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ABSTRACT

Objectives

This study sought to assess the differential adherence to transcatheter heart valve (THV)-oversizing principles between transesophageal echocardiography (TEE) and multislice computed tomography (CT) and its impact on the incidence of paravalvular leak (PVL).

Background

CT has emerged as an alternative to 2-dimensional TEE for THV sizing.

Methods

In our early experience, TEE-derived aortic annular diameters determined THV size selection. CT datasets originally obtained for vascular screening were retrospectively interrogated to determine CT-derived annular diameters. Annular dimensions and expected THV oversizing were compared between TEE and CT. The incidence of PVL was correlated to TEE- and CT-based oversizing calculations.

Results

Using TEE-derived annulus measurements, 157 patients underwent CoreValve implantation (23 mm: n = 66; 29 mm: n = 91). The estimated THV oversizing on the basis of TEE was 20.1 ± 8.2%. Retrospective CT analysis yielded larger annular diameters than TEE ($p < 0.0001$). When these CT diameters were used to recalculate the percentage of oversizing achieved with the TEE-selected CoreValve, the actual THV oversizing was only 10.4 ± 7.8%. Consequently, CT analysis suggested that up to 50% of patients received an inappropriate CoreValve size. When CT-based sizing criteria were satisfied, the incidence of PVL was 21% lower than that with echocardiography (14% vs. 35%; $p = 0.003$). Adherence to CT-based oversizing was independently associated with a reduced incidence of PVL (odds ratio 0.36; 95% confidence interval: 0.14 to 0.90; $p = 0.029$); adherence to TEE-based sizing was not.

Conclusions

Retrospective CT-based annular analysis revealed that CoreValve size selection by TEE was incorrect in 50% of patients. The percentage of oversizing with CT was one-half of that calculated with TEE resulting in the majority of patients receiving a THV that was too small.

Keywords: aortic stenosis, computed tomography, transcatheter aortic valve replacement, transcatheter heart valve, transesophageal echocardiography

Appropriate valve sizing is of critical importance to optimize outcomes in patients undergoing transcatheter aortic valve replacement (TAVR). Oversizing the transcatheter heart valve (THV) relative to the aortic annulus is required to generate interference between the prosthesis and the annulus and thus to provide adequate anchoring and sealing. Insufficient THV oversizing (i.e., selecting a valve that is too small) can be problematic and may result in intraprocedural valve embolization, or more commonly paravalvular leak (PVL), an independent predictor of poor long-term prognosis (1,2). However, excessive THV oversizing has been associated with annular rupture (balloon-expandable TAVR) and/or prosthesis dysfunction (3).

Historically, 2-dimensional (D) echocardiography was the imaging modality of choice for TAVR sizing. More recently, multislice computed tomography (CT) has emerged as an alternative and perhaps superior technique (4). CT provides a more reliable and detailed anatomical assessment of the aortic valvular complex and yields larger aortic annular diameters than echocardiography (5–11). Consequently, echocardiographic-based TAVR sizing may be inaccurate and may fail to provide the expected THV oversizing. Supporting this hypothesis is the observation that the rates of both PVL and mortality decline with CT-based sizing (5–11). Although it is axiomatic that the superiority of CT-based sizing is achieved through more accurate adherence to manufacturer THV-oversizing principles, this hypothesis has not been corroborated.

We sought to assess the differential adherence to THV-oversizing principles between 2D-echocardiography and multislice CT and to further correlate this difference with rates of PVL in a large series of patients undergoing TAVR.

METHODS

Patients

Between January 6, 2009 and June 6, 2010, 165 consecutive high-risk patients with severe aortic stenosis underwent vascular access screening with CT prior to TAVR at the German Heart Centre, Munich. Patients with symptomatic severe aortic stenosis (valve area ≤1.0 cm^2) were considered candidates for TAVR if surgery was deemed to be of high or excessive risk. The decision to proceed with TAVR was discussed by a dedicated Heart Team. Procedures were performed according to standard protocol as previously described (12). In this case series, all patients were treated with the self-expanding CoreValve system (Medtronic, S.a.r.l, Luxembourg).

TAVR sizing

Early in our experience, CT was routinely performed to evaluate the iliofemoral vasculature with the intention of proceeding to transfemoral TAVR. In all 165 cases, TAVR sizing was determined solely using transesophageal echocardiography (TEE)-derived aortic annular diameters and standard sizing criteria: annulus diameters of 20 to 23 mm and 23 to 27 mm for the 26- and 29-mm CoreValves, respectively. These sizing criteria yield THV oversizing of 13% to 30% for the 26-mm CoreValve and 7% to 26% for the 29-mm CoreValve (prosthesis diameter – annulus diameter / annulus diameter × 100). Appropriate valve sizing was defined as adherence to these criteria. The diameters of the sinuses of Valsalva and the ascending aorta, the extent of sinotubular and aortic root calcification, and the height of the coronary ostia were also considered when choosing the size of the THV. Only the 26- and 29-mm CoreValves were commercially available during study enrollment; however, the 31- and 23-mm CoreValves have more recently received Conformité Européenne–mark approval. We retrospectively assessed patient eligibility for these newer prostheses: annular diameter range of 18 to 20 mm and 26 to 29 mm for the 23- and 31-mm CoreValves, respectively.

Echocardiography

Pre-procedural 2D-TEE was performed in all subjects using a commercially available TEE transducer and ultrasound system (X7-2t Live 3D-TEE transducer, iE33, Philips Medical System, Andover, Massachusetts) according to standard techniques (13). All images were digitally stored for off-line analysis. The aortic root dimensions were measured during early systole in the 3-chamber long-axis view at approximately 120° angulation (14). Ineach patient, these measurements were used to calculate the percentage of THV oversizing and to select the appropriate valve size for implantation.

CT acquisition protocol

All examinations were performed using a Somatom Definition Flash CT scanner (Siemens Medical, Siemens, Munich, Germany). All CT were performed using the flash technique. Standard technical parameters were used: gantry rotation time 0.28 ms; axial coverage 0.75 mm (128 × 0.6 mm); 80 kV to 120 kV tube voltage according to body weight; milliampere intensity with Care Dose 4D modulation; and temporal resolution of 70 ms. Retrospective electrocardiographic gating was performed. Contrast enhancement was achieved with 60 to 100 ml of iomeprol 350 mg/ml (Iomeron, Bracco Imaging SpA, Milan, Italy). To achieve optimal synchronization, a bolus tracking method was used in the ascending aorta. Additional beta-blockade was not administered. The thickness of reconstructed images was 0.5 mm (increment 0.8 mm).

CT reconstruction and aortic annular measurements

Among 165 patients with a screening CT, 159 CT datasets were of sufficient quality for analysis and were retrospectively reconstructed using software from 3mensio Valves (version 4.1.sp1, Medical Imaging BV, Bilthoven, the Netherlands), as previously described (4). The aortic annulus dimensions were carefully assessed, including the major and orthogonal minor diameters, the area, and the perimeter. The CT_{mean} diameter was calculated as the mean of the major and minor diameters. The CT_{area}-derived diameter was calculated using the following equation: $2 \times \sqrt{[\text{area (mm}^2) / \pi]}$. The $CT_{perimeter}$-derived diameter was determined as: perimeter (mm) / π. These diameters were retrospectively calculated for each patient and were applied to the TEE-based CoreValve size in order to recalculate the CT-derived THV oversizing and adherence to recommended oversizing principles. The annular ellipticity index was calculated as the ratio of the major and minor diameters.

Calcification of the aortic root specifically associated with the valve leaflets was evaluated with the automated 3mensio software. Aortic valvular calcification was assessed between the sinotubular junction and 10 mm below the aortic annulus plane in the left ventricular outflow tract; calcification above and below the aortic leaflets was only included if it was continuous with that on the aortic leaflets. We selected an appropriate threshold value (Hounsfield units) to highlight and segment only calcified tissue from the aortic root. This threshold varied among patients due to differences in image acquisition, and therefore, multiple values were evaluated for each patient. Appropriate highlighting of the calcification (e.g., excluding opacified blood but not obvious calcification) was visually inspected in each case to determine the optimal threshold value. For each cusp, the calcification volumes were divided into quartiles and given a corresponding score of 1 to 4. Calcification volumes were then summed for each patient and classified as trivial (= 1), mild (= 2), moderate (= 3), or severe (= 4).

Depth of CoreValve implantation

The depth of CoreValve implantation was calculated using fluoroscopic imaging. The height of the CoreValve frame was assessed in the angiographic view with the least foreshortening for calibration so that the absolute depth could be measured. The distance from the bottom of each aortic sinus was measured as well as the total visible length of the device from inflow to outflow. The total length of the device was then compared to the known implanted device height and this ratio was used to calibrate the depth measurements. Length measurements were recorded in pixels and then converted to millimeters on the basis of the device length. The right- and left-sided depths were averaged to provide a single depth of implant. Suitable angiographic imaging was available in 135 patients.

Endpoints

For the purposes of this study, PVL was the primary outcome and was defined as post-procedural paravalvular aortic regurgitation grade ≥2 or the requirement for post-implantation balloon dilation despite appropriate CoreValve position. PVL was assessed using echocardiography during the index procedure and prior to discharge, and it was classified as mild, moderate, or severe according to the updated Valve Academic Research Consortium criteria (15). Post-implantation balloon dilation was performed with a 22- to 25-mm balloon for the 26-mm CoreValve and a 25- to 28-mm balloon for the 29-mm CoreValve. PVL cases resulting from THV malposition, defined as an implantation depth >9 mm, were excluded from the analyses. Clinical outcomes including vascular complications, bleeding, stroke, myocardial infarction, acute kidney injury, requirement for new pacemaker, and 30-day and 6-month mortality were assessed according to the updated Valve Academic Research Consortium criteria.

Statistical analysis

Continuous variables are presented as mean ± SD, or median and range, according to distribution. Categorical variables are presented as frequencies and percentages. Continuous variables were compared with either the Student *t* test or Mann-Whitney test. Multiple comparisons of the aortic annular diameters were analyzed using analysis of variance with Bonferroni correction or with the Kruskal-Wallis test. Categorical variables were compared using the chi-square or Fisher exact test, or McNemar test for related variables. Univariable and multivariable logistic regression analyses were performed to assess predictors of PVL. All variables that could plausibly be associated with PVL with a p value of <0.1 in the univariate analysis were entered into the multivariate model. Separate models were constructed for each sizing modality (if $p < 0.1$) due to multicollinearity of these variables. Receiver-operating characteristic (ROC) curves were developed and the areas under the curve (AUC) were calculated to compare the discriminatory power of TEE and CT to predict PVL. Comparisons of correlated AUC from the ROC analysis were compared with the method of DeLong. The nominal level of significance was 5%. Analyses were performed using SPSS (version 20.0, IBM Corp, Armonk, New York).

RESULTS

Patients, procedures, and outcomes

Among the 159 patients with CT datasets of suitable quality, 2 were excluded due to THV malposition (depth >9 mm). The baseline characteristics of the remaining 157 patients are presented in Table 1. Sixty-six patients (42%) received a 26-mm CoreValve and 91 (58%) received a 29-mm CoreValve.

TEE-derived diameters were significantly smaller than CT-based measurements ($p < 0.0001$) (Fig. 1A). Compared with CT_{area}-, CT_{mean}-, and $CT_{perimeter}$-derived diameters, TEE diameters were 1.3 mm (95% confidence interval [CI]: 0.7 to 2.0 mm), 1.5 mm (95% CI: 0.9 to 2.2 mm), and 2.0 mm (95% CI: 1.4 to 2.7 mm) smaller, respectively. Comparing the CT measurements, there was no significant difference between $CT_{perimeter}$ and CT_{mean} ($p = 0.32$), though $CT_{perimeter}$ was marginally larger than CT_{area} ($p = 0.05$). According to CT, aortic root calcification was classified as trivial in 26%, mild in 25%, moderate in 24%, and severe in 25% of patients.

Table 1 Study Population: Baseline and Procedural Characteristics (N = 157)

Baseline characteristics	
Age, years	79.7 ± 6.8
Male	56 (35.6)
Body mass index, kg/m^2	26.3 ± 4.6
Aortic valve indices	
Aortic valve area, mm^2	0.7 ± 0.2
Aortic valve peak gradient, mm Hg	76.7 ± 26.8
Aortic valve mean gradient, mm Hg	46.4 ± 17.1
Aortic regurgitation grade ≥2	21 (13.4)
Left ventricular EF ≤30%	30 (19.1)
NYHA functional class III/IV	156 (99.4)
Coronary artery disease	86 (54.8)
Prior aortocoronary bypass surgery	17 (10.8)
Peripheral vascular disease	23 (14.7)
Prior stroke	21 (13.4)
Diabetes mellitus	61 (38.8)
Chronic obstructive pulmonary disease	31 (19.8)
Pulmonary hypertension, PAP >60 mm Hg	33 (21.0)
Logistic EuroSCORE	17.8 ± 21.1
STS predicted mortality risk score	5.3 ± 3.4
Procedural characteristics	
26-mm CoreValve	66 (42.0)
29-mm CoreValve	91 (58.0)
Vascular access	
Femoral	131 (83.5)
Subclavian	22 (14.0)
Direct aortic	4 (2.5)

Values are mean ± SD or n (%).
EF = ejection fraction; EuroSCORE = European System for Cardiac Operative Risk Evaluation score; NYHA = New York Heart Association; PAP = pulmonary artery pressure; STS = Society of Thoracic Surgeons.

Suitability for available CoreValve sizes

We subsequently analyzed the number of patients whose annular dimensions fell within the range of the manufacturer's recommended sizing guidelines for the 23-, 26-, 29-, and 31-mm CoreValves using TEE and CT (Fig. 2). Some patients were eligible for treatment with 2 THV sizes due to overlap in the sizing criteria: for example, a 20-mm annulus can be treated with either a 23- or 26-mm CoreValve. According to TEE measurements, 95.5% of patients were suitable for either a 26-mm (35%) or 29-mm (60.5%) CoreValve; 10.8% were suitable for the 23-mm valve and 10.8% for the 31-mm CoreValve. In contrast, 18% fewer patients (78.3%)

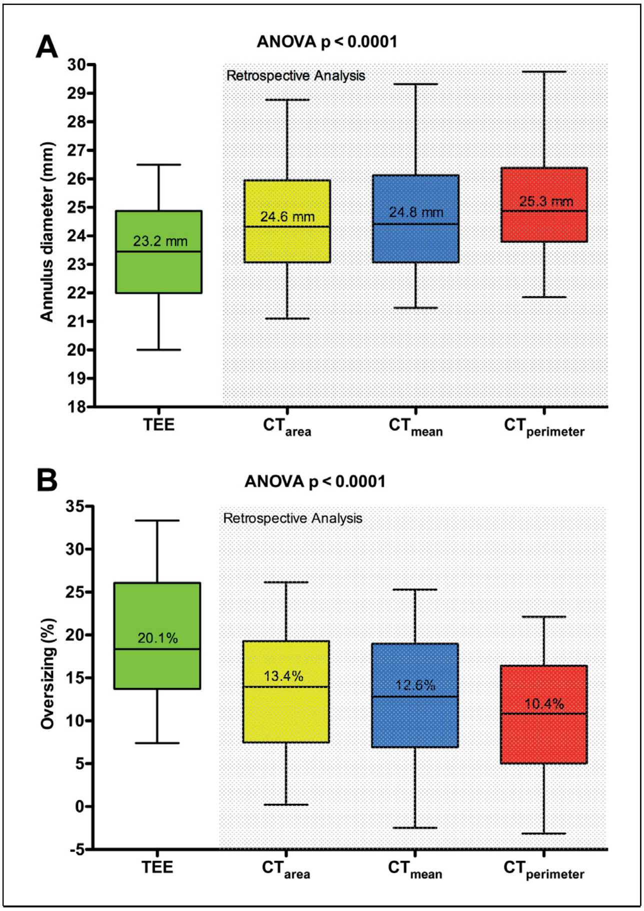

Figure 1 Annulus Diameter and Percentage Oversizing
(A) Mean aortic annulus diameters measured using transesophageal echocardiography (TEE) and computed tomography (CT). **(B)** Estimated THV oversizing according to TEE- and CT-derived annular diameters. Data are means and 95% confidence intervals. Shaded region represents retrospective CT analysis. ANOVA = analysis of variance.

were suitable for a 26- or 29-mm CoreValve, 11% more (21.7%) were suitable for a 31-mm device and 8.9% had annuli too large for currently available valve sizes using $CT_{perimeter}$. Furthermore, no patients were eligible for the 23-mm CoreValve using $CT_{perimeter}$.

Adherence to THV-oversizing criteria

The expected THV oversizing was calculated by relating the annular diameters measured with TEE and CT to the implanted CoreValve size (determined by TEE) (Fig. 1B). With TEE, the average THV-oversizing was 20.1 ± 8.2%. When CT data were applied retrospectively, the expected THV oversizing decreased considerably ($p < 0.0001$ for trend). Specifically, THV

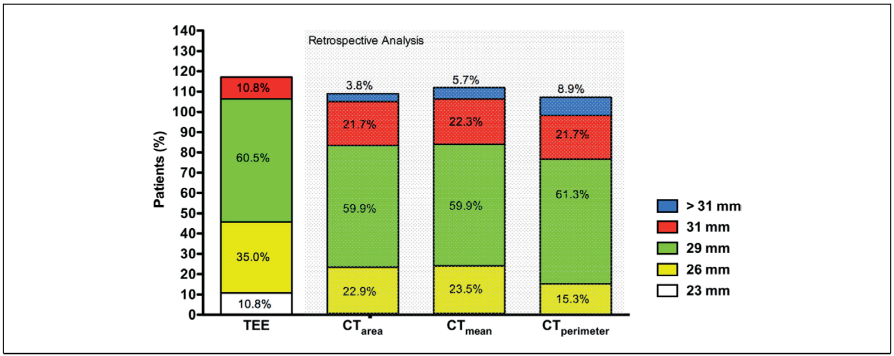

Figure 2 Suitability for CoreValve Sizes According to Imaging Modality
The proportion of patients suitable for currently available CoreValve sizes according to aortic annular measurements with TEE and CT. Note, some patients were eligible for treatment with 2 transcatheter heart valve sizes due to overlap in the sizing criteria. Shaded region represents retrospective CT analysis. Abbreviations as in Figure 1.

oversizing with CT_{area}, CT_{mean}, and $CT_{perimeter}$ was 13.4 ± 8.2%, 12.6 ± 8%, and 10.4 ± 7.8%, respectively. This meant that the absolute and relative difference in expected THV oversizing was 9.7% and 48.3% less using $CT_{perimeter}$ than when using TEE.

Using the TEE-derived annular measurements, 80.9% of patients realized the recommended THV oversizing and hence were deemed to have received the appropriate CoreValve size (Fig. 3); 19.1% did not achieve the recommended THV oversizing (12.7% excessive and 6.4% insufficient oversizing) and thus received an inappropriate valve size.

When CT data were applied retrospectively to the TEE-selected CoreValve size, the proportion of patients that satisfied the recommended THV-oversizing criteria decreased significantly ($p < 0.0001$ for trend). Using CT_{area} and CT_{mean}, 60.5% of cases achieved recommended THV-oversizing. Applying $CT_{perimeter}$ data, only 51% of patients achieved recommended THV oversizing, and thus 49% received an inappropriate CoreValve size. With $CT_{perimeter}$, 30.6% had annuli too large for the available CoreValve sizes at that time.

THV oversizing and PVL

Following CoreValve implantation, approximately one-quarter of patients (n = 38) met the criteria for significant PVL (paravalvular aortic regurgitation grade ≥2 in 16.1% or need for post- implantation dilation in 8.1%) (Table 2): 14 of 66 (21.2%) 26-mm and 24 of 91 (26.4%) 29-mm CoreValve ($p = 0.57$). With TEE, the proportion of patients with PVL was similar among those that satisfied THV-oversizing criteria and those that did not meet these criteria (23.6% vs. 26.7%; $p = 0.81$) (Fig. 4). According to $CT_{perimeter}$ data, however, the proportion of patients with PVL was 21% lower in those who satisfied THV-oversizing criteria than those who did not (13.8% vs. 35.1%; $p = 0.003$).

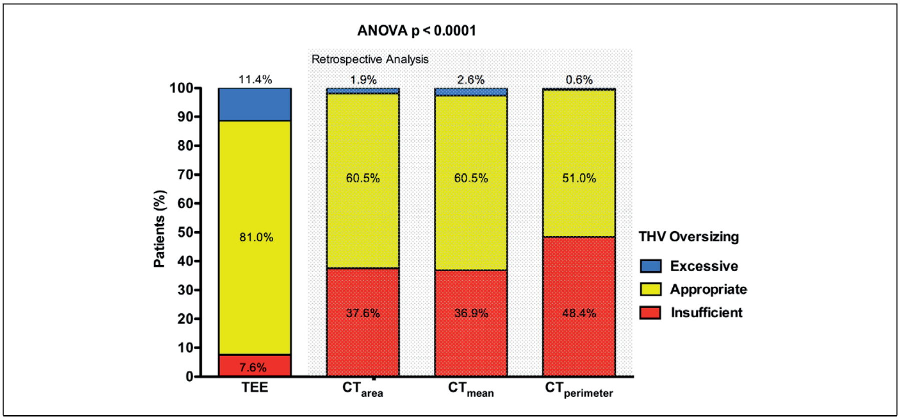

Figure 3 Excessive, Insufficient, or Appropriate THV Oversizing
The proportion of patients with excessive, insufficient, or appropriate transcatheter heart valve (THV) oversizing according to the manufacturer's sizing recommendations on the basis of TEE and CT. Shaded region represents retrospective CT analysis. Abbreviations as in Figure 1.

Table 2 Procedural and Clinical Outcomes (N = 157)

TAVR performance	
Aortic regurgitation grade ≥2 or post-implantation dilation	38 (17.8)
Aortic valve peak gradient, mm Hg	21.7 ± 7.3
Aortic valve mean gradient, mm Hg	11.3 ± 4.1
Vascular complications	
VARC major	14 (8.9)
VARC minor	18 (11.5)
Bleeding	
VARC life-threatening	4 (2.6)
VARC major	2 (1.3)
VARC minor	8 (5.1)
Stroke	4 (2.6)
Periprocedural myocardial infarction	1 (0.6)
Acute kidney injury, modified RIFLE criteria stage 2 or 3*	11 (19.3)
Pacemaker	39 (24.8)
30-day combined safety endpoint	32 (20.4)
30-day mortality	10 (6.4)
VARC cardiovascular	10 (6.4)
VARC noncardiovascular	0 (0.0)
6-month mortality	25 (15.9)

Values are n (%) or mean ± SD.
* Modified RIFLE criteria. RIFLE = Risk, Injury, Failure, Loss, and End-stage Kidney; TAVR = transcatheter aortic valve replacement; VARC = Valve Academic Research Consortium.

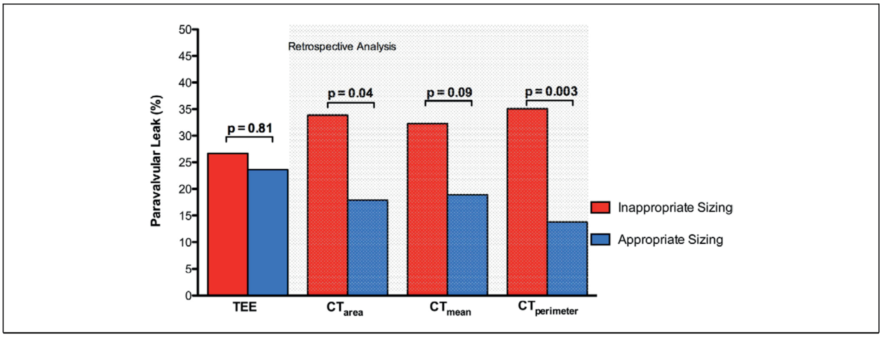

Figure 4 Appropriateness of THV Oversizing and PVL According to Imaging Modality
The proportion of patients with significant paravalvular leak (PVL) that achieved **(blue)** or did not achieve **(red)** appropriate THV oversizing according to TEE- and CT-based sizing. Shaded region represents retrospective CT analysis. Abbreviations as in Figures 1 and 3.

Using TEE, there was no difference in THV oversizing between patients with and without PVL (19.0 ± 8.6% vs. 20.5 ± 8.1%; p = 0.32) (Fig. 5). According to CT data, there was significantly less THV oversizing in those with PVL than those without PVL (CT_{area}: 9.0 ± 7.1% vs. 14.9 ± 8.0%, p < 0.0001; CT_{mean}: 9.0 ± 7.2% vs. 13.7 ± 8.0%, p < 0.001; and $CT_{perimeter}$: 6.2 ± 7.1% vs. 11.7 ± 7.5%, p = 0.0001).

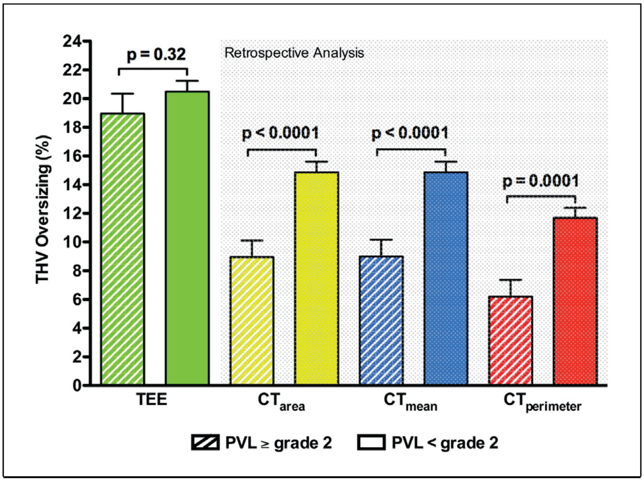

Figure 5 THV Oversizing and PVL According to Imaging Modality
Estimated percentage of THV oversizing according to TEE- and CT-based aortic annular diameters in patients with **(diagonal lines)** or without **(solid)** significant paravalvular leak. Shaded region represents retrospective CT analysis. Abbreviations as in Figures 1, 3, and 4.

Predictors of PVL

In the univariable analysis, several factors were associated with PVL (Table 3). Interestingly, increasing aortic annular diameter measured with CT, but not with TEE, was associated with a higher incidence of PVL. Similarly, adherence to CT-based rather than TEE-based THV-oversizing principles was associated with a reduction in PVL. In the multivariable analysis (Model 1), adherence to $CT_{perimeter}$-based TVH oversizing was independently associated with a reduction in the incidence of PVL (odds ratio [OR]: 0.36; 95% CI: 0.14 to 0.90; $p = 0.029$), whereas increasing depth of CoreValve implantation (OR: 1.19; 95% CI: 1.04 to 1.35; $p = 0.009$) and severe aortic root calcification (OR: 2.97; 95% CI: 1.2 to 7.38; $p = 0.019$) were both predictors of increased PVL.

Receiver-operating characteristic curves

ROC curves were used to compare the precision of TEE and CT to predict PVL (Fig. 6). TEE appeared to be the least efficacious imaging modality, with an intercept parallel to the line of equality (AUC: 0.51). The AUC for $CT_{perimeter}$ (0.65) was significantly greater than that of TEE ($p = 0.05$), but it was not significantly different from that calculated for CT_{area} (0.60) or CT_{mean} (0.59). Adhering to THV-oversizing criteria with $CT_{perimeter}$ gave a sensitivity, specificity, positive predictive value, and negative predictive value of predicting PVL of 71.1%, 58%, 35.1%, and 86.3%, respectively.

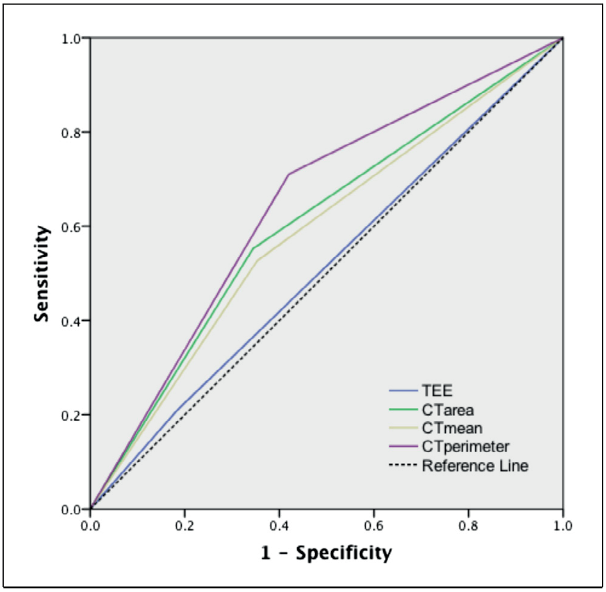

Figure 6 ROC Curves for Predicting PVL According to Adherence to Oversizing Criteria With TEE and CT
The receiver-operating characteristic (ROC) curves suggest that adherence to oversizing principles with $CT_{perimeter}$, CT_{mean}, and CT_{area} results in more accurate prediction of PVL than using TEE does. TEE = transesophageal echocardiography; other abbreviations as in Figures 1 and 4.

Table 3 Predictors of PVL

	Odds Ratio	95% CI	p Value
Univariable model			
Age, yrs	0.98	0.93–1.03	0.353
Male	1.44	0.68–3.03	0.343
BMI	0.76	0.13–4.57	0.765
Transfemoral TAVR	1.41	0.49–4.05	0.518
CoreValve size	1.10	0.87–1.41	0.457
Left ventricular EF	1.45	0.93–2.25	0.103
Aortic valve area	0.31	0.05–1.89	0.204
Aortic valve mean gradient	1.03	0.98–1.05	0.320
Logistic EuroSCORE	1.99	0.98–1.04	0.739
STS predicted mortality risk score	1.03	0.92–1.14	0.641
Depth of implant*	1.21	1.07–1.36	0.002
CT ellipticity	0.67	0.26–17.08	0.810
Severe aortic root calcification*	3.04	1.38–6.68	0.006
Annulus diameter			
TEE	1.14	0.94–1.37	0.175
CT_{area}*	1.32	1.12–1.16	0.001
CT_{mean}*	1.26	1.07–1.48	0.005
$CT_{perimeter}$*	1.30	1.11–1.53	0.001
Appropriate THV oversizing			
TEE	0.85	0.34–2.2	0.726
CT_{area}*	0.43	0.20–8.9	0.024
CT_{mean}*	0.49	0.23–1.03	0.059
$CT_{perimeter}$*	0.23	0.10–0.52	<0.0001
Multivariable model 1: $CT_{perimeter}$			
Depth of implant	1.19	1.04–1.35	0.009
Severe aortic root calcification	2.97	1.20–7.38	0.019
$CT_{perimeter}$	0.36	0.14–0.90	0.029
Multivariable model 2: CT_{area}			
Depth of implant	1.19	1.05–1.35	0.006
Severe aortic root calcification	3.31	1.35–8.10	0.009
CT_{area}	0.60	0.25–1.45	0.258
Multivariable model 3: CT_{mean}			
Depth of implant	1.19	1.05–1.35	0.006
Severe aortic root calcification	3.40	1.39–8.29	0.007
CT_{mean}	0.68	0.28–1.63	0.385

Univariate and multivariate predictors of PVL (grade ≥2 or post-implantation dilation). Separate multivariable analysis due to multicollinearity of CT variables.

* Variables associated with PVL in univariate analysis.

Further analysis of the $CT_{perimeter}$ data with sensitivity-specificity curves identified minimal oversizing thresholds of 9% for the 26-mm CoreValve and 9.6% for the 29-mm CoreValve that best predicted PVL (Fig. 7). Using this cut point, the sensitivity, specificity, positive predictive value, and negative predictive value for the 26-mm Core-Valve were 100%, 4.8%, 33%, and 100%. The corresponding values for the 29-mm CoreValve were 84.2%, 42.4%, 45.7%, and 82.4%. These $CT_{perimeter}$ thresholds predicted a higher incidence of PVL for both the 26 (33.3% vs. 11.1%; p = 0.037) and 29-mm CoreValves (42.1% vs. 15.1%; p = 0.007).

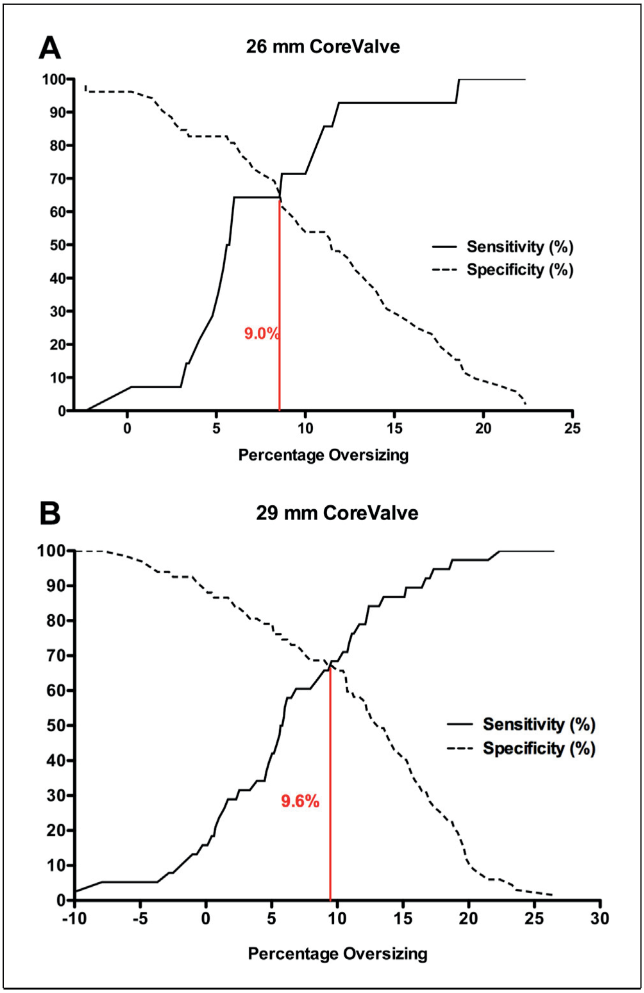

Figure 7 Sensitivity and Specificity Curves for $CT_{perimeter}$
The sensitivity and specificity curves identified $CT_{perimeter}$-derived oversizing thresholds of 9.0% **(A)** and 9.6% **(B)** for the 26-mm and 29-mm CoreValves to be predictive of PVL. Abbreviations as in Figures 1 and 4.

DISCUSSION

The current study confirms previous observations that CT-based aortic annular diameters are significantly larger than those obtained by 2D echocardiography. When these CT diameters were used to recalculate the oversizing relative to the TEE-selected CoreValve, the actual THV oversizing was reduced by 48%. Accordingly, the retrospective CT analysis suggested that up to 50% of patients did not achieve the manufacturer's recommended THV-oversizing criteria and therefore received an inappropriate CoreValve size. CT data also suggested that one-third of patients had annuli too large for available CoreValve sizes during the time of enrollment. Adherence to CT-based but not TEE-based oversizing was a predictor of reduced PVL. According to CT, significantly lower PVL rates were observed in those patients who received a correct CoreValve size than in those who did not. Finally, we identified a lower limit threshold for $CT_{perimeter}$-based THV oversizing associated with a reduced incidence of PVL: 9% and 9.6% for the 26-mm and 29-mm prostheses, respectively.

Transcatheter heart valve sizing

Pre-procedural anatomical screening is of considerable importance for TAVR. In particular, appropriate THV sizing is recognized to be a key factor for optimizing patient outcomes: PVL is an independent risk factor for mortality and has been reported in 9% to 21% of CoreValve and 6% to 13.9% of Edwards Sapien (Edwards Lifesciences Inc., Irvine, California) recipients (1,2,16). Appropriate THV sizing involves achieving a predefined amount of prosthesis oversizing relative to the aortic annulus. Previous studies have demonstrated that failing to achieve a 1:1 ratio of the THV relative to the aortic annulus (cover index: [TAVR area/annular area − 1] × 100) is associated with PVL (6,8,9,17). Evidently, accurate measurement of the dimensions of the aortic annulus is fundamental for accurate THV sizing.

Although there is no consensus as to the gold-standard technique for measuring the aortic annulus, CT provides more accurate annular measurements than TEE does, and the use of CT for THV sizing has been associated with improved clinical outcomes (4–10). CT multiplanar reformatting allows accurate 3D reconstruction of the aortic annulus in its true plane. The superiority of this technique over 2D TEE is explained by the oval shape and variable orientation of the aortic annulus and the likelihood that 2D echocardiographic imaging will measure a short-axis tangent across the annulus. Herein, we confirm previous observations that CT provides larger annular diameters than TEE does (4–10): $CT_{perimeter}$-derived diameters were on average 2.0 mm larger than TEE measurements.

The smaller diameters measured with TEE compared with CT have a significant impact on the amount of THV oversizing achieved. In 2007, the oversizing recommendations suggested by the manufacturer were based on the assumption that echocardiography was an accurate method of assessing the annular dimensions. This led us to believe that we were achieving approximately 20% THV oversizing among CoreValve recipients. When we retrospectively applied CT-based sizing to the TEE-based valve size, however, we were surprised to realize that the mean THV oversizing was only 10%. This translates into a 48% relative overestimation of THV oversizing with TEE versus CT. Obviously, this information would have had a substantial impact on THV size selection: up to one-half of all patients were deemed to have received the incorrect CoreValve size and approximately 30% would have been deemed ineligible for the available CoreValve prostheses at that time. The results of recent publications demonstrating enhanced clinical outcomes with CT-based THV sizing suggest that the initial THV-oversizing recommendations were appropriate, but the imaging modality (2D-echocardiography) was not (5–11).

BMI = body mass index; CI = confidence interval; CT = computed tomography; PVL = paravalvular leak; TEE = transesophageal echocardiography; THV = transcatheter heart valve; other abbreviations as in Tables 1 and 2.

In the present study, achieving TEE-based oversizing recommendations was insensitive for predicting PVL. In contrast, when $CT_{perimeter}$ data were retrospectively applied, the proportion of patients with PVL was significantly lower in those that achieved THV-oversizing criteria than in those that did not (13.8% vs. 35.1%; $p = 0.0026$). In those with significant PVL, oversizing was 3× more with TEE (19%) than with $CT_{perimeter}$ (6.2%). This reinforces the message that TEE led us to select valves that were too small for patients' anatomy, especially in those with significant PVL. Our ROC analysis further reinforces the hypothesis that TEE-based sizing was a poor predictor of PVL when compared with CT measures.

Moderate to severe PVL has been reported in 9% to 21% of CoreValve and 6% to 13.9% of Edwards Sapien valve recipients (17). We can speculate that this historical incidence of PVL with TAVR may reflect inaccurate TEE-based sizing in a considerable proportion of patients. Our data would appear to support previous observations that CT-sizing can reduce the incidence of significant PVL considerably (23.6% to 13.8%) (8). It is important to note, however, that appropriate THV sizing is not a panacea for eliminating PVL. Severe aortic root calcification and increasing depth of CoreValve implantation were also independent predictors of PVL, emphasizing the key role of pre-procedural CT for optimizing patient selection and the continued importance of refining procedural techniques.

Which CT diameter to choose?

Compared with CT_{area} and CT_{mean}, $CT_{perimeter}$ was found to yield larger annular diameters, affect TAVR sizing more frequently, and be a predictor of PVL in the multivariable analyses. Furthermore, $CT_{perimeter}$ had the greatest discrimination for PVL in the ROC analysis. Greater annular dimensions require THV of larger diameter, which increases the risk of annular rupture or coronary occlusion. Annular rupture, however, has not been reported with a self-expanding prosthesis, and coronary occlusion remains rare, particularly if guidelines regarding sinus of Valsalva width are respected (3,10). Previous investigators have suggested that CT_{area} or CT_{mean} are the most useful determinants of PVL in patients undergoing balloon-expandable TAVR

(6,8,9,11). The mechanistic differences in the structure and function between the Core-Valve and the Edwards Sapien valve may explain supremacy of $CT_{perimeter}$ in this analysis of CoreValve patients. Finally, $CT_{perimeter}$-oversizing thresholds of 9% and 9.6% for the 26-mm and 29-mm CoreValves were predictive of PVL. When CoreValve oversizing was less than these threshold values, we observed a 3-fold increase in the rate of PVL.

Study limitations

Post-implantation PVL may be caused by malposition, underexpansion, or undersizing of the THV. Differentiating between THV undersizing and underexpansion remains challenging. Thus, although we excluded THV-malposition from the analysis, our definition of PVL included cases where THV post-dilation was performed, and thus potentially included patients with THV-underexpansion rather than THV-undersizing. As underexpansion is more likely to occur with severe aortic root calcification, we performed detailed CT analysis of the aortic root to identify patients with heavy calcification. Significantly, after adjusting for both aortic root calcification and the depth of THV implantation, achieving CT-based oversizing criteria remained an independent predictor of reduced PVL. As the CT scans were obtained early in our TAVI experience, different acquisition protocols were used. A standardized acquisition protocol would have further optimized the CT analysis. Fluoroscopic assessment of THV malposition was only possible in 135 of 157 patients.

Although the results of this study suggest that CT-based annular measurements would result in larger valves being implanted in a large proportion of patients and, compared with 2D echocardiography, has the potential to reduce PVL, these strategies were not directly compared in a prospective manner. Therefore, the retrospective design and observational nature of the data imply that the conclusions should be viewed as hypothesis-generating. Furthermore, we did not use 3D TEE, which correlates more closely with CT-derived annular measurements, and could mitigate the inaccuracy associated with 2D TEE (18). Finally, this consecutive series of patients were treated with the Medtronic CoreValve and therefore the findings should not be extrapolated to other TAVR systems.

CONCLUSIONS

Aortic annular measurements are significantly larger when measured with CT than with TEE. Retrospective application of these CT-derived measurements to recalculate the oversizing of the TEE-selected CoreValve size revealed that the expected THV oversizing was overestimated 2-fold. Consequently, the TEE-selected CoreValve size was incorrect in one-half of all patients. $CT_{perimeter}$ appears to be the most sensitive CT-based measure for predicting PVL and is recommended for THV sizing in all patients undergoing CoreValve implantation.

ABBREVIATIONS AND ACRONYMS

AUC	= area under the curve
CI	= confidence interval
CT	= computed tomography
D	= dimensional
OR	= odds ratio
PVL	= paravalvular leak
ROC	= receiver-operating characteristic
TAVR	= transcatheter aortic valve replacement
TEE	= transesophageal echocardiography
THV	= transcatheter heart valve

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