

### Three-Dimensional Echocardiography for Transcatheter Aortic Valve Replacement Sizing: A Systematic Review and Meta-Analysis

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**Background**—Transcatheter aortic valve replacement (TAVR) is the standard of care for many patients with severe symptomatic aortic stenosis and relies on accurate sizing of the aortic annulus. It has been suggested that 3-dimensional transesophageal echocardiography (3D TEE) may be used instead of multidetector computed tomography (MDCT) for TAVR planning. This systematic review and meta-analysis compared 3D TEE and MDCT for pre-TAVR measurements.

*Methods and Results*—A systematic literature search was performed. The primary outcome was the correlation coefficient between 3D TEE– and MDCT-measured annular area. Secondary outcomes were correlation coefficients for mean annular diameter, annular perimeter, and left ventricular outflow tract area; interobserver and intraobserver agreements; mean differences between 3D TEE and MDCT measurements; and pooled sensitivities, specificities, and receiver operating characteristic area under curve values of 3D TEE and MDCT for discriminating post-TAVR paravalvular aortic regurgitation. A random effects model was used. Meta-regression and leave-one-out analysis for the primary outcome were performed. Nineteen studies with a total of 1599 patients were included. Correlations between 3D TEE and MDCT annular area, annular perimeter, annular diameter, and left ventricular outflow tract area measurements were strong (0.86 [95% CI, 0.80–0.90]; 0.89 [CI, 0.82–0.93]; 0.80 [CI, 0.70–0.87]; and 0.78 [CI, 0.61–0.88], respectively). Mean differences between 3D TEE and MDCT between measurements were small and nonsignificant. Interobserver and intraobserver agreement and discriminatory abilities for paravalvular aortic regurgitation were good for both 3D TEE and MDCT.

*Conclusions*—For pre-TAVR planning, 3D TEE is comparable to MDCT. In patients with renal dysfunction, 3D TEE may be potentially advantageous for TAVR measurements because of the lack of contrast exposure. (*J Am Heart Assoc.* 2019;8: e013463. DOI: 10.1161/JAHA.119.013463.)

**Key Words:** multidetector row computed tomography • transesophageal echocardiography • transfemoral aortic valve implantation

Transcatheter aortic valve replacement (TAVR) is currently the standard of care for many patients with severe symptomatic aortic stenosis. TAVR implantation relies on accurate sizing of the aortic annulus to optimize aortic valve flow dynamics while minimizing paravalvular aortic regurgitation (PVAR). Historically, efforts to measure the aortic annulus used 2-dimensional echocardiography; however, the current accepted gold standard has become multidetector computed tomography (MDCT) with the focus on area or perimeter measurements of the often eccentric annulus.<sup>1,2</sup> In recent years, several studies have shown accurate assessment of the aortic annulus with 3-dimensional transesophageal echocardiography (3D TEE). As 3D TEE does not require contrast medium, this could clinically benefit patients with impaired renal function.

In this systematic review and meta-analysis, we aim to summarize current evidence on the comparison between 3D TEE and MDCT for TAVR annular measurements.

Received May 30, 2019; accepted August 9, 2019.

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Accompanying Tables S1 through S4 and Figures S1 through S10 are available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.119.013463

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#### **Clinical Perspective**

#### What Is New?

- The main findings of this study are that 3-dimensional transesophageal echocardiography annular measurements (annular area, annular perimeter, and left ventricular outflow tract area) are strongly correlated to multidetector computed tomography measurements.
- Intraobserver and interobserver concordances for annular cross-sectional area, perimeter, and diameter were high for both techniques, with a correlation coefficient around 0.9.
- In a sensitivity analysis limited to 3 studies, multidetector computed tomography and 3-dimensional transesophageal echocardiography predicted post-transcatheter aortic valve replacement paravalular aortic regurgitation with similar accuracy.

#### What Are the Clinical Implications?

• Three-dimensional transesophageal echocardiography does not require contrast media and may potentially reduce the rate of kidney injury, which may be particularly beneficial in patients with impaired baseline renal function.

#### Methods

The authors declare that all supporting data are available within the article and its online supplementary file.

#### Search Strategy

A medical librarian performed comprehensive searches to identify randomized trials and observational studies comparing aortic valve measurements by different imaging techniques. Searches were run on September 5, 2018, in the following databases: Ovid MEDLINE (ALL; 1946 to August 10, 2018); Ovid Embase (1974 to present); and the Cochrane Library (Wiley). The search strategy included all appropriate controlled vocabulary and keywords for the interventions: "two-dimensional echocardiography," "three-dimensional echocardiography," "three-dimensional echocardiography," "three dimensional echocardiography," and "aortic valve." The full search strategy for Ovid MEDLINE is available in Table S1. To limit publication bias, there were no publication date, language, or article type restrictions on the search strategy.

#### Study Selection and Quality Assessment

Searches across the chosen databases retrieved 4960 results. After results were de-duplicated, 2 independent reviewers (I.H., M.R.) screened a total of 3835 citations. Discrepancies were resolved by the senior author (M.G.). Titles and abstracts were reviewed against predefined

Full text was pulled for the selected studies for a second round of eligibility screening. Reference lists for articles selected for inclusion in the study were also searched for relevant articles. The full Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram outlining the study selection process is available in Figure S1.<sup>3</sup> Two independent investigators (I.H., M.R.) reviewed all studies, and disagreements were resolved by the senior author (M.G.). For overlapping studies, the largest series were included.

Two investigators (I.H., F.K.) performed data extraction independently, and the extracted data were verified by a third investigator (M.R.) for accuracy. The following variables were included: study demographics (sample size, publication year, design, institution, and country) (Table 1),<sup>4–22</sup> patient demographics (age, sex, body mass index, body surface area, and comorbidities [hypertension, previous myocardial infarction, diabetes mellitus], normal aortic valve or aortic stenosis, aortic valve morphology [bicuspid or tricuspid]) (Table S2), imaging procedure–related variables, and correlations between MDCT and 3D TEE in assessing distance to the left coronary ostia (Table 2).

For the pooled receiver operating characteristic analysis on PVAR, the incidence of PVAR, sensitivity, specificity, and receiver operating characteristic area under the curve (AUC) values of: (1) absolute differences between TAVR prosthesis size and 3D TEE and MDCT annulus diameter, area, perimeter; and (2) the covering indices of 3D TEE– and MDCT-measured annular sizes in terms of nominal prosthesis sizes (diameter, area, and perimeter), as defined in the individual studies. Details of calculation of the pooled receiver operating characteristic are presented in Table S3.

The quality of the included studies was assessed using the Newcastle-Ottawa Scale for observational studies (Table S4).<sup>23</sup>

#### Measurements

The primary outcome was the correlation coefficient between 3D TEE and MDCT measurements of annular area. Secondary outcomes were the correlation coefficients between the 2 techniques for mean annular diameter, annular perimeter, left ventricular outflow tract area (LVOT-A), interobserver and intraobserver agreements, and mean differences between 3D TEE and MDCT measurements. In addition, sensitivity, specificity, and AUC value for prediction

#### Table 1. Summary of Included Studies

Study/Year	Study Period	Hospital/Country	Country	Type of Study	Total No. of Patients
Garcia-Martin/2016 <sup>4</sup>	2012-2014	Ramon y Cajal University Hospital	Spain	Retrospective	31
Guez/2017 <sup>5</sup>	2014-2015	Thomas Jefferson University	United States	Retrospective	74
Hafiz/2017 <sup>6</sup>	2012–2015	University of Massachusetts Medical School	United States	Retrospective	111
Hammerstingl/2014 <sup>7</sup>		University Hospital Bonn	Germany	Retrospective	138
Husser/2013 <sup>8</sup>	2011–2011	University of Regensburg Medical Center	Germany	Retrospective	57
Jilaihawi/2013 <sup>9</sup>		Cedars-Sinai Heart Institute	United States	Retrospective	256
Kato/2018 <sup>10</sup>	2016–2016	Tokyo Medical Dental University	Japan	Retrospective	43
Machida/2015 <sup>11</sup>	2011–2014	St. Marianna University School of Medicine	Japan	Prospective	126
Mediratta/2017 <sup>12</sup>		University of Chicago Medical Center	United States	Prospective	47
Otani/2010 <sup>13</sup>	2008–2009	University of Occupational and Environmental Health	Japan	Retrospective	35
Prihadi/2018 <sup>14</sup>		Leiden University Medical Centre	Netherlands	Retrospective	150
Stahli/2014 <sup>15</sup>	2008–2012	University Hospital Zurich	Switzerland	Retrospective	39
Tamborini/2012 <sup>16</sup>	2008–2011	Centro Cardiologico Monzino	Italy	Retrospective	119
Pinto Teixeira/2017 <sup>17</sup>	2014-2015	Hospital de Santa Marta	Portugal	Prospective	60
Vaquerizo/2016 <sup>18</sup>	2013-2014	McGill University Health Center	Canada	Prospective	50
Wu/2014 <sup>19</sup>		University of Occupational and Environmental Health	Japan	Retrospective	40
Ng/2010 <sup>20</sup>		Leiden University Medical Center	Netherlands	Retrospective	53
Khalique/2014 <sup>21</sup>	2011–2013	Columbia University Medical Center/New York Presbyterian Hospital	United States	Retrospective	100
Wiley/2016 <sup>22</sup>	2012–2014	Mount Sinai Medical Center	United States	Retrospective	70

of post-TAVR PVAR were calculated from the studies reporting this information.

#### **Data and Statistical Analyses**

The correlation coefficients between 3D TEE and MDCT measurements from each study were used as effect sizes and transformed using Fisher *z*. Summary estimates were then reconverted to correlations that were reported as correlation coefficient (*r*) and 95% Cls, while mean differences were pooled and reported as mean difference and 95% Cls using DerSimonian Laird (inverse variance) method and DerSimonian-Laird estimator for tau<sup>2</sup>.<sup>24,25</sup> Random and fixed effect models were used. The Cochran Q statistic and the  $l^2$  test were used to assess studies' heterogeneity.<sup>26</sup> Leave-one-out sensitivity analysis was performed for the primary outcome. Funnel plot and Egger's regression test were used to assess for potential publication bias (Figures S2 and S3).

Correlation coefficient (*r*) values between 0.7 and 1.0 (-0.7 and -1.0) were considered as indicating a strong positive (negative) correlation.

Meta-regression was used to explore the effects of age, sex, body mass index, body surface area, left ventricular ejection fraction, mean transaortic gradient, and baseline aortic valve area on the primary outcome using the DerSimonian-Laird method.

Pooled sensitivity and specificity with corresponding 95% CIs and pooled receiver operating characteristic for PVAR were estimated using a random effects model (DerSimonian-Laird method).

Statistical analyses were performed using "meta" and "metafor" packages<sup>27,28</sup> in R (version 3.3.3 R Project for Statistical Computing) within RStudio (0.99.489, http://www. rstudio.com) and Meta-DiSc software (version 1.4).

#### Results

#### Search, Study Selection, and Quality Assessment

A total of 3835 studies were retrieved, of which  $19^{4-22}$  met the inclusion criteria and were included in the final analysis.

Seven studies originated from the United States and Canada, 10 from Europe, and 2 from Japan. Overall, 1599 patients were included. The number of patients in the individual studies ranged from 31 to 256. The mean age ranged from 70 to 88 years. Men ranged from 22% to 63%, and mean body mass index and body surface area ranged from 25.4 to 27.0 kg/m<sup>2</sup> and 1.45 to 1.84 m<sup>2</sup>, respectively. Implanted TAVR size was determined by MDCT in 6 studies,

Table 2. Summary of Imaging Variables of the Included Studies

Baseline Echo- Measured AVA of Patients Pre-TAVR (SD), cm <sup>2</sup>	0.7 (0.2)	:	0.71 (0.19)	0.7 (0.2)	0.67 (0.22)	:	0.58 (0.12)	0.79 (0.22)	0.8 (0.2)	1.1 (0.4)	0.8 (0.3)		0.65 (0.16)	0.62 (0.20)	:	:	:
Baseline Echo-Measured Mean TAG (SD), m/s	46.3 (16)	:	43.33 (16.44)	42.7 (16.8)	50 (16)	:	47.0 (16.8)	34 (19)	40 (13)	38 (20)	43.5 (19.6)	41 (2.3)	52 (15)	49.4 (14.4)	:	:	:
Correlation (r) Between MDCT and 3D TEE in Assessing Distance to Left Coronary Ostia	N	N	N	NR	N	N	NR	N	N	0.89	NR	NR	0.83	NR	N	0.71	N
LVEF (SD)	58.2 (11)	÷	52.29 (13.57)	50.5 (14.8)	÷	÷	58.3 (10.2)	60 (13)	57 (16)	÷	50.0 (11.8)	56 (2)	58 (12)	59.8 (13.9)	56.2 (13.1)	49 (11)	61.1 (27.7)
Imaging Modality Used for TAVR Sizing	3D TEE and MDCT	MDCT	MDCT	3D TEE and MDCT	3D TEE and MDCT	3D TEE and MDCT	MDCT	NR	3D TEE and MDCT	MDCT	MDCT	NR	3D TEE and MDCT	NR	MDCT	3D TEE and MDCT	3D TEE and MDCT
Software for 3D Data Set Analysis	Philips Q-Lab	Philips Q-Lab	Philips Q-Lab	:	Philips Q-Lab	Philips Q-Lab	ACUSON SC2000 PRIME (Siemens Medical)	Philips Q-Lab	Philips Q-Lab	Philips Q-Lab	iE33 and EPIQ7 (Philips Medical)	Philips Q-Lab	Philips Q-Lab	Philips Q-Lab		X7-2t (Philips)	Philips Q-Lab
Measurement Phase	Systole	Systole	Systole	:	Systole	Systole	Systole	Systole	Systole	Systole	Systole	Systole	Systole	Systole	Systole	Systole	Systole
3D TEE Technique (Axis)	Automatic (long-axis)	Manual (long-axis)	Manual (long-axis)	:	Manual (long-axis)	Manual (long-axis)	Manual (long-axis)	Manual (long-axis)	Manual (long-axis)	Manual (long-axis)	Automatic (long-axis)	Manual (long-axis)	Manual (long-axis)	Manual (long-axis)	Manual (long-axis)	Manual (long-axis)	Manual (long-axis)
MDCT Technique	Manual (coronal and sagittal)	Manual (3-point measurement)	Manual (muttiplanar reformations)	:	Manual (coronal and sagittal)	Manual (coronal and sagittal)	Manual (coronal and sagittal)	Manual (coronal and sagittal)	Manual (coronal and sagittal)	Manual (coronal and sagittal)	Manual (coronal and sagittal)	Manual (coronal and sagittal)	Manual	Manual	Manual (coronal and sagittal)	Manual (coronal and sagittal)	Manual (coronal and sagittal)
Study/Year	Garcia-Martin/2016 <sup>4</sup>	Guez/2017 <sup>5</sup>	Hafiz/2017 <sup>6</sup>	Hammerstingl/2014 <sup>7</sup>	Husser/2013 <sup>8</sup>	Jilaihawi/2013 <sup>9</sup>	Kato/2018 <sup>10</sup>	Machida/2015 <sup>11</sup>	Mediratta/2017 <sup>12</sup>	0tani/2010 <sup>13</sup>	Prihadi/2018 <sup>14</sup>	Stahli/2014 <sup>15</sup>	Tamborini/2012 <sup>16</sup>	Pinto Teixeira/2017 <sup>17</sup>	Vaquerizo/2016 <sup>18</sup>	Wu/2014 <sup>19</sup>	Ng AC/2010 <sup>20</sup>

Continued

							(T)		
							Correlation (7) Between MDCT and 3D TFF in		
							Assessing		Baseline Echo-
							Distance	Baseline	Measured
							to Left	Echo-Measured	AVA of Patients
			Measurement	Software for 3D	Imaging Modality		Coronary	Mean TAG	Pre-TAVR (SD),
Study/Year	MDCT Technique	3D TEE Technique (Axis)	Phase	Data Set Analysis	Used for TAVR Sizing	LVEF (SD)	Ostia	(SD), m/s	cm <sup>2</sup>
Khalique/2014 <sup>21</sup>	Manual	Semiautomated	Systole	Philips Q-Lab	3D TEE and MDCT	:	NR	4.1 (0.76)	0.67 (0.17)
		(long-axis)							
Wiley/2016 <sup>22</sup>	Manual	:	:	Philips Q-Lab	3D TEE and MDCT	58.2 (11)	NR	46.3 (16)	0.7 (0.2)
3D indicates 3-dimensional	.: AVA. aortic valve area; LV	'EF, left ventricular ejection fr.	action: MDCT, mu	Iltidetector row computed	tomography; NR, not repo	rted; TAG, transaort	ic gradient: TAVR, tr	anscatheter aortic v	alve replacement: TEE.

transesophageal echocardiography

by both 3D TEE and MDCT in 10 studies, while 3 studies did not report this information. Correlations between 3D TEE and MDCT in assessing distance to the left main coronary ostia were reported by 3 studies and were generally high (Table 2). Description of the included studies and imaging modalities are presented in Tables 1and 2 and Table S3. The mean and SDs of 3D TEE– and MDCT-derived measures for annular area, annular diameter, annular perimeter, and LVOT-A are shown in Figure S4. The number of studies and patients analyzed for the primary and secondary outcomes are presented in Table 3. The assessment of the quality of the individual studies is reported in Table S4.

#### **Meta-Analysis**

The overall heterogeneity and results for pooled correlations, mean differences, and intraobserver and interobserver agreements are summarized in Table 3.

The correlations between 3D TEE and MDCT annular area, annular perimeter, annular diameter, and LVOT-A measurements were strong (0.86 [Cl, 0.80–0.90]; 0.89 [Cl, 0.82–0.93]; 0.80 [Cl, 0.70–0.87]; and 0.78 [Cl, 0.61–0.88], respectively) (Figure S5).

The mean differences between 3D TEE and MDCT for annular area, annular perimeter, and mean annular diameter measurements were small and not statistically different ( $-0.12 \text{ cm}^2$  [CI, -0.24 to 0.00], -0.02 cm [CI, -0.65 to 0.61], and -0.03 cm [CI, -0.15 to 0.10]). The mean difference between 3D TEE and MDCT for LVOT-A was  $-0.40 \text{ cm}^2$  [CI, -1.05 to 0.26] (Figure S6).

The pooled intraobserver agreements for:

- 1. Annular area in 3D TEE and MDCT were 0.94 (Cl, 0.90– 0.97) and 0.96 (Cl, 0.91–0.98), respectively.
- 2. Annular perimeter in 3D TEE and MDCT were 0.95 (Cl, 0.94–0.96) and 0.94 (Cl, 0.58–0.99), respectively.
- 3. Annular diameter in 3D TEE was 0.94 (Cl, 0.90–0.96) (Figure S7).

The pooled interobserver agreements for:

- 1. Annular area in 3D TEE was 0.92 (Cl, 0.88-0.95).
- 2. Annular perimeter in 3D TEE was 0.94 (Cl, 0.87-0.97).
- 3. Annular diameter in 3D TEE was 0.92 (Cl, 0.88-0.94).
- 4. Annular perimeter in MDCT was 0.88 (Cl, 0.52–0.97) (Figure S8).

On meta-regression, mean body mass index, body surface area, and transaortic gradient were associated with lower correlations between 3D TEE and MDCT annular area measurement (Table 4).

The pooled sensitivities, specificities, and receiver operating characteristic of 3D TEE and MDCT included 3 studies and

#### Table 3. Outcomes Summary

			Random Effects Model			Fixed Effect Model		
Outcome	No. of Patients	No. of Studies	Effect Estimate (95% CI)	Heterogeneity, I <sup>2</sup> (P Value)	Tau <sup>2</sup>	Effect Estimate (95% CI)	Heterogeneity I <sup>2</sup> (P Value)	Tau <sup>2</sup>
Correlation (3D TEE and MDCT)	)							
Annular area	1321	15	<i>⊧</i> =0.86 (0.80–0.90)	92.0% ( <i>P</i> <0.001)	0.1399	<i>⊧</i> =0.86 (0.80–0.90)	92.0% ( <i>P</i> <0.001)	0.1399
Annular perimeter	378	5	<i>⊧</i> =0.89 (0.82–0.93)	82.1% ( <i>P</i> =0.001)	0.0676	<i>r</i> =0.90 (0.88−0.92)	82.1% ( <i>P</i> =0.001)	0.0676
Annular diameter	1093	12	<i>r</i> ≡0.80 (0.70–0.87)	91.9% ( <i>P</i> <0.001)	0.1347	<i>⊧</i> =0.78 (0.76–0.81)	91.9% ( <i>P</i> <0.001)	0.1347
LVOT-A	99	2	≠=0.78 (0.61–0.88)	60.8% ( <i>P</i> =0.11)	0.0352	<i>⊧</i> =0.78 (0.69–0.85)	60.8% ( <i>P</i> =0.11)	0.0352
Mean difference between 3D T	EE and MD	CT						
Annular area, cm <sup>2</sup>	681	9	MD=-0.12 (-0.24 to 0.00)	0.0% ( <i>P</i> =0.64)	0	MD=-0.12 (-0.24 to 0.00)	0.0% ( <i>P</i> =0.64)	0
Annular perimeter, cm	243	3	MD=-0.02 (-0.65 to 0.61)	49.4% ( <i>P</i> =0.14)	0.1536	MD=0.04 (-0.40 to 0.47)	49.4% ( <i>P</i> =0.14)	0.1536
Annular diameter, cm	357	4	MD=-0.03 (-0.15 to 0.10)	0.0% ( <i>P</i> =0.95)	0	MD=-0.03 (-0.15 to 0.10)	0.0% ( <i>P</i> =0.94)	0
LVOT-A, cm <sup>2</sup>	92	2	MD=-0.40 (-1.05 to 0.26)	0.0% ( <i>P</i> =0.88)	0	MD=-0.40 (-1.05 to 0.26)	0.0% ( <i>P</i> =0.88)	0
Intraobserver agreement						-		
Annular area (MDCT)	428	6	/=0.96 (0.91−0.98)	92.3% ( <i>P</i> <0.001)	0.1846	<i>r</i> =0.96 (0.95−0.97)	92.3% ( <i>P</i> <0.001)	0.1846
Annular area (3D TEE)	691	9	<i>⊧</i> =0.94 (0.90–0.97)	92.3% ( <i>P</i> <0.001)	0.1682	<i>r</i> =0.95 (0.94−0.96)	92.3% ( <i>P</i> <0.001)	0.1682
Annular perimeter (MDCT)	185	2	<i>r</i> ≡0.94 (0.58–0.99)	97.6% ( <i>P</i> <0.001)	0.6003	<i>r</i> =0.96 (0.95−0.97)	97.6% ( <i>P</i> <0.001)	0.6003
Annular perimeter (3D TEE)	288	2	<i>r</i> ≡0.95 (0.94–0.96)	0.0% ( <i>P</i> =1.00)	0	<i>r</i> =0.95 (0.94−0.96)	0.0% ( <i>P</i> =1.00)	0
Annular diameter (3D TEE)	288	2	<i>r</i> =0.94 (0.90−0.96)	75.9% ( <i>P</i> =0.04)	0.0224	<i>r</i> =0.94 (0.92−0.95)	75.9% ( <i>P</i> =0.04)	0.0224
Interobserver agreement								
Annular area (3D TEE)	582	8	<i>r</i> =0.92 (0.88−0.95)	85.3% ( <i>P</i> <0.001)	0.0875	<i>r</i> =0.92 (0.91−0.93)	85.3% ( <i>P</i> <0.001)	0.0875
Annular perimeter (MDCT)	185	2	<i>r</i> =0.88 (0.52–0.97)	95.1% ( <i>P</i> =0.001)	0.2951	<i>⊧</i> =0.91 (0.88–0.93)	95.1% ( <i>P</i> =0.001)	0.2951
Annular perimeter (3D TEE)	288	2	<i>r</i> =0.94 (0.87–0.97)	91.9% ( <i>P</i> =0.001)	0.0804	<i>r</i> =0.94 (0.93–0.95)	91.9% ( <i>P</i> =0.001)	0.0804
Annular diameter (3D TEE)	419	4	<i>r</i> =0.92 (0.88−0.94)	72.4% ( <i>P</i> =0.01)	0.0277	<i>r</i> =0.91 (0.90−0.93)	72.4% ( <i>P</i> =0.01)	0.0277

3D indicates 3-dimensional; LVOT-A, left ventricular outflow tract area; MD, mean difference; MDCT, multidetector row computed tomography contrast angiography; r, correlation coefficient; TEE transesophageal echocardiography.

are presented in Table 5. Discriminatory abilities for PVAR were good for both 3D TEE (annular area cover index AUC 0.83, standard error [SE] 0.04 and annular perimeter cover index AUC 0.93, SE 0.06; mean difference between prosthetic valve and 3D TEE–measured diameter AUC 0.63, SE 0.10) and MDCT (annular area cover index AUC 0.89, SE 0.03 and annular perimeter cover index AUC 0.93, SE 0.04; mean difference between prosthetic valve and MDCT-measured diameter AUC 0.75, SE 0.13, respectively) (Figure and Figures S9 and S10).

#### Discussion

Evaluation of aortic root anatomy has undergone significant evolution since the early days of TAVR. Minor axis assessment

via 2-dimensional echocardiography was the sole modality used to measure aortic annulus for sizing in early trials. These measurements often correlated loosely with true annular dimensions.<sup>29</sup> Not surprisingly, PVAR rates were high and many of these were more than mild in nature.<sup>30</sup>

The introduction of MDCT imaging developed the ability to accurately assess annular dimensions. Significant data were also gained on root anatomy including coronary heights and sinus of Valsalva and sinotubular junction diameters.<sup>31</sup> With this additional data in hand, it became possible to plan for and prevent many potential root complications such as coronary obstruction and root rupture. Guidelines were developed for valve selection based on annular perimeters and areas.<sup>32</sup> As MDCT was included as a mandatory part of the evaluation of patients for entry into TAVR clinical trials, the contrast requirements were not of major concern as patients with

Table 4.Meta-Regression of Patient and Imaging Variableson the Primary Outcome of Correlation Between 3D TEE andMDCT Annular Area Measurement

Variable	No. of Studies	β±SD* ( <i>P</i> Value)
Age	13	0.00090±0.022 ( <i>P</i> =0.98)
Male sex	13	-0.0075±0.0065 ( <i>P</i> =0.24)
Body mass index	4 <sup>†</sup>	−2.78±0.82 ( <i>P</i> <0.001) <sup>†</sup>
Body surface area	3 <sup>†</sup>	−2.55±0.68 ( <i>P</i> <0.001) <sup>†</sup>
Left ventricular ejection fraction	9	-0.040±0.029 ( <i>P</i> =0.16)
Transaortic gradient	10 <sup>†</sup>	−0.036±0.013 ( <i>P</i> <0.01) <sup>†</sup>
Aortic valve area	10	0.61±0.94 ( <i>P</i> =0.52)

3D indicates 3-dimensional; MDCT, multidetector row computed tomography contrast angiography; TEE, transesophageal echocardiography.

\*Positive  $\beta$  implies stronger correlation with increase in the explored variable while negative  $\beta$  implies weaker correlation with increase in the explored variable. ^P-value significant.

significant renal insufficiency were excluded from participation by trial guidelines.<sup>33</sup>

As the technology gained commercial approval, the realworld experience began to include patients with significantly impaired renal function. In this setting, 3D TEE was introduced as an alternative to standard MDCT evaluation. As all manufacturer-provided sizing tables are based on MDCT measurements, an assumption was made that 3D TEE measurements could correlate closely with those obtained by MDCT. This study is the most comprehensive attempt to validate this assumption.

The main findings of this study are that: (1) 3D TEE annular measurements (annular area, annular perimeter, and LVOT-A are strongly correlated with MDCT measurements; (2) intraobserver and interobserver concordance for annular cross-sectional area, perimeter, and diameter was high for both techniques, with a correlation coefficient around 0.9; (3) in a sensitivity analysis limited to 3 studies,<sup>13,15,27</sup> MDCT and 3D TEE predicted post-TAVR PVAR with similar accuracy.

There has been only one previous attempt to systematically compare 3D TEE and MDCT for TAVR sizing.<sup>34</sup> In a metaanalysis of 13 studies and 1228 patients, Elkaryoni and colleagues<sup>34</sup> described a high correlation between the 2 techniques for annular area, the only outcome that was investigated. However, the authors focused on a single measurement and did not evaluate correlation in terms of other important variables usually considered when planning TAVR.

Our study expands on the previous finding to include aortic annular perimeter and LVOT-A measurements, which are important for TAVR preparation. Additionally, we compared both modalities in terms of prediction of post-valve deployment PVAR and evaluated interobserver and intraobserver agreement for both techniques.

There are modality-specific reasons for differences in annular measurements between 3D TEE and MDCT. Due to different imaging techniques, the cross-sectional plane chosen for annular measurements may be different. This may also explain the relatively large difference of 0.40 cm<sup>2</sup> in LVOT-A between 3D TEE and MDCT, where the location of the LVOT-A cross-sectional area measured by both modalities may not be consistent. Also, because of the differences in temporal resolution and appearance of calcifications, the image analysis may have been performed at different points in the cardiac cycle, as well as have different errors introduced by calcification.<sup>35</sup>

There are also modality-specific strengths specific to 3D TEE and MDCT. Three-dimensional TEE can provide real-time intraoperative guidance, assess and aid in the decision-making process for PVAR, and diagnose intraoperative complications such as annular rupture or coronary occlusion. If MDCT measurements are imprecise or fall in between 2 valve sizes (a common occurrence), 3D TEE may be used to add key information for sizing. MDCT instead is key in providing information on vascular access, coronary height, aortic valve, and LVOT-A calcifications. Although 3D TEE is not primarily used for coronary height, there was good correlation for left coronary height with MDCT (Table 2).

Table 5. Diagnostic Performance of 3D TEE and MDCT in Discriminating Post-TAVR PVAR

Parameter	Imaging Modality	Pooled Sensitivity (95% CI)	Pooled Specificity (95% CI)	Pooled ROC (AUC, SE)
$\Delta$ Mean annular diameter	MDCT	0.83 (0.73–0.90)	0.63 (0.58–0.68)	0.75 (0.13)
	3D TEE	0.80 (0.70–0.87)	0.54 (0.49–0.59)	0.63 (0.10)
Cover index area	MDCT	0.81 (0.71–0.88)	0.78 (0.74–0.82)	0.89 (0.03)
	3D TEE	0.73 (0.62–0.82)	0.67 (0.62–0.71)	0.83 (0.04)
Cover index perimeter	MDCT	0.81 (0.71–0.88)	0.75 (0.70–0.79)	0.93 (0.04)
	3D TEE	0.73 (0.62–0.82)	0.64 (0.59–0.69)	0.93 (0.06)

Δ Indicates the difference between prosthetic valve and measured size; 3D, 3-dimensional; AUC, area under curve; MDCT, multidetector row computed tomography; PVAR, paravalvular aortic regurgitation; ROC, receiver operating characteristic curve; SE, standard error; TAVR, transcatheter aortic valve replacement; TEE, transesophageal echocardiography.



**Figure.** Pooled receiver operating characteristic curves of (**A**) 3-dimensional transesophageal echocardiography (3D TEE) and (**B**) multidetector row computer tomography (MDCT) annular area covering index for predicting paravalvular aortic regurgitation (PVAR). The red circles of different diameters represent different studies. Their true positive rates (sensitivity) and false positive rates (1-specificity) for determining PVAR can be traced to the *y*- and *x*-axes, respectively. Both 3D TEE and MDCT annular area cover indices are good in predicting PVAR (area under curve [AUC] 0.8268, standard error [SE] 0.0371; and AUC 0.8914, SE 0.337, respectively).

Recent studies have shown that 3D TEE may underestimate annulus cross-sectional area by  $\approx 10\%$  compared with MDCT.<sup>9,20,35</sup> Our data confirm that 3D TEE measurements are on average smaller than corresponding MDCT measurements for annular area, diameter, and perimeter measurements. However, the mean differences (-0.12 cm<sup>2</sup> [Cl, -0.24 to 0.00] and -0.02 cm [Cl, -0.65 to 0.61], respectively) may be irrelevant for TAVR planning purposes and are not statistically significant.

The clinical relevance may be inferred from whether this difference resulted in a different valve size, and possible undersizing, of the implanted valve, which may lead to increased risk of PVAR. A subset of 4 studies (Husser, Kato, Prihadi, Vaquerizo) analyzed transcatheter valve sizing agreement between 3D TEE and MDCT with considerable heterogeneity and varying results. Husser et al<sup>8</sup> found that 3D TEE predicted final valve size in 84% of patients, while MDCT predicted 79%, with a 77% agreement between both modalities. Kato et al<sup>10</sup> found that semiautomated 3D TEE measurements showed 77% agreement with final prosthesis implanted. Prihadi et al<sup>14</sup> did not compare the 2 modalities to size of prosthesis implanted but found that there was 93.3% agreement in valve size between 3D TEE and MDCT. Finally, Vaquerizo et al<sup>18</sup> found that there was only 38% agreement between MDCT and 3D TEE for valve size with up to 50% of patients measured by 3D TEE as having a hypothetical inappropriate valve size according to manufacturer-recommended sizing algorithms (based on MDCT). Future studies including the incidence of PVAR and agreement in valve sizing may offer clinical information to the correlations found in this study.

The incidence of MDCT contrast-related kidney injury in patients evaluated for TAVR range from 7% to 10.5%.<sup>36</sup> Threedimensional TEE does not require contrast media and may potentially reduce the rate of kidney injury, which may be particularly beneficial in patients with impaired baseline renal function. Analysis of the Society of Thoracic Surgery/American College of Cardiology Transcatheter Valve Therapy Registry shows that among the overall population of 44 778 TAVR candidates, there were 19 266 (43.03%) patients with stage 3 chronic kidney disease, 2413 (5.39%) with stage 4 chronic kidney disease, and 206 (0.46%) with stage 5 chronic kidney disease, suggesting that 3D TEE may be more appropriate than MDCT for TAVR measurements in a significant proportion of the current TAVR population.

While 3D TEE can substantially reduce contrast load requirements with MDCT, it does not address the issue of access and evaluation therein. With the elimination of MDCT evaluation of the aortic root, patients may have isolated iliofemoral computed tomography angiography with a substantially reduced contrast load. Alternatively, a noncontrast study can provide adequate measurements as well.

#### **Study Limitations**

Our study has several important limitations that must be acknowledged. Statistical heterogeneity ( $l^2$ ) was high for most outcomes. However, this is to be expected in meta-analyses evaluating continuous outcomes where traditional interpretations of heterogeneity may not be appropriate.<sup>37</sup> A few studies used automated software for calculation of annular

area, but most used manual tracing techniques, which are more likely operator dependent. However, we found little interobserver variability between studies, so this effect was likely minimal. Additionally, some heterogeneity between studies may be attributable to varying numbers of bicuspid and tricuspid valves included, although only one study mentioned bicuspid valves and we assumed that the other studies were performed in patients with tricuspid valves.

#### Conclusions

The present data suggest that 3D TEE is comparable to MDCT for TAVR planning. As 3D TEE does not require the use of contrast media, it may be advantageous in patients with preexisting renal dysfunction. Since the first TAVR performed in 2002, TAVR has transitioned from a novel procedure to standard of care for many patients with aortic stenosis. Early on, procedural safeguards such as general anesthesia and intraprocedural TEE were recommended.<sup>38</sup> As TAVR has become increasingly safer with fewer complications, many programs are taking a minimalist approach including percutaneous transfemoral vascular access, sedation without general anesthesia, lack of intraprocedural TEE guidance, and early discharge protocols. This has not been shown to have improved outcomes, however, and some studies show that there is an increased incidence of PVAR from this approach. In the future, there may be a role for 3D TEE in patients presenting for TAVR with renal dysfunction, patients with indeterminate valve sizing with MDCT, and patients with complex anatomy at high risk for PVAR.

#### Sources of Funding

Rong is supported in part by the Foundation for Anesthesia Research and Education Training Grant (FAER MTRG-CT-08-15-2018-Rong)—significant. Wijeysundera reports research funding from Edwards Lifesciences and Medtronic—significant. Fremes is supported in part by the Bernard S. Goldman Chair in Cardiovascular Research—significant.

#### **Disclosures**

Angiolillo reports receiving payments as an individual for: consulting fee or honorarium from Amgen, Aralez, AstraZeneca, Bayer, Biosensors, Boehringer Ingelheim, Bristol-Myers Squibb, Chiesi, Daiichi-Sankyo, Eli Lilly, Haemonetics, Janssen, Merck, PLx Pharma, Pfizer, Sanofi, and The Medicines Company; participation in review activities from CeloNova and St. Jude Medical; institutional payments for grants from Amgen, AstraZeneca, Bayer, Biosensors, CeloNova, CSL Behring, Daiichi-Sankyo, Eisai, Eli-Lilly, Gilead, Janssen, Matsutani Chemical Industry Co., Merck, Novartis, Osprey Medical, and Renal Guard Solutions—modest. Salemi reports being a clinical proctor for Medtronic and Edwards Lifesciences. The remaining authors have no disclosures to report.

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# SUPPLEMENTAL MATERIAL

#### Table S1. Ovid MEDLINE search strategy.

#### Ovid MEDLINE® ALL - 1946 to September 04, 2018

Searched on September 5, 2018

No language, article type, or publication date restrictions

#### Line # | Search term

- 1 Echocardiography/ or Echocardiography, Doppler/ or Echocardiography, Doppler, Color/ or Echocardiography, Doppler, Pulsed/ or Echocardiography, Stress/ or Echocardiography, Transesophageal/
- 2 ((2D or 2-D or 2 dimensional or two dimensional) adj3 (echocardiography or echocardiographic or echocardiographies or cardiac echography or cardiac scanning or cardial echography or cardioechography or echo cardiogram or echo cardiography or heart echo sounding or echocardiogram or heart echography or heart scanning or myocardium scanning or ultrasound cardiography)).tw.
- 3 1 or 2
- 4 Echocardiography, Three-Dimensional/
- 5 (((3D or 3-D or 3 dimensional or three dimensional) adj3 (echocardiography or echocardiographic or echocardiographies or cardiac echography or cardiac scanning or cardial echography or cardioechography or echo cardiogram or echo cardiography or heart echo sounding or echocardiogram or heart echography or heart scanning or myocardium scanning or ultrasound cardiography)) or (planimetry or ellipse or biplane)).tw.
- 6 4 or 5
- 7 Multidetector Computed Tomography/
- 8 (MDCT or MSCT or multidetector computed tomography or multi-detector computed tomography or multidetector computer assisted tomography or multi-detector computer assisted tomography or multidetector helical computed tomography or multi-detector helical computed tomography or multidetector spiral computed tomography or multi-detector spiral computed tomography or multisection computed tomography or multi-section computed tomography or multislice computed tomography or multi-slice computed tomography or multislice helical computed tomography or multislice helical computed tomography or multislice spiral computed tomography or multi-slice spiral computed tomography or multidetector-row computed tomography or multi-detector row computed tomography).tw.
- 9 (multidetector CT or multi-detector CT or multi-detector helical CT or multidetector helical CT or multidetector spiral CT or multi-detector spiral CT or multisection CT or multi-section CT or multislice CT or multi-slice CT or multislice helical CT or multi-slice helical CT or multislice spiral CT or multi-slice spiral CT or multidetector-row CT or multi-detector row CT).tw.

- 10 or/7-9
- 11 Aortic Valve/ or Aortic Valve Stenosis/ or Transcatheter Aortic Valve Replacement/ or Ventricular Outflow Obstruction/
- 12 (aorta or aortic or valva aortae or TAVR or left ventricular outflow or LVOT or left cardiac ventricle outflow or left heart ventricle outflow or left outflow tract).tw.
- 13 11 or 12
- 14 3 and 6 and 13
- 15 3 and 10 and 13
- 16 6 and 10 and 13
- 17 14 or 15 or 16

Table S2. Demographics of included patients.

Study/Year	Age (Mean±SD)	Male (%)	Body mass index (kg/m²) (Mean±SD)	Body surface area (m²) (Mean±SD)	Normal aortic valve or aortic stenosis	Aortic valve type- Bicuspid or Tricuspid	Hypertension (%)	Previous myocardial infarction (%)	Diabetes (%)
Garcia-Martin/2016 <sup>1</sup>	84	22	NR	NR	AS	NR	100	NR	22.6
Guez/2017 <sup>2</sup>	84	50	NR	NR	AS	NR	NR	NR	NR
Hafiz/2017 <sup>3</sup>	85±7	55	26.89±5.01	NR	AS	NR	91.9	5.4	25.2
Hammerstingl/2014 <sup>4</sup>	81±6	52	NR	NR	AS	NR	NR	13.8	NR
Husser/2013 <sup>5</sup>	79±6	42	27.0±5	NR	AS	NR	67	5	32
Jilaihawi/2013 <sup>6</sup>	NR	NR	NR	NR	AS	NR	NR	NR	NR
Kato/2018 <sup>7</sup>	84±5	37	NR	1.45±0.18	AS	NR	81	NR	9
Machida/2015 <sup>8</sup>	74±10	59	NR	NR	AS	bicuspid and tricuspid	57	NR	35
Mediratta/2017 <sup>9</sup>	81±8	47	NR	NR	AS	NR	NR	NR	NR
Otani/2010 <sup>10</sup>	71±10	NR	NR	NR	Both normal and AS	NR	NR	NR	NR
Prihadi/2017 <sup>11</sup>	81±7	49	26.7±5.5	NR	AS	NR	NR	NR	NR
Stahli/2014 12	82±1	54	25.4±0.7	1.79±0.03	AS	NR	80	NR	15
Tamborini/2012 <sup>13</sup>	81±7	49	NR	1.70±0.2	AS	NR	NR	NR	NR
Teixeira/2017 <sup>14</sup>	82±5	46	NR	NR	AS	NR	NR	NR	NR
Vaquerizo/2016 <sup>15</sup>	83±7	60	26.9±4.3	NR	AS	NR	NR	NR	NR
Wu/2014 <sup>16</sup>	70±13	63	NR	1.53±0.19	Both normal and AS	NR	NR	NR	NR
Ng AC/2010 17	80±8	53	NR	1.84±0.2	AS	NR	NR	NR	NR
Khalique/2014 <sup>18</sup>	88±8	45	NR	NR	AS	NR	NR	NR	NR
Wiley/2016 19	NR	NR	NR	NR	AS	NR	NR	NR	NR

AS- aortic stenosis

NR- not reported

Table S3. Details of calculation of pooled receiver operating characteristic (PROC) on para-valvular aortic regurgitation. The table shows the raw data used to PROC curves.

Cover index	perimeter (usi	ing MDCT)			
Study	TP	FP	FN	TN	Total
Khalique 2014 <sup>18</sup>	39	21	11	29	100
Jilaihawi 2013 <sup>6</sup>	22	57	4	173	256
Hammerstingl 2014 <sup>4</sup>	10	24	2	102	138

Hammerstingl 2014 reported sensitivity of 80% and specificity of 81.2%, PVAR incidence of 12/138 (7.2%) (consequently, patients with no incidence of PVAR constituted 126 of 138 patients.

True positive (TP) = (Sensitivity \* PVAR occurrence)/100 = (80 \* 12)/100=10

True negative (TN) = (Specificity\* Non-PVAR occurrence)/100 = (81.2\* 126)/100=102

False positive (FP) = Non-PVAR occurrence -TN = 126-102=24

False negative (FN) = PVAR occurrence - TP = 12 - 10 = 2

Table S4. Summary of critical appraisal of included observational studies using the Newcastle-Ottawa Quality Assessment Scale for Cohort Studies.

Author/ Year	Selection	Comparability	Outcome
Garcia-Martin/2016 <sup>1</sup>	****	*	***
Guez/2017 <sup>2</sup>	***	*	***
Hafiz/2017 <sup>3</sup>	****	*	***
Hammerstingl/2014 <sup>4</sup>	****	*	***
Husser/2013 <sup>5</sup>	****	*	***
Jilaihawi/2013 <sup>6</sup>	***	*	***
Kato/2018 <sup>7</sup>	****	*	***
Machida/2015 <sup>8</sup>	* * * *	*	NA
Mediratta/2017 <sup>9</sup>	****	*	***
Otani/2010 10	* * * *	*	* * *
Prihadi/2017 <sup>11</sup>	****	*	***
Stahli/2014 12	* * * *	*	* * *
Tamborini/2012 <sup>13</sup>	***	*	***
Teixeira/2017 <sup>14</sup>	***	*	***
Vaquerizo/2016 <sup>15</sup>	****	*	***
Wu/2014 <sup>16</sup>	****	*	* * *
Ng AC/2010 <sup>17</sup>	****	*	***
Khalique/2014 <sup>18</sup>	***	*	***
Wiley/2016 19	***	*	***

#### Selection

1) Representativeness of intervention cohort- a) truly representative of the average in the community \*; b) somewhat representative of the average \*; c) only selected group of users; d) no description of the derivation of the cohort.

2) Selection of non-intervention cohort – a) drawn from same community as intervention cohort\*; b) drawn from a different source; c) no description of the derivation of the non-exposed cohort.

3) Ascertainment of exposure- a) secure record\*; b) structured interview\*; c) written self-report; d) no description.

4) Demonstration that outcome of interest was not present at start of study- a) yes\*; b) no.

#### Comparability

1) Comparability of cohorts on the basis of the design or analysis- a) study controls for age, and sex\*; b) study controls for any additional factor\*.

#### Outcome

1) Assessment of outcome- a) independent blind assessment\*; b) record linkage\*; c) self-report; d) no description.

2) Was follow-up long enough for outcomes to occur- a) yes\*; b) no

3) Adequacy of follow up of cohorts- a) complete follow up\*; b) subjects lost to follow up unlikely to introduce bias- < 20 % lost follow up\*; c) follow up rate < 80% and no description of those lost; d) no statement

Figure S1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart of our analysis.



Figure S2. (A) Leave-one-out analysis and (B) funnel plot of included studies reporting correlation between 3-dimensional transesophageal echocardiography (3D TEE) and multidetector-row computed tomography (MDCT) for primary outcome (annular area).



Figure S3. Funnel plots (with trim and fill method) of included studies reporting correlation or mean difference between 3-dimensional transesophageal echocardiography (3D TEE) and multidetector-row computed tomography (MDCT) for A) Annular area (correlation; Bias=1.62,P=0.60), B) Annular perimeter (correlation; Bias=5.14,P=0.28), C) Annular diameter (correlation; Bias=1.92,P=0.59), D) Annular area (mean difference; Bias=-0.70,P=0.04), E) Annular perimeter (mean difference; Bias=-8.09,P=0.23), F) Annular diameter (mean difference; Bias=-1.37, P=0.17). Only two studies reported left ventricular outflow tract area and could not be analyzed by funnel plot.



Figure S4. The mean and standard deviations of 3-dimensional transesophageal echocardiography (orange) vs multidetector computed tomography (MDCT) (blue)-derived measures: A) annular area (cm<sup>2</sup>); B) annular diameter (cm); C) annular perimeter (cm); and D) left ventricular outflow tract area (LVOT-A) (cm<sup>2</sup>).





Β.

Mean and standard deviation of MDCT vs 3D-TEE- derived annular diameter (cm)



C.



#### Mean and standard deviation of MDCT vs 3D-TEE- derived annular perimeter (cm)

D.



Figure S5. Correlation between 3-dimensional transesophageal echocardiography (3D TEE) and multidetector-row computed tomography (MDCT) in measuring (A) annular area, (B) annular perimeter, (C) annular diameter, and (D) left ventricular outflow tract area (LVOT-A).

#### Α.



#### Β.

Study	Total	Corre	lation	COR	95%-CI	Weight (fixed)	Weight (random)
Khalique 2014	100			- 0.93	[0.90; 0.95]	26.7%	21.6%
Hammerstingl 2014	138			+ 0.92	[0.89; 0.94]	37.2%	22.5%
Vaquerizo 2016	50			0.70	[0.52; 0.82]	12.9%	19.0%
Mediratta 2017	47			🕂 0.90	[0.83; 0.94]	12.1%	18.7%
Kato 2018	43			+ 0.90	[0.82; 0.94]	11.0%	18.2%
Fixed effect model	378			0.90	[0.88; 0.92]	100.0%	
Random effects mod	el			o.89 🔶	[0.82; 0.93]		100.0%
Heterogeneity: 12 = 82%	$\tau^2 = 0.0676$	p < 0.01					
		-0.5 0	0.5				

#### C.

Weight Weight Study Total Correlation COR 95%-CI (fixed) (random) Tamborini 2012 119 0.68 [0.57: 0.77] 11.0% 8.7% Khalique 2014 100 0.90 [0.85; 0.93] 9.2% 8.6% Husser 2013 57 0.75 [0.61; 0.85] 5.1% 8.2% Wiley 2016 70 0.74 [0.61; 0.83] 6.3% 8.4% Jilaihawi 2013 256 0.69 [0.62; 0.75] 23.9% 9.0% Hammerstingl 2014 138 • 0.94 [0.92: 0.96] 12.8% 8.8% 7.7% Wu 2014 0.77 40 0.60: 0.87 3.5% Garcia-Martin 2016 31 0.90 [0.80; 0.95] 2.6% 7.4% Vaquerizo 2016 50 0.69 [0.51; 0.81] 4.4% 8.0% Mediratta 2017 47 0.89 [0.81; 0.94] 4.2% 8.0% Guez 2017 74 0.77 [0.66; 0.85] 6.7% 8.4% Hafiz 2017 111 0.52 [0.36; 0.64] 10.2% 8.7% Fixed effect model 1093 0.79 [0.76; 0.81] 100.0% 0.80 [0.70; 0.87] 100.0% Random effects model  $\diamond$ Heterogeneity:  $I^2 = 92\%$ ,  $\tau^2 = 0.1347$ , p < 0.01-0.5 0 0.5

D.

Study	Total	Corre	ation		COR	95%-CI	Weight (fixed)	Weight (random)
Stahli 2014 Teixeira 2017	39 60				0.69 0.83	[0.48; 0.83] [0.73; 0.90]	38.7% 61.3%	45.6% 54.4%
Fixed effect model Random effects model Heterogeneity: $l^2 = 61\%$ , $\tau^2$	<b>99</b> <sup>2</sup> = 0.0352	, p = 0.11 -0.5	0	 0.5	0.78 0.78	[0.69; 0.85] [0.61; 0.88]	100.0%	 100.0%

Figure S6. Mean difference between 3-dimensional transesophageal echocardiography (3D TEE) and multidetector-row computed tomography (MDCT) in measuring (A) annular area ( $cm^2$ ) (p = 0.05), (B) annular perimeter (cm) (p = 0.95), (C) annular diameter (cm) (p = 0.68), and (D) left ventricular outflow tract area (LVOT-A) ( $cm^2$ ) (p = 0.23). Negative numbers indicate 3D TEE underestimation compared to MDCT.

Α.

Study	Mean Diffe	rence MD	95%-CI	Weight (fixed)	Weight (random)
Otani 2010	<	-0.49	[-1.37; 0.39]	1.8%	1.8%
Ng AC 2010		-0.45	[-1.00; 0.10]	4.7%	4.7%
Tamborini 2012	<→	→ -0.20	[-2.16; 1.76]	0.4%	0.4%
Khalique 2014		0.08	[-0.48; 0.64]	4.6%	4.6%
Husser 2013	- <mark></mark> -	-0.10	[-0.22; 0.03]	87.1%	87.1%
Vaquerizo 2016	<		[-18.48; 2.22]	0.0%	0.0%
Prihadi 2017			[-7.72; 5.70]	0.0%	0.0%
Guez 2017	<	-0.30	[-1.36; 0.76]	1.3%	1.3%
Kato 2018	<	→ <b>-</b> 0.18	[-5.28; 1.58]	0.1%	0.1%
Fixed effect model		-0.12	[-0.24; 0.00]	100.0%	
Random effects model	$\diamond$	-0.12	[-0.24; 0.00]		100.0%
Heterogeneity: $I^2 = 0\%$ , $\tau^2$	= 0, p = 0.63				
	-1 -0.5 0	0.5 1			

### Β.

Study	Mean Diffe	rence	MD	95%-CI	Weight (fixed)	Weight (random)
Vaquerizo 2016	•	-	-0.65	[-1.52; 0.22]	25.3%	29.4%
Prihadi 2017 -	<b>_</b>		-0.02	[-0.84; 0.80]	28.4%	31.3%
Kato 2018		•	→ 0.45	[-0.19; 1.09]	46.2%	39.3%
Fixed effect model	- li		0.04	[-0.40; 0.47]	100.0%	
Random effects model			-0.02	[-0.65; 0.61]		100.0%
Heterogeneity: $I^2 = 50\%$ , $\tau^2 = 0.7$	1561, p = 0.13	I				
-1	-0.5 0	0.5	1			

### C.

Study	Mean Differend	ce MD	95%-CI	Weight (fixed)	Weight (random)
Husser 2013		-0.03	[-0.33; 0.27]	16.4%	16.4%
Khalique 2014	<mark></mark>	0.01	[-0.18; 0.20]	40.1%	40.1%
Vaguerizo 2016	<b>_</b>	-0.10	[-0.39; 0.19]	17.0%	17.0%
Prihadi 2017		-0.03	[-0.27; 0.21]	26.5%	26.5%
Fixed effect model	4	-0.03	[-0.15; 0.10]	100.0%	
Random effects model	$\diamond$	-0.03	[-0.15; 0.10]		100.0%
Heterogeneity: $I^2 = 0\%$ , $\tau^2 = 0$ , $p$	= 0.94				
-1	-0.5 0 (	0.5 1			

D.

Study		Mean	Differe	ence		MD	95%-CI	Weight (fixed)	Weight (random)
Ng AC 2010 Stahli 2014	÷	•		_		-0.37 -0.50	[-1.10; 0.36] [-1.97; 0.97]	80.4% 19.6%	80.4% 19.6%
Fixed effect model Random effects mode Heterogeneity: $l^2 = 0\%$ , $\tau^2$	<sup>2</sup> ± 0, p	= <b>d</b> .88				-0.40 -0.40	[-1.05; 0.26] [-1.05; 0.26]	100.0%	 100.0%
	-1	-0.5	0	0.5	1				

Figure S7. Intra-observer agreement in (A) multidetector-row computed tomography (MDCT) annular area, (B) 3-dimensional transesophageal echocardiography (3D TEE) annular area, (C) MDCT annular perimeter, (D) 3D TEE annular perimeter and (E) 3D TEE annular diameter.

### Α.

Study	Total	Correlation	COR	95%-CI	Weight (fixed)	Weight (random)
Ng AC 2010 Khalique 2014 Wu 2014 Hammerstingl 2014 Vaquerizo 2016 Mediratta 2017	53 100 40 138 50 47		0.99 0.94 0.98 0.97 0.97 0.94  0.80	[0.98; 0.99] [0.91; 0.96] [0.96; 0.99] [0.96; 0.98] [0.90; 0.97] [0.67; 0.88]	12.2% 23.7% 9.0% 32.9% 11.5% 10.7%	16.5% 17.3% 15.9% 17.6% 16.4% 16.3%
Fixed effect model Random effects mod Heterogeneity: $l^2 = 92\%$ ,	<b>428</b> el τ <sup>2</sup> = 0.1846, μ	o < d.01 -0.5 0 0.5	0.96 ♦ 0.96	[0.95; 0.97] [0.91; 0.98]	100.0%	100.0%

### Β.

Study	Total	Cor	relation		COR	95%-CI	Weight (fixed)	Weight (random)
Ng AC 2010	53			1	0.99	[0.98; 0.99]	7.5%	10.9%
Khalique 2014	100				0.94	[0.91; 0.96]	14.6%	11.5%
Wiley 2016	70			- <b></b>	0.81	[0.71; 0.88]	10.1%	11.2%
Wu 2014	40				0.97	[0.94; 0.98]	5.6%	10.5%
Hammerstingl 2014	138			•	0.96	[0.94; 0.97]	20.3%	11.7%
Vaguerizo 2016	50				0.79	[0.66; 0.88]	7.1%	10.9%
Prihadi 2017	150			•	0.97	[0.96; 0.98]	22.1%	11.8%
Mediratta 2017	47			-	0.89	[0.81; 0.94]	6.6%	10.8%
Kato 2018	43			•	0.96	[0.93; 0.98]	6.0%	10.7%
Fixed effect model	691				0.95	[0.94; 0.96]	100.0%	
Random effects mod	el			0	0.94	[0.90; 0.97]		100.0%
Heterogeneity: /2 = 92%	$\tau^2 = 0.1691$	p < 0.01		Г				
		-0.5	0 (	0.5				

### C.

Study	Total	Cor	relatior	ı	COR	95%-CI	Weight (fixed)	Weight (random)
Hammerstingl 2014 Mediratta 2017	138 47				0.98 0.83	[0.97; 0.99] [0.71; 0.90]	75.4% 24.6%	50.6% 49.4%
Fixed effect model Random effects mode Heterogeneity: $I^2 = 98\%$ ,	<b>185</b> ε <b>Ι</b> τ <sup>2</sup> = 0.6003, <i>ρ</i>	o < <mark>0.01</mark> −0.5	0	0.5	0.97 0.94	[0.95; 0.97] [0.58; 0.99]	100.0%	 100.0%

### D.

Study	Total	Corre	elation	COR	95%-CI	Weight (fixed)	Weight (random)
Hammerstingl 2014 Prihadi 2017	138 150			• 0.95 • 0.95	[0.93; 0.96] [0.93; 0.96]	47.9% 52.1%	47.9% 52.1%
Fixed effect model Random effects model Heterogeneity: $I^2 = 0\%$ , $\gamma$	<b>288</b> el e <sup>2</sup> = 0, <i>p</i> = 1.00	0.5	0 0.5	0.95 0.95	[0.94; 0.96] [0.94; 0.96]	100.0% 	100.0%

### Ε.

Study	Total Co	orrelatio	on	COR	95%-CI	Weight (fixed)	Weight (random)
Hammerstingl 2014 Prihadi 2017	138 150			+ 0.92 • 0.95	[0.89; 0.94] [0.93; 0.96]	47.9% 52.1%	49.5% 50.5%
Fixed effect model Random effects model Heterogeneity: $l^2 = 76\%$ , $\tau^2$	<b>288</b> $^{2} = 0.0224, p = 0.04 - 0.5$	0	0.5	♦ 0.94 ♦ 0.94	[0.92; 0.95] [0.90; 0.96]	100.0%	100.0%

Figure S8. Inter-observer agreement in (A) 3-dimensional transesophageal echocardiography (3D TEE) annular area, (B) 3D TEE annular perimeter, (C) 3D TEE annular diameter, (D) multidetectorrow computed tomography (MDCT) annular perimeter, (E) MDCT annular diameter, and (F) MDCT annular area.

Α.

Study	Total	Corr	elation		COR	95%-CI	Weight (fixed)	Weight (random)
Ng AC 2010	53				0.98	[0.96; 0.99]	9.0%	12.3%
Wiley 2016	70			- 🖷	0.91	[0.86; 0.94]	12.0%	12.9%
Hammerstingl 2014	138			+	0.92	[0.89; 0.94]	24.2%	14.0%
Garcia-Martin 2016	31			-	0.95	[0.90; 0.98]	5.0%	10.8%
Prihadi 2017	150			-	0.93	[0.90; 0.95]	26.3%	14.0%
Vaquerizo 2016	50				0.79	[0.66; 0.88]	8.4%	12.2%
Mediratta 2017	47				0.80	[0.67: 0.88]	7.9%	12.0%
Kato 2018	43			- 📮	0.95	[0.91; 0.97]	7.2%	11.8%
Fixed effect model	582				0.92	[0.91; 0.93]	100.0%	
Random effects mod	el			4	0.92	[0.88; 0.95]		100.0%
Heterogeneity: 12 = 85%,	$\tau^2 = 0.0875$	p < 0.01	1 1					
		-0.5	0 05					

Β.

Study	Total	Co	rrelatio	on	COR	95%-CI	Weight (fixed)	Weight (random)
Hammerstingl 2014 Prihadi 2017	138 150				+ 0.91 • 0.96	[0.88; 0.93] [0.95; 0.97]	47.9% 52.1%	49.8% 50.2%
Fixed effect model Random effects mode Heterogeneity: $I^2 = 92\%$ ,	<b>288</b> el τ <sup>2</sup> = 0.0804	, p < 0.01 -0.5	0	0.5	∮ 0.94 ⊲ 0.94	[0.93; 0.95] [0.87; 0.97]	100.0% 	100.0%

### C.

Study	Total	Corr	elatio	n		COR	95%-CI	Weight (fixed)	Weight (random)
Khalique 2014	100				-	0.90	[0.85; 0.93]	23.8%	26.4%
Hammerstingl 2014	138				-+	0.88	[0.84; 0.91]	33.2%	28.5%
Garcia-Martin 2016	31				- 👎	0.94	[0.89; 0.97]	6.9%	16.1%
Prihadi 2017	150				+	0.94	[0.92; 0.96]	36.1%	29.0%
Fixed effect model	419				0	0.91	[0.90; 0.93]	100.0%	
Random effects mode	el				0	0.92	[0.88; 0.94]		100.0%
Heterogeneity: 12 = 73%,	τ <sup>2</sup> = 0.0291, p =	0.01	I I	1					
	-	0.5	0	0.5					

# D.

Study	Total	Correlation		COR	95%-CI	Weight (fixed)	Weight (random)
Hammerstingl 2014	138		-	0.94	[0.92; 0.96]	75.4%	51.2%
Mediratta 2017	47			0.74	[0.58; 0.85]	24.6%	48.8%
Fixed effect model	185		•	0.91	[0.88; 0.93]	100.0%	
Random effects mode	el		$\sim$	0.88	[0.52; 0.97]		100.0%
Heterogeneity: $I^2 = 95\%$ ,	$\tau^2 = 0.2951, p < 0.0$	01					
	-0.5	5 0	0.5				

Ε.

Study	Total	Co	orrelation	ı	COR	95%-CI	Weight (fixed)	Weight (random)
Khalique 2014 Hammerstingl 2014	100 138				+ 0.92 + 0.91	[0.88; 0.95] [0.88; 0.93]	41.8% 58.2%	41.8% 58.2%
Fixed effect model Random effects mod Heterogeneity: $I^2 = 0\%$ ,	<b>238</b> el $t^2 = 0, p = 0.64$	4 -0.5	0	0.5	♦ 0.91 ♦ 0.91	[0.89; 0.93] [0.89; 0.93]	100.0% 	 100.0%

## F.

Study	Total	Cor	relation	1		COR	95%-CI	Weight (fixed)	Weight (random)
Ng AC 2010 Hammerstingl 2014 Vaquerizo 2016 Mediratta 2017	53 138 50 47				-	0.99 0.95 0.92 0.83	[0.99; 1.00] [0.93; 0.96] [0.87; 0.96] [0.71; 0.90]	18.1% 48.9% 17.0% 15.9%	24.9% 25.6% 24.8% 24.7%
Fixed effect model Random effects mode Heterogeneity: $I^2 = 96\%$ ,	<b>288</b> I t <sup>2</sup> = 0.3970,	р < 0.01 -0.5	0	0.5	•	0.96 0.96	[0.94; 0.96] [0.85; 0.99]	100.0% 	 100.0%

Figure S9. Pooled receiver operating characteristic curves of (A) 3-dimensional transesophageal echocardiography (3D TEE) and (B) multidetector-row computer tomography (MDCT) annular perimeter covering index for predicting paravalvular aortic regurgitation (PVAR).



The red circles of different diameters represent different studies. Their true positive rates (sensitivity) and false positive rates (1-specificity) for determining PVAR can be traced to the y- and x-axes, respectively. Both 3D TEE and MDCT annular perimeter cover indices are good in predicting PVAR (area under curve [AUC] 0.9279, standard error [SE] 0.0549; and AUC 0.9306, SE 0.0417 respectively).

Figure S10. Pooled receiver operating characteristic curves of (A) 3-dimensional transesophageal echocardiography (3D TEE) and (B) multidetector-row computer tomography (MDCT) difference between measured mean annular diameter and diameter of prosthetic valve for predicting paravalvular aortic regurgitation (PVAR).



The red circles of different diameters represent different studies. Their true positive rates (sensitivity) and false positive rates (1-specificity) for determining PVAR can be traced to the y- and x-axes, respectively. Both 3D TEE and MDCT differences between measured mean annular diameter and diameter of prosthetic valve are good in predicting PVAR (area under curve [AUC] 0.6268, standard error [SE] 0.1001; and AUC 0.7479, SE 0.1279 respectively).

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