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The Impact of Integration of a Multidetector Computed Tomography Annulus Area Sizing Algorithm on Outcomes of Transcatheter Aortic Valve Replacement

A Prospective, Multicenter, Controlled Trial

Ronald K. Binder, MD,* John G. Webb, MD,* Alexander B. Willson, MBBS,* Marina Urena, MD,† Nicolaj C. Hansson, MD,‡ Bjarne L. Norgaard, MD, PhD,‡ Philippe Pibarot, MD,† Marco Barbanti, MD,* Eric Larose, MD,† Melanie Freeman, MBBS,* Eric Dumont, MD,† Chris Thompson, MD,* Miriam Wheeler, MBChB,* Robert R. Moss, MD,* Tae-hyun Yang, MD,* Sergio Pasian, MD,† Cameron J. Hague, MD,* Giang Nguyen, MD,* Rekha Raju, MD,* Stefan Toggweiler, MD,* James K. Min, MD,§ David A. Wood, MD,‖ Josep Rodés-Cabau, MD,† Jonathon Leipsic, MD*

Vancouver and Quebec City, Canada; Aarhus, Denmark; and Los Angeles, California

Objectives This study prospectively investigated the impact of integration of a multidetector computed tomography (MDCT) annular area sizing algorithm on transcatheter aortic valve replacement (TAVR) outcomes.

Background Appreciation of the 3-dimensional, noncircular geometry of the aortic annulus is important for transcatheter heart valve (THV) sizing.

Methods Patients being evaluated for TAVR in 4 centers underwent pre-procedural MDCT. Recommendations for balloon-expandable THV size selection were based on an MDCT sizing algorithm with an optimal goal of modest annulus area oversizing (5% to 10%). Consecutive patients who underwent TAVR with the algorithm (MDCT group) were compared with consecutive patients without the algorithm (control group). The primary endpoint was the incidence of more than mild paravalvular regurgitation (PAR), and the secondary endpoint was the composite of in-hospital death, aortic annulus rupture, and severe PAR.

Results Of 266 patients, 133 consecutive patients underwent TAVR (SAPIEN XT THV) in the MDCT group and 133 consecutive patients were in the control group. More than mild PAR was present in 5.3% (7 of 133) of the MDCT group and in 12.8% (17 of 133) in the control group ($p = 0.032$). The combined secondary endpoint occurred in 3.8% (5 of 133) of the MDCT group and in 11.3% (15 of 133) of the control group ($p = 0.02$), driven by the difference of severe PAR.

Conclusions The implementation of an MDCT annulus area sizing algorithm for TAVR reduces PAR. Three-dimensional aortic annular assessment and annular area sizing should be considered for TAVR. (J Am Coll Cardiol 2013;62:431–8)

The aortic annulus is a complex, 3-dimensional, nearly uniformly oval-shaped structure (1). Appreciation of its geometry is important for appropriate transcatheter heart valve (THV) size selection (1,2). For transcatheter aortic valve replacement (TAVR), the dimensions of the aortic annulus have been traditionally described by a single diameter measurement

From the *St. Paul's Hospital, University of British Columbia, Vancouver, British Columbia, Canada; †Quebec Heart and Lung Institute, Laval University, Quebec City, Quebec, Canada; ‡Aarhus University Hospital Skejby, Aarhus, Denmark; §Cedars-Sinai Heart Institute, Los Angeles, California; and the ‖Vancouver General Hospital, University of British Columbia, Vancouver, British Columbia, Canada. Edwards Lifesciences funded the image transfer but had no involvement in data collection, data analysis, or manuscript writing. Drs. Binder, Webb, Norgaard, Dumont, Wood, Rodés-Cabau, and Leipsic are consultants to Edwards Lifesciences. Drs. Binder and Toggweiler received unrestricted research grants from the Swiss National Foundation. Drs. Hansson and Pibarot received research grants from Edwards Lifesciences. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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Abbreviations and Acronyms

MDCT = multidetector computed tomography

PAR = paravalvular regurgitation

TAVR = transcatheter aortic valve replacement

TEE = transesophageal echocardiography

THV = transcatheter heart valve

TTE = transthoracic echocardiography

from 2-dimensional transesophageal echocardiography (TEE) (3). However, the appropriateness of this method for THV sizing has recently been questioned (1,4,5). Inappropriate THV size selection is associated with paravalvular regurgitation (PAR) (2,4), aortic annular rupture (6), coronary occlusion (7), and device embolization (8). These complications strongly impact morbidity and mortality after TAVR (7). Three-dimensional assessments of the aortic annulus by TEE (9,10) or multidetector computed tomography (MDCT) have been shown to predict PAR (2,4) because of better appreciation of its complex 3-dimensional structure. Our group previously found that MDCT annular area oversizing was the strongest predictor for PAR (2) in a retrospective, multicenter analysis. However, it is unknown whether this knowledge can be translated into improved clinical outcomes when practically applied by a readily available, reproducible MDCT annulus area sizing algorithm (5). We therefore performed a prospective, multicenter, controlled trial to evaluate the impact of integration of an MDCT annular area sizing algorithm on TAVR outcomes (5).

Methods

Patients with high surgical risk or inoperable symptomatic severe aortic stenosis, planed for TAVR in 4 experienced centers (St. Paul's Hospital, University of British Columbia, Vancouver, British Columbia, Canada; Quebec Heart and Lung Institute, Laval University, Quebec City, Quebec, Canada; Aarhus University Hospital Skejby, Aarhus, Denmark; and Vancouver General Hospital, University of British Columbia, Vancouver, British Columbia, Canada) were considered for this trial, which was approved by the local ethical committees. Exclusion criteria were an estimated glomerular filtration rate of less than 35 ml/min (except for patients on chronic hemodialysis), previous aortic valve replacement ("valve-in-valve"), and TAVR with a THV other than the SAPIEN XT balloon-expandable valve (Edwards Lifesciences, Irvine, California). Prospectively enrolled, consecutive patients who underwent TAVR with the implementation of the MDCT annular area sizing algorithm (MDCT group) were compared with consecutive patients who underwent TAVR without the algorithm (control group) prior to trial initiation. For both groups, the available THV sizes were 20-, 23-, 26-, and 29-mm diameters. Each center contributed equal numbers of patients to the MDCT group and the control group. Because the trial was initiated in the beginning of 2012, consecutive patients in the control group were treated in 2011 just before trial initiation. Sizing of the THV in the control group was based on an integration of echocardiography measurements and angiography (without standardized measurements) but not on 3-dimensional MDCT area assessment.

Study endpoints. The primary endpoint was the incidence of more than mild PAR, and the secondary endpoint was the composite of in-hospital death, aortic annular rupture (as a marker of excessive oversizing), and severe PAR (as a marker of excessive undersizing). Study endpoint analysis was performed by intention to treat.

MDCT and THV size selection. All MDCT scans were read by 1 experienced level 3 cardiac MDCT reader at St. Paul's Hospital (MDCT core laboratory) in concert and by consensus with the local site. Examinations were performed with either a 64-slice scanner (Discovery HD 750, GE Healthcare, Waukesha, Wisconsin) or a second-generation dual-source CT system (Siemens Somatom Definition Flash, Siemens Healthcare, Erlangen, Germany). The protocol for the single-source scanner included the injection of 80 to 120 ml of radio-contrast medium at 5 ml/s followed by 30 ml of normal saline (2). Electrocardiogram-gated dose modulation was used, but heart rate reduction with beta-blockade was not performed. Depending on patient size, maximum tube current ranged between 450 and 700 mA with a fixed tube voltage of 100 kVp for patients with a body mass index (BMI) <30 kg/m^2 and 120 kVp for larger patients. For the dual-source scanner, a contrast-enhanced MDCT examination in the caudocranial direction with retrospective gating was performed. Commercially available contrast media (ioversol 350 mg/ml, Mallinckrodt Inc., Hazelwood, Missouri) was used (20 ml for the test bolus and 70 ml for the spiral scan). Contrast injection was followed by a 50-ml saline flush. Heart rate reduction with beta-blockade was not performed. MDCT was performed with a 128 $\times$ 0.625 mm collimation, z-flying spot, gantry rotation time 280 ms, and scan pitch 0.20 to 0.40 (depending on heart rate). Maximum tube current ranged from 450 to 750 mA with fixed tube potential of 100 (BMI <30 kg/m^2) or 120 kV (BMI >30 kg/m^2). Electrocardiogram-controlled tube current modulation was applied with reduction of the current to 20% and full pulsing applied only from 30% to 70% of the RR interval.

MDCT annular area measurements were performed in systole at 25% or 35% of the RR interval when the annulus is the largest (5), depending on which of the 2 phase reconstructions displayed better image quality. Recommendations for THV size were based on an MDCT sizing algorithm with an optimal goal of modest annulus area oversizing (nominal THV area/MDCT annular area = 5% to 10%) (Table 1) (5). The algorithm ensures routine oversizing of the MDCT aortic annular area (nominal THV area > MDCT annular area), calculating a percentage of annular oversizing (nominal THV area/MDCT annular area). Nominal external THV areas for the 20-, 23-, 26-, and 29-mm SAPIEN XT THV are 3.14 cm^2, 4.15 cm^2, 5.31 cm^2, and 6.61 cm^2, respectively. Implantation with nominally filled deployment balloons was performed by full injection of the indeflator volume. When more than 20% area oversizing was anticipated (or more than 15% oversizing in the presence of adverse aortic

Table 1 Multidetector Computed Tomography Annular Area Sizing Algorithm

Annular Area, mm^2	Percentage of Annular Area Oversizing, %			
	20-mm THV	23-mm THV	26-mm THV	29-mm THV
230	NR			
240	NR (30.9)			
250	25.7 UE			
260	20.8 UE			
270	16.4			
280	12.2			
290	8.3			
300	4.7			
310	1.3	NR		
320	NR (−1.9%)	29.8 UE		
330		25.9 UE		
340		22.2 UE		
350		18.7		
360		15.4		
370		12.3		
380		9.3		
390		6.5		
400		3.9	NR	
410		1.3	NR (29.5)	
420		NR (−1.1)	26.4 UE	
430			23.5 UE	
440			20.7 UE	
450			18.0	
460			15.4	
470			13.0	
480			10.6	
490			8.4	
500			6.2	
510			4.1	NR
520			2.1	NR (27.0)
530			0.2	24.6 UE
540				22.3 UE
550				20.1 UE
560				17.9
570				15.9
580				13.9
590				12.0
600				10.1
610				8.3
620				6.5
630				4.8
640				3.2
650				1.6
660				0.1
670				NR

The recommendation is to select a prosthesis with a cross-sectional area modestly larger than that of the aortic annulus. A target of 5% to 10% area oversizing with upper and lower limits of 1% to 20% is suggested. The highlighted grey zones represent annular areas in which valve selection is challenging. Selecting the larger valve will result in oversizing >20% and the smaller valve will result in undersizing. Oversizing the annulus >20% may increase the risk of annular injury. Options include underfilling the transcatheter heart value balloon or selecting a smaller valve size with an attendant risk of paravalvular regurgitation.

NR = not recommended; UE = underexpansion.

root features), intentional underexpansion of the THV was suggested. This was accomplished by reducing the volume of fluid within the valve deployment balloon by 10%. Adverse root features included more than minimal left ventricular outflow tract calcification and shallow sinuses of Valsalva. Although 5% to 10% area oversizing was considered optimal, most patients will not meet this target due to the large increments between manufactured prosthesis sizes. We therefore considered a range from 1% to 15% (20% in the absence of adverse root features) as acceptable margins in the sizing algorithm, with the integration of balloon underfilling for those who would require oversizing in excess of 20% by area.

In the MDCT group, TAVR operators were informed about the MDCT area sizing recommendation before the procedure. Operators were not obliged to follow the MDCT area sizing recommendations but could choose the THV size they considered most appropriate.

Echocardiography. Intraprocedural TEE was routinely performed by level 3 echocardiographers highly experienced in TAVR assessments. The aortic annulus was 2-dimensionally imaged by periprocedural TEE in a 3-chamber view, and a single diameter was documented. Echocardiographers were blinded toward the MDCT measurements and the MDCT sizing recommendation. Prior to discharge, transthoracic echocardiography (TTE) was performed to assess PAR, valve area, and transvalvular gradients. The grade of PAR was rated as none, mild, moderate, or severe according to Valve Academic Research Consortium criteria (11).

Statistical analysis. Analyses were performed using SPSS statistics software (version 20.0, SPSS Inc., Chicago, Illinois). Continuous variables are reported as mean ± SD and categorical variables by percentages. Continuous variables were tested for a normal distribution (QQ plot) and compared by the Student *t* test. For comparison of more than 2 continuous parametric variables, an analysis of variance was used. Categorical variables were compared by the Fisher exact test. All tests were 2-tailed, and a p value <0.05 was considered statistically significant.

Results

Baseline characteristics. Of 266 patients in the trial, 133 consecutive patients underwent TAVR with the MDCT sizing algorithm recommendation (MDCT group) and 133 consecutive patients without the algorithm (control group) (University of British Columbia (2 sites): 166 patients; Laval University: 56 patients; Aarhus University Hospital: 44 patients) (Fig. 1). Baseline characteristics are shown in Table 2. Patients in the control group had a 1.2% higher Society of Thoracic Surgeons score ($p = 0.007$), which reflects the broadening of TAVR indications to lower-risk patients over the study period.

Valve selection and procedure. All patients received a SAPIEN XT THV (Edwards Lifesciences) with valve sizes of 20-, 23-, 26-, or 29-mm diameter available for both groups. Prosthesis sizes and procedural characteristics are shown in Table 3. Within the MDCT group, sizing recommendations were followed in 80.5% of patients (107 of 133). In the 26 patients for which MDCT recommendations

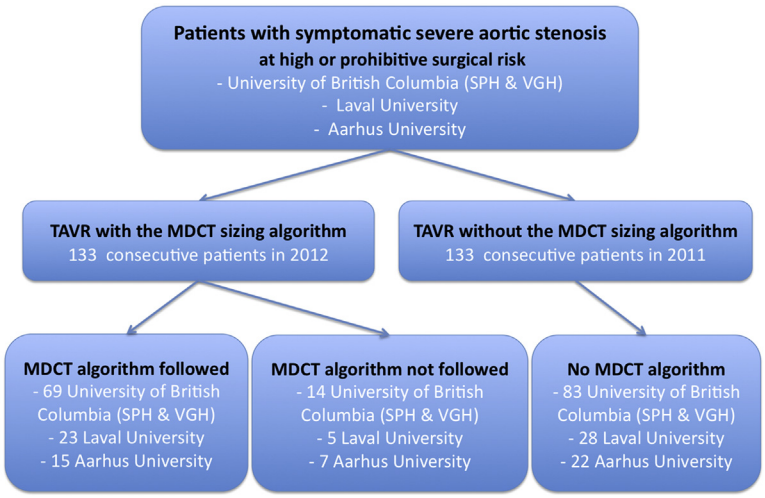

Figure 1 Study Flowchart

MDCT = multidetector computed tomography; SPH = St. Paul's Hospital; TAVR = transcatheter aortic valve replacement; VHG = Vancouver General Hospital.

were not followed, the implanted THV size was chosen because of conflicting echocardiography recommendations in 14 patients, balloon aortic valvuloplasty assessment in 2 patients, and operator preference (prosthesis size in discordance with MDCT as well as echocardiography recommendations) in 10 patients. In 9 patients, the MDCT algorithm would have recommended a larger size and in 17 patients a smaller THV size. In this group (26 patients), there were no cases of severe PAR, no annulus rupture, and no in-hospital mortality. Compared with the control group, the MDCT group was more often associated with the use of an underfilled deployment balloon (13.5% vs. 0%; $p < 0.001$) and implantation of the largest available (29-mm diameter) prosthesis (27.1% vs. 16.5%; $p = 0.038$). Whether deployment balloons were nominally filled or underfilled did not influence the rates of more than mild PAR (9.3% vs. 5.6%; $p = 0.595$), aortic annulus rupture (0.8% vs. 0%; $p = 0.702$), THV embolization (0.8% vs. 0%; $p = 0.702$), or post-dilation (13.3% vs. 5.6%; $p = 0.342$) (Fig. 2).

Post-implant echocardiography. Pre-discharge TTE documented comparable valve function in both MDCT and control groups. Aortic valve area was 1.6 ± 0.3 cm^2 versus 1.6 ± 0.4 cm^2 ($p = 0.923$) and mean gradient 10.0 ± 3.8 mm Hg versus 9.9 ± 4.6 mm Hg ($p = 0.96$) in the MDCT group versus control group, respectively. However, more than mild PAR was less common in the MDCT group: 5.3% (7 of 133) versus 12.8% (17 of 133) ($p = 0.032$). Similarly, severe PAR was less common in the MDCT group: 0% versus 4.5% (6 of 133) ($p = 0.013$) (Fig. 3). The degree of annulus area oversizing was significantly associated with a reduction in PAR. Annulus area oversizing was $16.4 \pm 12.1\%$ in patients with no PAR, $10.4 \pm 10.7\%$ in patients with mild PAR, and $0.5 \pm 9.4\%$ in patients with more than mild PAR ($p = 0.001$). In as-treated analysis, more than mild PAR occurred nearly twice as often in the control group (6 of 107 patients [5.6%] vs. 15 of 159 [9.4%]; $p = 0.111$). There was no difference in baseline aortic regurgitation grades between the MDCT group and the control group (Table 2). The rates of more than mild post-procedural PAR did not differ between patients with or without more than mild pre-procedural aortic regurgitation (19 of 225 patients [8.4%] vs. 5 of 41 [12.2%]; $p = 0.389$). Of the patients with severe pre-procedural aortic regurgitation, none had more than mild post-procedural PAR.

Outcomes. Procedural outcomes are shown in Table 3. There were 5 (3.8%) in-hospital deaths in the MDCT group and 9 (6.8%) in the control group ($p = 0.272$). The rates of annular rupture were 0.8% versus 0.8% ($p = 1.0$). The combined secondary endpoint of in-hospital mortality, aortic annular rupture, and severe PAR occurred in 3.8% (5 of 133) in the MDCT group and 11.3% (15 of 133) in the control group ($p = 0.02$). In as-treated analysis, the secondary endpoint occurred twice as often in the control group (5 of 107 patients [4.7%] vs. 15 of 159 [9.4%]; $p = 0.149$), albeit without statistical significance. There was no significant difference in the occurrence of the primary endpoint between the first and second halves of the control group (17.6% vs. 7.7%; $p = 0.119$) or the first and second halves of the MDCT group (2.9% vs. 7.7%; $p = 0.267$) (Table 4).

Discussion

In this prospective, multicenter, controlled trial, the integration of an MDCT annular area sizing algorithm reduced the incidence of more than mild PAR and the composite endpoint of in-hospital death, aortic annular rupture, and

Table 2 Patient Baseline Characteristics

	MDCT Group (n = 133)	Control Group (n = 133)	p Value
Age, yrs	82 ± 8	81 ± 8	0.207
Male	57 (76)	63 (84)	0.316
Height, cm	168 ± 10	168 ± 9	0.991
Weight, kg	77 ± 18	75 ± 18	0.464
BMI, kg/m^2	27 ± 6	27 ± 6	0.414
Diabetes	32 (43)	35 (47)	0.604
Hypertension	84 (112)	79 (105)	0.268
Dyslipidemia	68 (90)	74 (99)	0.224
Smoking history	43 (58)	38 (50)	0.318
COPD	38 (50)	26 (35)	0.065
NYHA functional class			0.088
Class I	1 (1)	0	
Class II	27 (36)	16 (21)	
Class III	63 (84)	76 (101)	
Class IV	9 (12)	8 (11)	
Pre-procedural aortic regurgitation			0.926
None	29.3 (39)	21.8 (29)	
Mild	55.6 (74)	62.4 (83)	
Moderate	13.5 (18)	14.3 (19)	
Severe	1.5 (2)	1.5 (2)	
Prior cerebrovascular accident	16 (21)	14 (19)	0.732
Prior open heart surgery	29 (39)	40 (53)	0.094
Porcelain aorta	11 (15)	10 (13)	0.689
Prior permanent pacemaker	12 (16)	13 (17)	0.852
Prior myocardial infarction	21 (28)	30 (40)	0.092
Hemodialysis	3 (4)	2 (3)	0.702
Pulmonary hypertension	40 (53)	29 (38)	0.039
Peripheral vascular disease	20 (26)	19 (25)	0.876
Atrial fibrillation	38 (51)	39 (52)	0.900
STS PROM, %	5.8 ± 3.2	7.0 ± 3.5	0.007
GFR, ml/min	62 ± 24	53 ± 20	0.001

Values are mean ± SD or % (n).
BMI = body mass index; COPD = chronic obstructive pulmonary disease; GFR = glomerular filtration rate; MDCT = multidetector computed tomography; NYHA = New York Heart Association; PCI = percutaneous coronary intervention; STS PROM = Society of Thoracic Surgeons Predicted Risk of Mortality.

Table 3 Annulus, Echocardiography Assessments, and Procedural Characteristics

	MDCT Group (n = 133)	Control Group (n = 133)	p Value
Left ventricular ejection fraction, %	53 ± 14	51 ± 15	0.175
Mean gradient, mm Hg	42 ± 18	38 ± 15	0.055
Aortic valve area, cm^2	0.7 ± 0.2	0.7 ± 0.2	0.440
TEE annulus diameter, mm	22.9 ± 2.2	22.5 ± 3.0	0.224
MDCT short-axis diameter, mm	21.5 ± 2.2	n/a	n/a
MDCT long-axis diameter, mm	27.3 ± 2.9	n/a	n/a
MDCT mean diameter, mm	24.4 ± 2.3	n/a	n/a
MDCT annulus area, cm^2	4.8 ± 0.8	n/a	n/a
Access type			
Transfemoral	74 (99)	71 (95)	0.581
Transapical	18 (24)	28 (37)	0.058
Transaortic	8 (10)	1 (1)	0.006
Labeled prosthesis size			
20 mm	0.8 (1)	1.5 (2)	0.561
23 mm	26.3 (35)	30.8 (41)	0.415
26 mm	45.9 (61)	51.1 (68)	0.390
29 mm	27.1 (36)	16.5 (22)	0.038
MDCT area oversizing, %	11.6 ± 11.5	n/a	n/a
Underfilled deployment balloon	13.5 (18)	0	< 0.001

Values are mean ± SD or % (n).
n/a = not applicable; TEE = transesophageal echocardiography; other abbreviation as in Table 2.

severe PAR, driven by the difference in severe PAR. The strength of our study manifests in a clear, reproducible, and readily available sizing algorithm, which was prospectively implemented for THV sizing in 4 TAVR centers (3 in Canada and 1 in Europe) and evaluated in a large cohort of consecutive patients.

Although TAVR is an approved alternative to surgical aortic valve replacement in selected patients (12,13), the widening of its application to lower-risk patients may be hampered by complications such as PAR and aortic root injury. These TAVR complications can, to some extent, be attributed to inappropriate THV size selection. Operators performing TAVR have to rely on indirect measurements of the aortic annulus for annular sizing and THV selection. Since its inception, the traditional measurement of the aortic annulus for TAVR was a single diameter from 2-dimensional TEE imaging (3), but recently this method has been challenged by 3-dimensional annular assessments with MDCT (2,4,5,14). In comparison to sizing by direct surgical inspection of the aortic annulus as a gold standard, some studies have shown superiority of MDCT over echocardiographic measurements (15,16). Our knowledge of the complex 3-dimensional geometry of the consistently oval-shaped annulus is expanding (1), and new sizing algorithms that address the limitations of 2-dimensional imaging are needed (5). A single-center retrospective study by Jilaihawi et al. (4) compared the annulus area–derived diameter from MDCT with the TEE diameter and found that MDCT sizing reduced the incidence of PAR. Another study by Hayashida et al. (17) implemented MDCT sizing prospectively in 40 patients and found a lower rate of PAR compared with that in a retrospective cohort of patients treated with TEE sizing. They studied the cross-sectional maximum diameter, area-derived diameter, and perimeter-derived diameter. Although there was a small, prospective cohort in their retrospective, single-center trial, this did not translate into a clear and practical sizing algorithm. In contrast, in our study, a clear and reproducible algorithm was applied prospectively, which was found to be practical and useful by TAVR operators across different centers for THV selection.

MDCT versus TEE. It was not the aim of this trial to perform a head-to-head comparison of TEE sizing versus MDCT sizing. Operators were not bound by recommendations from one or the other imaging modality but were able to freely choose the THV size based on all available information, including the MDCT area sizing recommendation, TEE measurements, TTE evaluation, and aortic root angiograms. For borderline cases, an aortic root angiogram during balloon aortic valvuloplasty may also provide valuable insight for

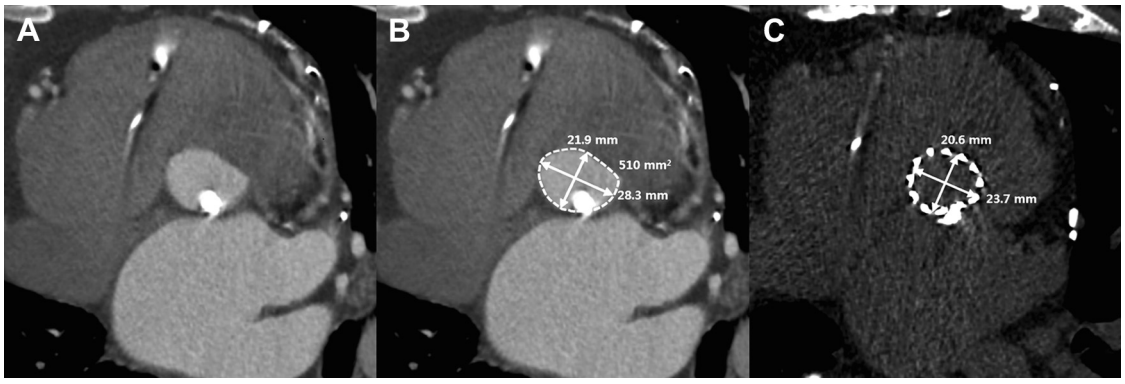

Figure 2 **Pre- and Post-TAVR MDCT in a Patient With Adverse Root Features and Intentional Underexpansion of the Transcatheter Heart Valve**

Because of adverse aortic root features **(A, B)** (large calcium nodule in the left ventricular outflow tract), the 26-mm transcatheter heart valve was intentionally underexpanded by removing 10% of the nominal deployment balloon volume. With this strategy, there was more controlled annular stretch, and displacement of the calcium nodule toward the ventricular septum was avoided **(C)**, thereby reducing the risk of aortic annulus injury. Abbreviations as in Figure 1.

the aortic annular dimensions (18). Because there is no prospective, randomized comparison of MDCT versus TEE sizing reported in the literature, it is unknown whether THV sizing by one of these imaging modalities may be superior. We do not think that it is prudent to randomize patients between imaging modalities nor to blind the operator to any pre-procedural data because TAVR remains a complex procedure with results that are supported by as much pre-procedural data as possible. Importantly, though, our data do confirm the benefit of integration of 3-dimensional MDCT measurements on TAVR-related outcomes, emphasizing their importance in THV selection and solidifying their role in TAVR.

Rationale for annulus area sizing. We elected to use annular area for sizing because we have consistently found it to be the most reproducible annular measurement (1,2,5) and the most predictive of greater than mild PAR (2). Others have suggested that annular sizing should be performed with perimeter measures of the annulus owing to its lesser variability across the cardiac cycle (19). Importantly, although perimeter may be less dynamic, there are growing amounts of data to suggest that it does in fact change through the cardiac cycle (20) and there remain significant limitations with these measurements owing to the lack of appropriate tools on all MDCT image review workstations, resulting in at times erroneous measurements and a lower degree of reproducibility (5). Should these tools become available on all workstations, the area oversizing guidelines used for this trial could be replaced with a perimeter-based sizing guideline but would require modification because annular perimeter oversizing does not translate to the same percentage of area oversizing. As an example, 10% annular

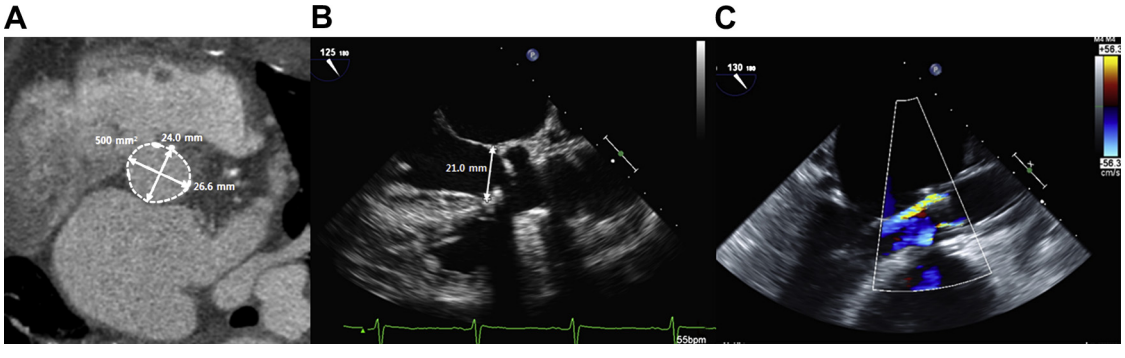

Figure 3 **Pre- and Post-TAVR Imaging in an 80-Year-Old Male Patient With Severe Symptomatic Aortic Stenosis Enrolled Before Integration of the MDCT Sizing Guideline Showing the Value of 3-Dimensional Imaging of the Aortic Annulus**

(A) Double oblique transverse reformat of the basal ring/annulus on MDCT with a mean annular diameter of 25.3 mm and an area of 5.0 cm^2. **(B)** The long-axis 2-dimensional echocardiogram suggests an annular diameter of 21.0 mm. **(C)** A 23-mm balloon-expandable prosthesis was selected on the basis of the 2-dimensional echocardiogram with significant resultant paravalvular regurgitation. Abbreviations as in Figure 1.

Table 4 Procedural Outcomes

	MDCT Group (n = 133)	Control Group (n = 133)	p Value
Procedural mortality	0 (0)	0.8 (1)	0.316
In-hospital mortality	3.8 (5)	6.8 (9)	0.272
30-day mortality	5.3 (7)	6.8 (9)	0.606
Annular rupture	0.8 (1)	0.8 (1)	1.000
THV embolization	0 (0)	1.5 (2)	0.156
THV-in-THV implantation	0.8 (1)	2.3 (3)	0.314
Procedural myocardial infarction	0.8 (1)	0 (0)	0.316
Post-dilation	12.8 (17)	12.8 (17)	1.000
Permanent pacemaker implantation	8.3 (11)	9 (12)	0.827
Paravalvular regurgitation			
None	27.8 (37)	28.6 (38)	0.892
Mild	66.9 (89)	58.6 (78)	0.163
More than mild	5.3 (7)	12.8 (17)	0.032
Severe	0 (0)	4.5 (6)	0.013

Values are % (n).
THV = transcatheter heart valve; other abbreviation as in Table 2.

area oversizing is mathematically equivalent to 5% perimeter oversizing.

Intentional THV underexpansion. The sizes of most currently available THVs differ by 3-mm increments. This is more than the typical increments of surgical bioprosthesis (2 mm). For borderline aortic annulus dimensions, THV size selection may be challenging because excessive oversizing increases the risk of aortic annulus rupture (6) and coronary occlusion (7) and excessive undersizing increases the risk for PAR (2) and valve embolization (8). In vitro studies and post-implant MDCT in patients with intentionally underexpanded balloon-expandable THVs (unpublished data) have shown that current manufacturers' recommended deployment balloon fill volumes routinely result in THV inflow diameters very slightly below the stated nominal THV diameter, and reducing the volume of fluid within the deployment balloon by 10% below the nominal volume results in a reduction of the deployed inflow diameter to a value intermediate between the fully expanded THV and the next smaller THV (e.g., when a 26-mm balloon-expandable THV is deployed, reducing the balloon volume by 10% results in an inflow diameter between a 23- and 26-mm THV). We therefore developed a strategy to manage borderline cases by intentional underexpanding balloon-expandable THVs, thereby minimizing the risks associated with excessive oversizing. Our data showed that intentional underexpansion in 18 selected patients led to comparable hemodynamics and favorable clinical outcomes. However, the durability of underexpanded THVs is unknown, and this strategy may become less necessary as more THV sizes with lower diameter increments become available.

Study limitations. Randomized trials render high levels of evidence; however, choosing the appropriate THV size during TAVR should be based on all available information and not one single measurement. We therefore chose not to perform a randomized comparison of different sizing modalities but rather study the impact of implementation of an MDCT area sizing algorithm on overall outcomes. Therefore, 26 patients received THV sizes not in accordance with MDCT recommendations. Even if operators decided not to go with the recommendations, size selection may still have been influenced by the proposed valve size. This non–pre-specified subgroup is too small for valuable primary or secondary endpoint comparisons. However, expert opinion appeared effective in achieving procedural success in this subgroup.

The control group consisted of consecutive patients from all 4 centers who underwent TAVR before the MDCT area sizing recommendations were implemented. A learning effect, which may have led to improved outcomes, could be postulated. However, highly experienced operators, each having performed more than 200 cases prior to the control group, performed this trial in high-volume centers. We therefore do not think that the differences were generated by a learning curve.

Not all baseline characteristics were the same between groups. The Society of Thoracic Surgeons score was lower in the MDCT group, and the estimated glomerular filtration rate was lower in the control group. Although this discrepancy was statistically significant, the absolute difference is clinically less relevant because it is not anticipated to impact the primary endpoint of this trial.

Whereas all MDCT scans were read in a core laboratory, the TTE and TEE were read locally at the participating site. Grading of PAR may be heterogeneous across readers and sites. However, all sites contributed equal numbers of patients to both groups, which may counterbalance possible heterogeneity of echocardiography readings. Furthermore, all local site reads were performed by level 3 echocardiographers with significant experience in TAVR and graded according to standardized definitions (11).

All patients received a SAPIEN XT balloon-expandable THV. Because self-expandable and balloon-expandable THVs engage differently with the aortic annulus and leaflets, our findings and algorithm may not be suitable for self-expanding THVs. Furthermore, newer-generation devices with paravalvular sealing systems (e.g., the SAPIEN 3 [Edwards Lifesciences] or the Sadra Medical Lotus [Boston Scientific, Boston, Massachusetts]) may need less oversizing or even tolerate prudent undersizing without an increased risk of PAR (21).

Conclusions

In this prospective, multicenter, controlled trial the implementation of an MDCT annulus area sizing algorithm for TAVR reduced PAR. Three-dimensional aortic annular assessment and annular area sizing should be considered for TAVR.

Reprint requests and correspondence: Dr. Jonathon Leipsic, St. Paul's Hospital, 1081 Burrard Street, V6Z 1Y6 Vancouver, British Columbia, Canada. E-mail: jleipsic@providencehealth.bc.ca.

REFERENCES

1. Gurvitch R, Webb JG, Yuan R, et al. Aortic annulus diameter determination by multidetector computed tomography: reproducibility, applicability, and implications for transcatheter aortic valve implantation. J Am Coll Cardiol Intv 2011;4:1235–45.
2. Willson AB, Webb JG, Labounty TM, et al. 3-dimensional aortic annular assessment by multidetector computed tomography predicts moderate or severe paravalvular regurgitation after transcatheter aortic valve replacement: a multicenter retrospective analysis. J Am Coll Cardiol 2012;59:1287–94.
3. Moss RR, Ivens E, Pasupati S, et al. Role of echocardiography in percutaneous aortic valve implantation. J Am Coll Cardiol Img 2008; 1:15–24.
4. Jilaihawi H, Kashif M, Fontana G, et al. Cross-sectional computed tomographic assessment improves accuracy of aortic annular sizing for transcatheter aortic valve replacement and reduces the incidence of paravalvular aortic regurgitation. J Am Coll Cardiol 2012;59: 1275–86.
5. Willson AB, Webb JG, Freeman M, et al. Computed tomography-based sizing recommendations for transcatheter aortic valve replacement with balloon-expandable valves: comparison with transesophageal echocardiography and rationale for implementation in a prospective trial. J Cardiovasc Comput Tomogr 2012;6:406–14.
6. Blanke P, Reinohl J, Schlensak C, et al. Prosthesis oversizing in balloon-expandable transcatheter aortic valve implantation is associated with contained rupture of the aortic root. Circ Cardiovasc Interv 2012;5:540–8.
7. Gurvitch R, Tay EL, Wijesinghe N, et al. Transcatheter aortic valve implantation: lessons from the learning curve of the first 270 high-risk patients. Catheter Cardiovasc Interv 2011;78:977–84.
8. Tay EL, Gurvitch R, Wijeysinghe N, et al. Outcome of patients after transcatheter aortic valve embolization. J Am Coll Cardiol Intv 2011; 4:228–34.
9. Santos N, de Agustin JA, Almeria C, et al. Prosthesis/annulus discongruence assessed by three-dimensional transoesophageal echocardiography: a predictor of significant paravalvular aortic regurgitation after transcatheter aortic valve implantation. Eur Heart J Cardiovasc Imaging 2012;13:931–7.
10. Gripari P, Ewe SH, Fusini L, et al. Intraoperative 2D and 3D transoesophageal echocardiographic predictors of aortic regurgitation after transcatheter aortic valve implantation. Heart 2012;98:1229–36.
11. Kappetein AP, Head SJ, Genereux P, et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. J Am Coll Cardiol 2012;60:1438–54.
12. Kodali SK, Williams MR, Smith CR, et al. Two-year outcomes after transcatheter or surgical aortic-valve replacement. N Engl J Med 2012; 366:1686–95.
13. Makkar RR, Fontana GP, Jilaihawi H, et al. Transcatheter aortic-valve replacement for inoperable severe aortic stenosis. N Engl J Med 2012; 366:1696–704.
14. Altiok E, Koos R, Schroder J, et al. Comparison of two-dimensional and three-dimensional imaging techniques for measurement of aortic annulus diameters before transcatheter aortic valve implantation. Heart 2011;97:1578–84.
15. Kempfert J, Van Linden A, Lehmkuhl L, et al. Aortic annulus sizing: echocardiographic versus computed tomography derived measurements in comparison with direct surgical sizing. Eur J Cardiothorac Surg 2012;42:627–33.
16. Yano M, Nakamura K, Nagahama H, Matsuyama M, Nishimura M, Onitsuka T. Aortic annulus diameter measurement: what is the best modality? Ann Thorac Cardiovasc Surg 2012;18:115–20.
17. Hayashida K, Bouvier E, Lefevre T, et al. Impact of CT-guided valve sizing on post-procedural aortic regurgitation in transcatheter aortic valve implantation. EuroIntervention 2012;8:546–55.
18. Babaliaros VC, Junagadhwalla Z, Lerakis S, et al. Use of balloon aortic valvuloplasty to size the aortic annulus before implantation of a balloon-expandable transcatheter heart valve. J Am Coll Cardiol Intv 2010; 3:114–8.
19. Hamdan A, Guetta V, Konen E, et al. Deformation dynamics and mechanical properties of the aortic annulus by 4-dimensional computed tomography: insights into the functional anatomy of the aortic valve complex and implications for transcatheter aortic valve therapy. J Am Coll Cardiol 2012;59:119–27.
20. Blanke P, Russe M, Leipsic J, et al. Conformational pulsatile changes of the aortic annulus: impact on prosthesis sizing by computed tomography for transcatheter aortic valve replacement. J Am Coll Cardiol Intv 2012;5:984–94.
21. Binder RK, Rodés-Cabau J, Wood DA, et al. Transcatheter aortic valve replacement with the SAPIEN 3: a new balloon-expandable transcatheter heart valve. J Am Coll Cardiol Intv 2013;6:293–300.

Key Words: annulus area ■ multidetector computed tomography ■ transcatheter aortic valve replacement ■ transcatheter heart valve sizing.