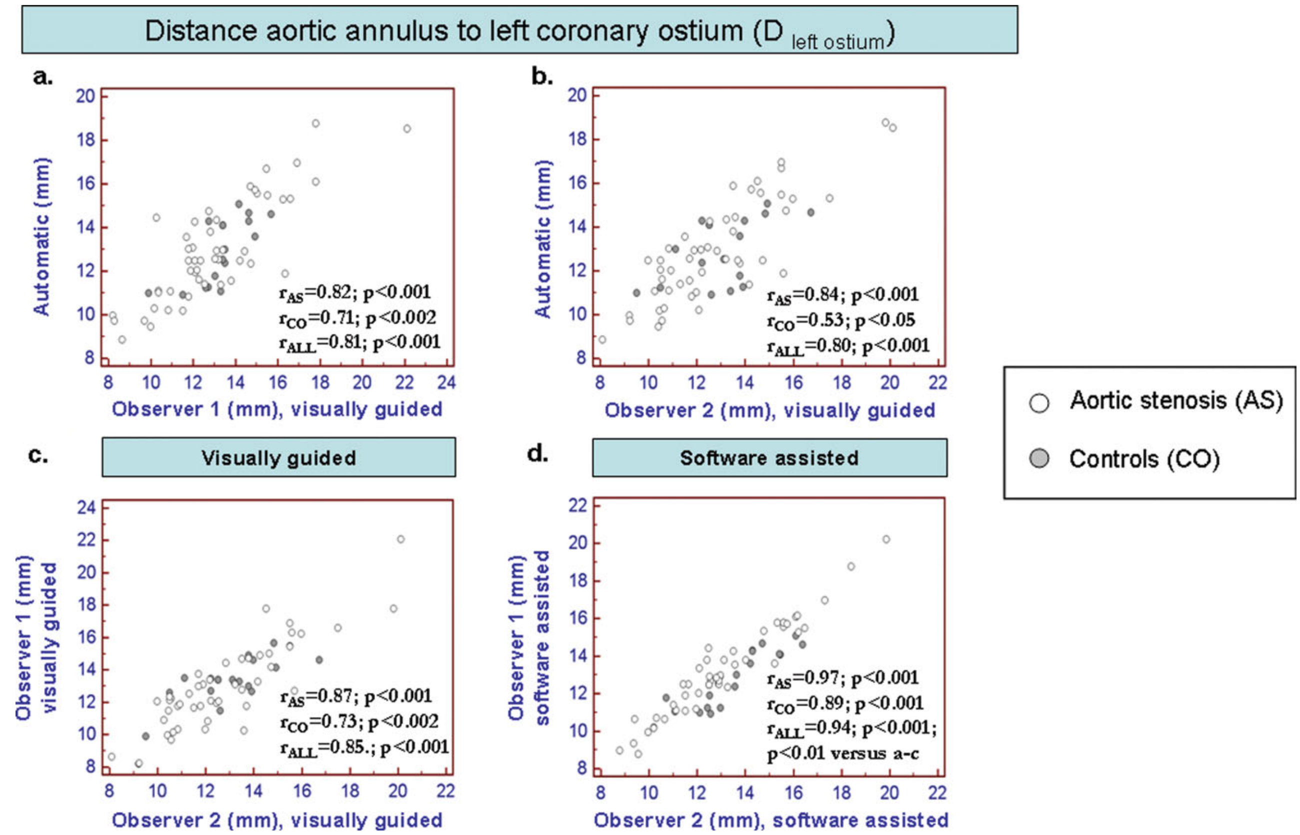

Fig. 4. For assessment of $D_{left\ ostium}$ correlation coefficients of r = 0.81 and 0.80 were acquired between observers and model-based measures and of r = 0.85 between observers to each other (a–c). Software-assisted assessment of $D_{left\ ostium}$ significantly improved the agreement between observers (r = 0.94 in d). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

datasets. Furthermore, interobserver agreement could be significantly improved by software-assisted quantification of the aortic annulus and its distance to coronary ostia, compared with manual assessment. Using software-assisted measurements, very narrow limits of agreement (<1 mm) could be achieved for the diameter of the aortic annulus. Considering the faster automated analysis, compared with manual measurements, this tool seems very promising for translation into the clinical reality.

Consistent assessment of the aortic annulus diameter is crucial to circumvent peri- and post-procedural complications in patients undergoing TAVI. TAVI represents nearly 13% of all aortic valve procedures, and it is forecasted that by 2012 transcatheter valve therapies will account for ∼ 40% of the total heart valve procedures performed in Europe [18]. Currently, two devices are commercialised for TAVI: (1) the balloon expandable Edwards Sapien XT valve, which consists of three bovine pericardial leaflets mounted within a tubular cobalt chromium frame and which exists in 23 and 26 mm sizes and (2) the CoreValve system, which consists of three porcine pericardial leaflets mounted in a self-expanding nitinol frame and which exists in 26 and 29 mm sizes. Preprocedural sizing of the aortic annulus is crucial for both devices, because implanting a too large prosthesis may cause aortic root damage or impair optimal valve expansion [19]. Implanting a too small prosthesis on the other hand, may prevent solid anchoring of the valve into the annulus. This may result in paravalvular regurgitation or dislocation of the valve, which is associated with significantly increased rates for severe complications and death [5,6]. Particularly with the Edwards valve, deployment of the covered lower part of the prosthesis at the level of coronary ostia may cause coronary artery occlusion [20]. Therefore the assessment of the distance between the aortic annulus and coronary ostia is also important.

Previous studies successfully used contrast aortography or echocardiography for the preprocedural evaluation of aortic valve structures including device sizing and placement [21,22]. However, the two-dimensional nature of these techniques may limit their ability to consistently assess the complex 3D-geometry of the

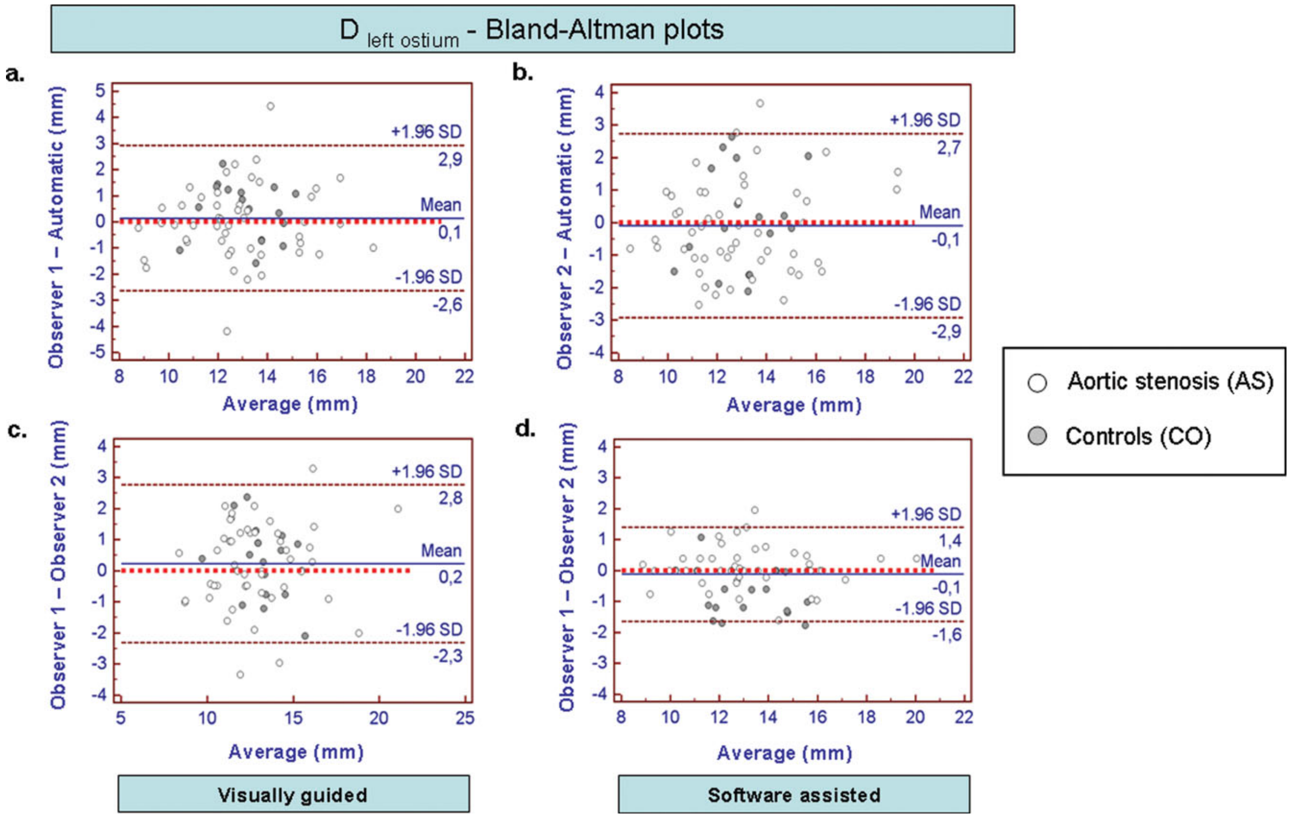

Fig. 5. No trend for over- or underestimation of $D_{left\ ostium}$ was present between observers and model-based measures (a–c). Using software-assisted measurements low limits of agreement (95%CI of −1.6 to 1.4 mm) were observed (d). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

TABLE II. Mean Values for Annulus Diameters and Their Distance to the Coronary Ostia

	Fully automatic	Observer 1 (manually)	Observer 2 (manually)	Observer 1 (software-assisted)	Observer 2 (software-assisted)
$D_{annulus\ coronal}$	27.1 ± 2.7*	25.4 ± 3.2	25.7 ± 3.0	n.a.	n.a.
$D_{annulus\ short}$	22.4 ± 2.5	22.3 ± 2.5	22.5 ± 2.6	22.4 ± 2.5	22.7 ± 2.5
$D_{annulus\ long}$	27.4 ± 2.7	27.6 ± 3.0	27.0 ± 3.0	27.5 ± 2.7	27.7 ± 2.7
$D_{right\ ostium}$	15.4 ± 2.2	15.4 ± 2.5	14.9 ± 2.4	14.9 ± 2.6	15.5 ± 2.3
$D_{left\ ostium}$	13.1 ± 2.3	13.1 ± 2.4	12.8 ± 2.3	13.1 ± 2.2	13.3 ± 2.3

Data are presented as numbers and standard deviation. N.A., not applicable.
*$P < 0.01$ for fully automatic versus manual assessment of $D_{annulus\ coronal}$.

TABLE III. Correlation Coefficients Between Observers 1 and 2 to Each Other by Manual or Soft-Assisted Assessment and to Fully Automatic Measurements

	Observer 1 versus Automatic	Observer 2 versus Automatic	Observer 1: manually software-assisted	Observer 2: manually software-assisted	Observer 1 versus Observer 2 (manually)	Observer 1 versus Observer 2 (software-assisted)
$D_{annulus\ coronal}$	0.65	0.62	n.a.	n.a.	0.67	n.a.
$D_{annulus\ short}$	0.87**	0.84**	0.88	0.84	0.81**	0.98*
$D_{annulus\ long}$	0.84**	0.84**	0.83	0.82	0.73	0.99*
$D_{right\ ostium}$	0.78	0.67	0.76	0.70	0.78	0.92*
$D_{left\ ostium}$	0.81	0.80	0.83	0.78	0.85	0.94*

Data are presented as numbers. N.A., not applicable.
*$P < 0.01$ for software-assisted versus manual measures of the aortic annulus and its distance to the coronary ostia;
**$P<0.05$ for measures of the aortic annulus on 2D-coronal ($D_{annulus\ coronal}$) versus multiple oblique views ($D_{annulus\ short}$ and $D_{annulus\ long}$); all tested by z-statistics.

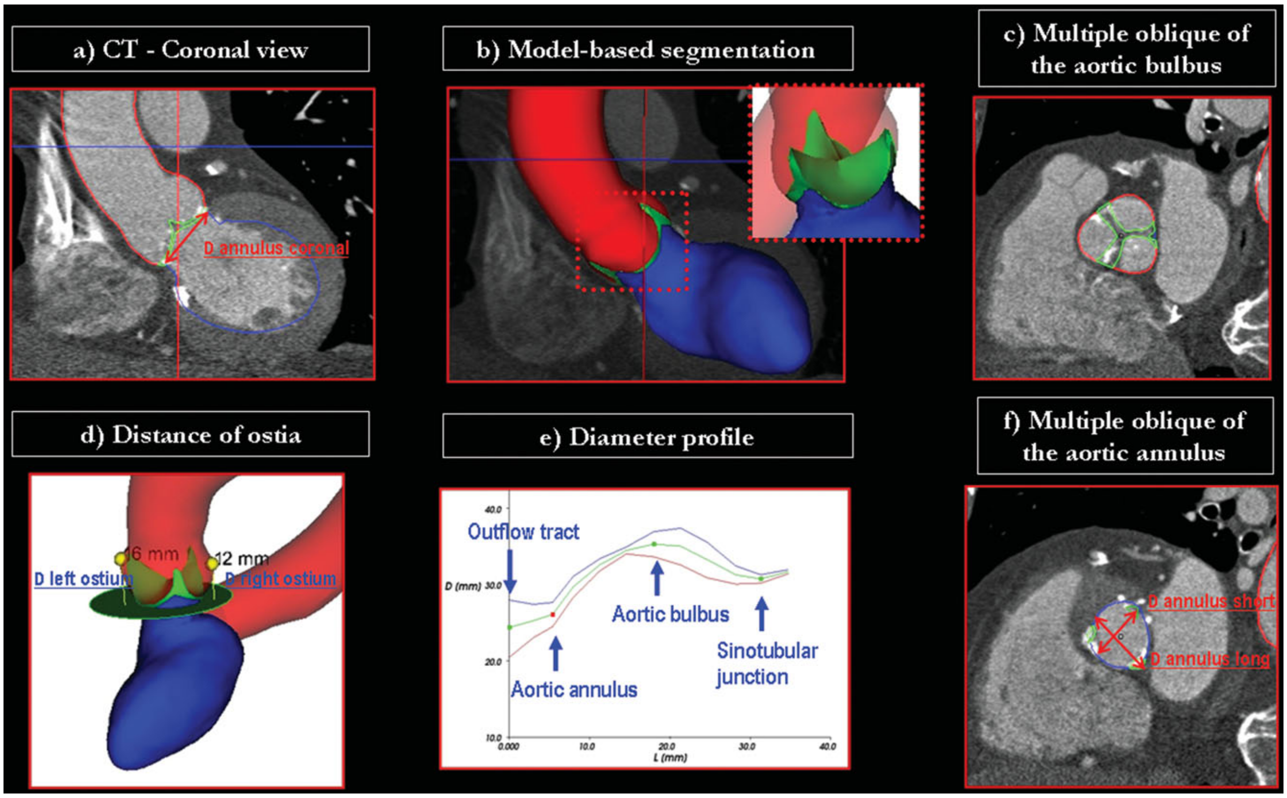

Fig. 6. Using model-based segmentation of the aortic root, measures of $D_{annulus\ coronal}$ (a) and of the distance between annulus and coronary ostia ($D_{left\ ostium}$ and $D_{right\ ostium}$ in d) were automatically provided. By taking into account the complex 3D-geometry and the crown-like shape of the aortic annulus (b), with magnification of the "crown" on the right upper side, the diameters of the aortic root were calculated as a function of distance from the left ventricular outflow tract [red, green, and purple line, indicating the short, mean, and long diameter of the aortic root, respectively in (e)] at different levels as for e.g. in aortic bulbus (c) and at the level of the aortic annulus (f). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

aortic annulus. In agreement with these theoretical considerations, recent studies indicated that echocardiography systematically underestimates the diameter of the aortic annulus diameter (~2 mm) compared with cardiac CT [11]. In this regard, 3D trans-esophageal echocardiography (3D TEE) has been previously proposed as a valuable modality for improving the correlation of echocardiographic measurements of the aortic annulus to those assessed by cardiac CT [23,24].

Although echocardiography is a very practical imaging technique we chose to assess aortic valve structures using computed tomography in our study. In this regard we demonstrated a "proof of concept" that such measurements can be assessed consistently and easily by using a model based segmentation approach with 3D CT images. Hereby, using the 2D-coronal approach based on CT image datasets resulted in underestimation of the aortic annulus diameters (~1–2 mm) compared with 3D model-based measures, which may be attributed to the fact that such measures do not transect the full diameter of the aortic annulus but instead cut a tangent across the root [8]. Furthermore prosthesis sizing by model-based 3D- instead of 2D-measures would have modified the implantation strategy in 25% of our patients. This is in agreement with previous trials, where a clinical decision based on cardiac CT measurements would have modified the implantation strategy in a substantial number of patients (~40%) undergoing TAVI based on echocardiographic criteria, highlighting the rather poor agreement between the two modalities [25]. In the above study moderate postprocedural aortic regurgitation was observed in 15% of the patients. In the same line, we observed aortic regurgitation in 17% of our patients. In this regard, assessment of the congruence between the device considered for implantation and the aortic annulus together with more precise 3D measures may further help reducing the incidence of moderate or severe aortic regurgitation in future trials [26].

In addition, in our study, for the first time in the current literature a model-based segmentation of the aortic root is presented, which allows (1) for fully automatic assessment of aortic valve structures and (2) for software-assisted measures by adjustment of the automatic

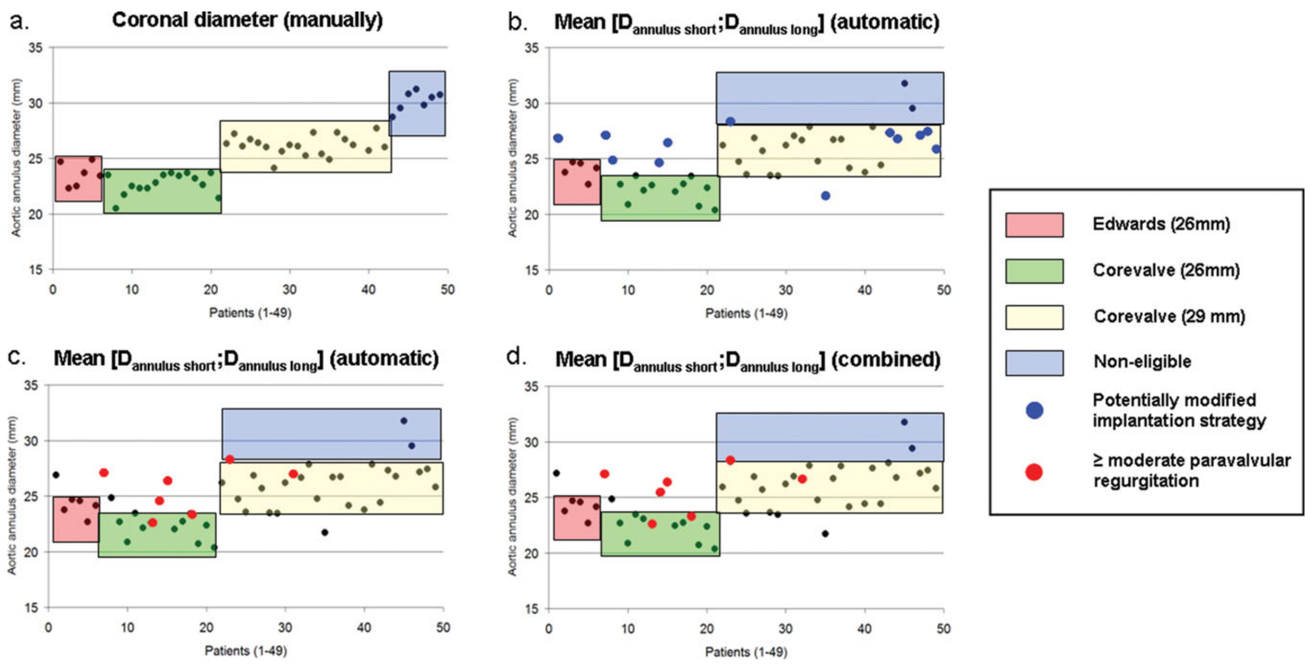

Fig. 7. Based on the ***manual assessment of 2D-coronal annulus diameter***, 6 received the Edwards Sapien XT valve (26 mm), 15 the CoreValve system (26 mm), and 21 received the CoreValve system (29 mm), while the 7 remaining were deemed as ineligible for TAVI due to annulus diameter >27 mm (a). If prothesis sizing had been assessed by the automatically model-based mean of $D_{annulus\ short}$ and $D_{annulus\ long}$ however, implantation strategy would have been modified in 12 of 49 (25%) cases (blue dots in b). Thus, of seven patients deemed inappropriate for TAVI, five patients would have received Corevalve (29 mm); two patients who received Corevalve (29 mm) and Edwards Sapien (26 mm), respectively would have been deemed inappropriate for transfemoral and transapical TAVI, respectively; four patients who received Corevalve (26 mm) would have received Corevalve (29 mm) and one patient who received Corevalve (29 mm) would have received Corevalve (26 mm). Postprocedural moderate paravalvular regurgitation was observed in 33% (4 of 12) patients with potentially modified versus 8% (3 of 37) patients with nonmodified implantation strategy (c). Similar results were obtained for software-assisted measures of $D_{annulus\ short}$ and $D_{annulus\ long}$ (d). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

measurements by the clinical observers. The utilized model-based approach yielded good agreement with standardized 3D-measures, while the agreement with 2D-coronal measures was lower. This is in agreement with methods previously proposed for standardized 3D-measurements on CT images, which yielded a high degree of interobserver agreement for the estimation of the aortic annulus when multiple oblique cutplanes are used [27]. Therefore, in the meanwhile such 3D multiple oblique cutplanes are used for the assessment of the aortic annulus. In addition, the software-assisted model-based approach resulted in substantial improvement of interobserver agreement versus manual assessment, and by software-assisted measures overall correlation coefficients of $r > 0.9$ were acquired. The improvement of the interobserver agreement is crucial to guarantee for reproducibility of the acquired variables (both annulus diameter and its distance to the coronaries) and is expected to gain even more importance when vendors deliver a wider range of more specialized devices of varying dimensions. Certainly, the clinical value of the observed higher reproducibility remains to be elucidated in future studies, as in our study model-based measures were not used to structure prosthesis sizing for patient treatment compared with conventional measures. In contrast to previous studies all patients included underwent ECG-gated cardiac CT using a state-of -the-art 256-slice scanner which encompasses high temporal resolution and an isotropic submillimeter spatial resolution.

Limitations

The number of patients included in our study was relatively small and long term follow-up data in patients who underwent TAVI are not yet available at this time point. Furthermore, no comparison to echocardiography or TEE data was available and no standard reference was defined for the “real” size of the aortic annulus, which are both limitation. Such “real” size measures can be for e.g. assessed during intraoperative measurement of the aortic annulus with a neutral sizer after excision of the native valve. However, as preprocedural assessment of the aortic annulus is usually performed in patients who are not ineligible for conventional surgery, such reference measures are not expected to be available in such trials. In addition, iodine injection and exposure are known limitations with cardiac CT. In our study however, all CT scans were clinically indicated in order to assess both the aortic annulus and peripheral femoro-iliac artery dimensions to guide our clinical decision between a transfemoral or transapical approach and cardiac scan were performed using dose modulation techniques [28]. In future trials, methods such as prospective triggering combined with lower tube voltages and iterative reconstructions [28,29] or high-pitch dual-source CTA [30] of the aortic root would represent ways to reduce radiation exposure for such patients.

CONCLUSIONS

This is to our knowledge the first study to demonstrate that a model-based segmentation of the aortic root can be used to objectively and consistently quantify the diameter of the aortic annulus and its distance to the coronary ostia on ECG-gated cardiac CT images. Interobserver variability could be significantly improved by software-assisted versus manual quantification of aortic valve structures, and software-assisted measurements exhibited extremely narrow limits of agreement and acceptable time-spent for implementation in the clinical work flow.

REFERENCES

1. Cribier A, Eltchaninoff H, Tron C, Bauer F, Agatiello C, Sebagh L, Bash A, Nusimovici D, Litzler PY, Bessou JP, Leon MB. Early experience with percutaneous transcatheter implantation of heart valve prosthesis for the treatment of end-stage inoperable patients with calcific aortic stenosis. J Am Coll Cardiol 2004;43:698–703
2. Grube E, Laborde JC, Gerckens U, Felderhoff T, Sauren B, Buellesfeld L, Mueller R, Menichelli M, Schmidt T, Zickmann B, Iversen S, Stone GW. Percutaneous implantation of the corevalve self-expanding valve prosthesis in high-risk patients with aortic valve disease: The siegburg first-in-man study. Circulation 2006;114:1616–1624.
3. Vahanian A, Alfieri O, Al-Attar N, Antunes M, Bax J, Cormier B, Cribier A, De Jaegere P, Fournial G, Kappetein AP, Kovac J, Ludgate S, Maisano F, Moat N, Mohr F, Nataf P, Pierard L, Pomar JL, Schofer J, Tornos P, Tuzcu M, van Hout B, Von Segesser LK, Walther T. Transcatheter valve implantation for patients with aortic stenosis: A position statement from the European association of cardio-thoracic surgery (eacts) and the European society of cardiology (esc), in collaboration with the European association of percutaneous cardiovascular interventions (eapci). Eur Heart J 2008;29:1463–1470.
4. Webb JG, Chandavimol M, Thompson CR, Ricci DR, Carere RG, Munt BI, Buller CE, Pasupati S, Lichtenstein S. Percutaneous aortic valve implantation retrograde from the femoral artery. Circulation 2006;113:842–850.
5. Kahlert P, Eggebrecht H, Erbel R. Corevalve dislocation: Breaking the wave of enthusiasm? Circ Cardiovasc Interv 2010;3:523–525.
6. Geisbusch S, Bleiziffer S, Mazzitelli D, Ruge H, Bauernschmitt R, Lange R. Incidence and management of corevalve dislocation during transcatheter aortic valve implantation. Circ Cardiovasc Interv 2010;3:531–536.
7. Cribier A, Eltchaninoff H, Tron C, Bauer F, Agatiello C, Nercolini D, Tapiero S, Litzler PY, Bessou JP, Babaliaros V. Treatment of calcific aortic stenosis with the percutaneous heart valve: Mid-term follow-up from the initial feasibility studies: The French experience. J Am Coll Cardiol 2006;47:1214–1223.
8. Piazza N, de Jaegere P, Schultz C, Becker AE, Serruys PW, Anderson RH. Anatomy of the aortic valvar complex and its implications for transcatheter implantation of the aortic valve. Circ Cardiovasc Interv 2008;1:74–81.
9. Korosoglou G, Mueller D, Lehrke S, Steen H, Hosch W, Heye T, Kauczor HU, Giannitsis E, Katus HA. Quantitative assessment of stenosis severity and atherosclerotic plaque composition using 256-slice computed tomography. Eur Radiol 2010;20: 1841–1850.
10. Schultz CJ, Weustink A, Piazza N, Otten A, Mollet N, Krestin G, van Geuns RJ, de Feyter P, Serruys PW, de Jaegere P. Geometry and degree of apposition of the corevalve revalving system with multislice computed tomography after implantation in patients with aortic stenosis. J Am Coll Cardiol 2009;54:911–918.
11. Tops LF, Wood DA, Delgado V, Schuijf JD, Mayo JR, Pasupati S, Lamers FP, van der Wall EE, Schalij MJ, Webb JG, Bax JJ. Noninvasive evaluation of the aortic root with multislice computed tomography implications for transcatheter aortic valve replacement. JACC Cardiovasc Imaging 2008;1:321–330.
12. Schultz CJ, Moelker A, Piazza N, Tzikas A, Otten A, Nuis RJ, Neefjes LA, van Geuns RJ, de Feyter P, Krestin G, Serruys PW, de Jaegere PP. Three dimensional evaluation of the aortic annulus using multislice computer tomography: Are manufacturer's guidelines for sizing for percutaneous aortic valve replacement helpful? Eur Heart J 2010;31:849–856.
13. Waechter I, Kneser R, Korosoglou G, Peters J, Bakker NH, van der Boomen R, Weese J. Patient specific models for planning and guidance of minimally invasive aortic valve implantation. Med Image Comput Comput Assist Interv 2010;13:526–533.
14. Wood DA, Tops LF, Mayo JR, Pasupati S, Schalij MJ, Humphries K, Lee M, Al Ali A, Munt B, Moss R, Thompson CR, Bax JJ, Webb JG. Role of multislice computed tomography in transcatheter aortic valve replacement. Am J Cardiol 2009; 103:1295–1301.
15. Ecabert O, Peters J, Schramm H, Lorenz C, von Berg J, Walker MJ, Vembar M, Olszewski ME, Subramanyan K, Lavi G, Weese J. Automatic model-based segmentation of the heart in ct images. IEEE Trans Med Imaging 2008;27:1189–1201.
16. Gorlin R, Gorlin SG. Hydraulic formula for calculation of the area of the stenotic mitral valve, other cardiac valves, and central circulatory shunts. I. Am Heart J 1951;41:1–29.
17. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986;1:307–310.
18. Piazza N, Tzikas A, de Jaegere P, Serruys PW. Transcatheter aortic valve implantation: What lies ahead? Hospital Chronicles 2010;5:64–69.
19. Chin D. Echocardiography for transcatheter aortic valve implantation. Eur J Echocardiogr 2009;10:i21–i29.
20. Stabile E, Sorropago G, Cioppa A, Cota L, Agrusta M, Lucchetti V, Rubino P. Acute left main obstructions following tavi. EuroIntervention 2010;6:100–105.

21. Tzikas A, Schultz C, Van Mieghem NM, de Jaegere PP, Serruys PW. Optimal projection estimation for transcatheter aortic valve implantation based on contrast-aortography: Validation of a prototype software. Catheter Cardiovasc Interv 2010;76:602–607.
22. Moss RR, Ivens E, Pasupati S, Humphries K, Thompson CR, Munt B, Sinhal A, Webb JG. Role of echocardiography in percutaneous aortic valve implantation. JACC Cardiovasc Imaging 2008;1:15–24.
23. Mesa Rubio D, Suarez de Lezo Cruz Conde J, Alvarez-Osorio MP, Ruiz Ortiz M, Delgado Ortega M, Leon del Pino Mdel C, Toledano Delgado F, Segura Saint-Gerons J, Ojeda Pineda S, Garcia Fuertes D, Crespin Crespin M, Espejo S, Ysamat R. Measurement of aortic valve annulus using different cardiac imaging techniques in transcatheter aortic valve implantation: Agreement with finally implanted prosthesis size. Echocardiography 2011;28:388–396.
24. Altiok E, Koos R, Schroder J, Brehmer K, Hamada S, Becker M, Mahnken AH, Almalla M, Dohmen G, Autschbach R, Marx N, Hoffmann R. Comparison of two-dimensional and three-dimensional imaging techniques for measurement of aortic annulus diameters before transcatheter aortic valve implantation. Heart 2011;97:1578–1584.
25. Messika-Zeitoun D, Serfaty JM, Brochet E, Ducrocq G, Lepage L, Detaint D, Hyafil F, Himbert D, Pasi N, Laissy JP, Iung B, Vahanian A. Multimodal assessment of the aortic annulus diameter: Implications for transcatheter aortic valve implantation. J Am Coll Cardiol 2010;55:186–194.
26. Detaint D, Lepage L, Himbert D, Brochet E, Messika-Zeitoun D, Iung B, Vahanian A. Determinants of significant paravalvular regurgitation after transcatheter aortic valve: Implantation impact of device and annulus discongruence. JACC Cardiovasc Interv 2009;2:821–827.
27. del Valle-Fernandez R, Jelnin V, Panagopoulos G, Dudiy Y, Schneider L, de Jaegere PT, Schultz C, Serruys PW, Grube E, Ruiz CE. A method for standardized computed tomography angiography-based measurement of aortic valvar structures. Eur Heart J 2010;31:2170–2178.
28. Hosch W, Heye T, Schulz F, Lehrke S, Schlieter M, Giannitsis E, Kauczor HU, Katus HA, Korosoglou G. Image quality and radiation dose in 256-slice cardiac computed tomography: Comparison of prospective versus retrospective image acquisition protocols. Eur J Radiol 2011;80:127–135.
29. Hausleiter J, Martinoff S, Hadamitzky M, Martuscelli E, Pschierer I, Feuchtner GM, Catalan-Sanz P, Czermak B, Meyer TS, Hein F, Bischoff B, Kuse M, Schomig A, Achenbach S. Image quality and radiation exposure with a low tube voltage protocol for coronary ct angiography results of the protection ii trial. JACC Cardiovasc Imaging 2010;3:1113–1123.
30. Karlo C, Leschka S, Goetti RP, Feuchtner G, Desbiolles L, Stolzmann P, Plass A, Falk V, Marincek B, Alkadhi H, Baumuller S. High-pitch dual-source ct angiography of the aortic valve-aortic root complex without ecg-synchronization. Eur Radiol 2011;21:205–212.