Multimodality Imaging in Transcatheter Aortic Valve Implantation and Post-Procedural Aortic Regurgitation

Comparison Among Cardiovascular Magnetic Resonance, Cardiac Computed Tomography, and Echocardiography

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Objectives
The purpose of this study was to determine imaging predictors of aortic regurgitation (AR) after transcatheter aortic valve implantation (TAVI) and the agreement and reproducibility of cardiovascular magnetic resonance (CMR), cardiac computed tomography (CT), and transthoracic echocardiography (TTE) in aortic root assessment.

Background
The optimal imaging strategy for planning TAVI is unclear with a paucity of comparative multimodality imaging data. The association between aortic root morphology and outcomes after TAVI also remains incompletely understood.

Methods
A total of 202 consecutive patients assessed by CMR, CT, and TTE for TAVI were studied. Agreement and variability among and within imaging modalities was assessed by Bland-Altman analysis. Postoperative AR was assessed by TTE.

Results
Of the 202 patients undergoing TAVI assessment with both CMR and TTE, 133 also underwent CT. Close agreement was observed between CMR and CT in dimensions of the aortic annulus (bias, 0.4 mm; 95% limits of agreement: -5.7 to 5.0 mm), and similarly for sinus of Valsalva, sinotubular junction, and ascending aortic measures. Agreement between TTE-derived measures and either CMR or CT was less precise. Intraobserver and interobserver variability were lowest with CMR. The presence and severity of AR after TAVI were associated with larger aortic valve annulus measurements by both CMR \((p = 0.03)\) and CT \((p = 0.04)\) but not TTE-derived measures \((p = 0.10)\). Neither CT nor CMR measures of annulus eccentricity, however, predicted AR after TAVI \((p = 0.33\) and \(p = 0.78,\) respectively).

Conclusions
In patients undergoing imaging assessment for TAVI, the presence and severity of AR after TAVI were associated with larger aortic annulus measurements by both CMR and CT, but not TTE. Both CMR and CT provide highly reproducible information in the assessment of patients undergoing TAVI. (J Am Coll Cardiol 2011;58:2165–73)

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Transcatheter aortic valve implantation (TAVI), compared with conventional therapy, reduces mortality in patients with severe aortic stenosis (AS) considered to be unsuitable for surgical aortic valve (AV) replacement (1). Paravalvular aortic regurgitation (AR) is usually mild after TAVI (2); however, significant \((\geq 2+)\) AR is a predictor of adverse outcomes (3). The occurrence of significant AR after TAVI can be predicted by pre-procedural aortic root imaging; however, the limited studies investigating this prediction have been small and are generally limited to single imaging modality analysis (4,5). Accurate prosthesis size selection is important in preventing complications after TAVI includ-
ing embolization and AR (6). Although TAVI size selection is currently based on echocardiography-derived AV annulus measures, this 2-dimensional imaging strategy only measures the AV annulus in a single plane, preventing analysis of its ellipsoid architecture (7). Cardiovascular magnetic resonance (CMR) and cardiac computed tomography (CCT) allow routine assessment of AV annulus and aortic root morphology in multiple imaging planes, affording assessment of their ellipsoid nature, which may better guide TAVI size selection (8,9).

This study sought to determine whether pre-procedural AV annulus and aortic root measures by CMR, CCT, and transthoracic echocardiography (TTE) were associated with AR after TAVI and to establish both the agreement and reproducibility of each modality in this assessment.

Methods

Study population. A total of 202 consecutive patients with severe AS (AV area <1 cm²) who underwent both CMR and TTE at the Royal Brompton Hospital as part of the assessment for TAVI were included. Of these, 133 also underwent CCT. All cases were discussed at a multidisciplinary team meeting, which included cardiothoracic surgeons, cardiologists, and radiologists, where all available imaging was reviewed. Patients were excluded from analysis if they had inadequate images (TTE [n = 12, poor echo windows], CCT [n = 1, movement artifact], CMR [n = 2, poor breath hold]), or previous AV replacement (n = 3). The study was approved by our institutional review board, and all patients gave written informed consent.

TAVI. Selection and technical aspects of TAVI were consistent with published guidelines (10). Both the Medtronic CoreValve (MCV) (Medtronic, Minneapolis, Minnesota) and Edwards SAPIEN valve (ESV) (Edwards Lifesciences, Irvine, California) were implanted. Prosthesis size was determined by consensus at the multidisciplinary team meeting after reviewing all 3 imaging modalities.

CMR image acquisition and analysis. All scans were conducted with a 1.5-T scanner (Siemens Avanto, Erlangen, Germany) following our standardized protocol (8). Transaxial and coronal half-Fourier acquisition single-shot turbo spin-echo multislice pilot images were acquired in diastole. During held expiration, balanced steady-state free precession cine acquisitions were acquired using the following parameters: echo time of 1.57 ms, 15 segments; repetition time of 46 ms without view sharing, slice thickness of 7 mm, field of view of 350 × 263 mm, and resolution of 1.4 × 2.2 mm. Measurements were made in the following cine planes: an oblique sagittal cine in the axis of the left ventricular outflow tract (LVOT) and an oblique coronal cine located orthogonal to the oblique sagittal cine (LVO Tx). These images were then used to align cine planes transecting the AV annulus. Serial short-axis cine were acquired (6-mm slice thickness) rising from 5 mm below the AV annulus at 2-mm distances with no gap until the entire aortic root was imaged.

Images were analyzed by an experienced cardiovascular imaging specialist blinded to the CCT and TTE measurements, using CMR tools (Cardiovascular Imaging Solutions, London, United Kingdom). The aortic annulus was measured from the LVOT and LVOTx, as demonstrated in Figures 1A and 1B. All measures were made using the 70% or 80% cardiac phase (R-R interval) cine images, which were chosen to most closely replicate CCT imaging. The internal dimensions of the sinotubular junction were likewise measured in 2 orthogonal planes from the same images (Figs. 1A and 1B). The dimensions of the sinuses of Valsalva were acquired from the short-axis cine with the largest cusp commissure measurements (Fig. 1C). The internal ascending aorta dimensions were measured from a transaxial half-Fourier acquisition single-shot turbo spin-echo image at the level of the right pulmonary artery. After the largest diameter was plotted, the diameter at 90° to this line was then measured (Fig. 1D).

CCT acquisition and analysis. For CCT, imaging was routinely performed using a prospective scanning protocol (z-axis coverage, 0.75 mm; acquisition time, 0.5 to 5 s; tube current, 370 mA [with electrocardiography-gated milliampereme modulation control]; tube voltage, 100 or 120 kV [depending on a patient’s weight]; gantry rotation time, 0.28 s; and scanning field of view, 200 mm unless the heart rate exceeded 75 beats/min or a significant arrhythmia was present, in which case a retrospective protocol was used [acquisition time, 7.5 to 8.5 s; tube current], 320 mA [with electrocardiography-gated milliampereme modulation control]).

Images were reconstructed at 0.75-mm thickness every 0.5 mm. Total radiation dose was 8 to 11 mSv for prospectively gated studies and 23 to 30 mSv for retrospectively gated CCT and CTA of the thoracic and abdominal aorta. Breath-hold times ranged from 8 to 13 s for CCT alone and 20 to 25 s for combined CCT/CTA.

In retrospectively gated studies, phases were reconstructed at 10% increments from 10% to 100% of the R-R interval to allow functional analysis of the left and right ventricles. In the prospectively gated studies, only the 40%, 50%, 60%, and 70% cardiac cycle phases were acquired.

Aortic root measurements were made by 2 experienced cardiovascular imaging specialists blinded to the CMR and TTE measurements. Images were reconstructed (Aquarius
Workstation, Terarecon, Inc., San Mateo, California) using the best diastolic phase images to allow assessment of aortic root dimensions in the same 3 orthogonal planes used in the CMR analysis (Figs. 2A, 2B, and 2C). Likewise, the internal ascending aorta dimensions were measured from a transaxial image at the level of the right pulmonary artery (Fig. 2D).

TTE acquisition and analysis. All patients underwent standard pre-procedural TTE (iE33, Philips Medical Systems, Andover, Massachusetts) and a second study 3 days after TAVI (12). The AV annulus was measured in peak systole between the hinge points of the AV leaflets (inner edge to inner edge) in the parasternal long-axis view (Fig. 3A). The sinuses of Valsalva (Fig. 3B), sinotubular junction (Fig. 3B), and proximal ascending aorta (1 cm above the sinotubular junction) (Fig. 3B) were measured at end-diastole, also in the parasternal long-axis view. The degree of post-procedural AR was assessed semiquantitatively with color flow Doppler according to current guidelines and was considered significant if moderate or greater (13,14).

Intraobserver and interobserver variability, agreement, and interstudy reproducibility. Twenty consecutive patients from the cohort who had undergone CMR, CCT, and TTE were selected for the assessment of intraobserver and interobserver variability within and agreement among each modality. Two blinded specialists reported the same patient studies. One blinded specialist then reported the same studies again on a separate day. The CMR and TTE measurements were made from preformatted images; however, CCT measurements were performed from an unreconstructed axial dataset, potentially introducing further variability. Given this, an additional 20 patients with severe...
AS who had serial CMR scans at our center (<12 months apart) were studied to assess the interstudy reproducibility of CMR. These studies were performed by different technologists under the supervision of different doctors, but reported twice by a single blinded specialist.

**Statistical analysis.** Intraobserver and interobserver variability and interstudy reproducibility were defined by the coefficient of variation (15). Agreement and bias among modalities was assessed using Bland-Altman analysis (16). The agreement between the different imaging methods regarding implantation decision was determined by contingency analysis and expressed by Cohen’s kappa value. The associations between AR after TAVI and imaging parameters were assessed by Spearman’s correlation coefficient. Two-tailed values of p < 0.05 were considered significant. Analyses were performed using SPSS version 19.0 (SPSS, Inc., Chicago, Illinois) and Prism version 5.0 (GraphPad Software, San Diego, California).

**Results**

**Baseline characteristics.** A total of 202 consecutive patients with severe AS were studied. All patients underwent both CMR and TTE, of whom 133 patients also underwent CCT. Baseline patient characteristics and echocardiographic parameters are listed in **Table 1**. Of the 87 patients who subsequently underwent TAVI, 91% had an MCV and 9% had an ESV implanted.

**Variability and reproducibility.** The interobserver and intraobserver variability of CMR-derived aortic root measurements was low (**Table 2**). Although the interobserver and
intraobserver variability of CMR-derived AV annulus measures was lowest, both CMR- and CCT-derived measures displayed lower intraobserver variability than TTE-derived measures (Table 2). Interstudy reproducibility of CMR was similar to its interobserver and intraobserver reproducibility. Specifically, the coefficient of variation of the largest AV annulus diameter was 2.6%; it was 2.1% for the sinus of Valsalva, 2.8% for the sinotubular junction, and 2.9% for the ascending aorta.

**Agreement.** Close agreement was observed between CMR and CCT (Table 3). Similar bias and 95% limits of agreement were observed between the smallest, largest, and average AV annulus diameters (Fig. 4). No clinically significant bias was observed between CMR and CCT; however, TTE significantly underestimated the largest AV annulus diameter compared with both CMR and CCT (p < 0.0001) (Table 3, Figs. 5 and 6). TTE also displayed wider 95% limits of agreement compared with CMR and CCT relative to the CMR-CCT limits of agreement (Fig. 5).

**TAVI size selection.** Based on recommended manufacturer sizing for the CoreValve prosthesis, in the 133 patients in whom all 3 imaging modalities were performed, CMR and CCT agreed on the same TAVI size in 67 patients (50%, kappa = 0.31), CMR and TTE agreed in 18 patients (14%, kappa = −0.06) and CCT and TTE in 25 patients (19%, kappa = 0.002).

TAVI would have been precluded for too large an annulus by CMR alone in 38 patients (29%), by CCT in 30 patients (23%), and by TTE in 7 patients (5%) and precluded for too small an annulus by CMR in 3 patients (2%), by CCT in 3 patients (2%), and by TTE in 31 patients (23%).

**Aortic regurgitation.** Based on a multimodality imaging TAVI selection strategy, the incidence of significant AR...
after TAVI was low. TTE 3 days after TAVI was performed in 85 of 87 patients. One procedural death occurred after the need for a second TAVI to attempt correction of high positioning of the first (AV annulus 24 mm by CMR, 32 mm by TTE). All other implantations were successful. A second patient did not have a day 3 TTE for logistic reasons. No AR was observed in 35 patients (41%); mild AR was seen in 33 patients (39%), mild to moderate AR in 11 patients (13%), moderate AR in 5 patients (6%), and moderate to severe AR in 1 patient (1%). No severe AR developed in any patients. All AR was paravalvular. The severity of AR after TAVI was associated with increasing AV annulus diameter by both CMR ($r = 0.24$, $p = 0.03$) and CCT ($r = 0.34$, $p = 0.01$) but not TTE ($r = 0.20$, $p = 0.07$).

Annulus eccentricity was also assessed by CMR and CCT and calculated as: 1 − smallest diameter/largest diameter, with higher values denoting a more ellipsoid annulus (5). The mean eccentricity index by CMR was 0.093 ± 0.06 and 0.093 ± 0.08 by CCT with reasonable agreement between modalities (bias, 0.0038; 95% limits of agreement: −0.169 to 0.176). Neither CCT- nor CMR-derived eccentricity indices were associated with AR after TAVI ($p = 0.34$ and $p = 0.88$, respectively).

### Discussion

This study demonstrates that aortic root measurements made by both CMR and CCT are highly reproducible and show close agreement. In contrast, TTE-derived measures display higher variability and significantly underestimate AV annulus size compared with CMR and CCT. This has clinical implications for predicting outcome after TAVI. Using a TAVI selection strategy that involved multimodality imaging, significant AR after TAVI was associated with larger AV annulus measures by both CMR and CCT but not TTE.

### Aortic valve annulus measurement

The most accurate method for measuring AV annulus diameter remains to be determined. In the absence of a gold standard, a highly reproducible and comprehensive imaging modality is pref-

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**Table 1**

Baseline Clinical and Echocardiographic Characteristics

| Imaging | CMR and TTE | 202 |
| TAVI inserted | Medtronic CoreValve | 79 (91) |
| Edwards SAPIEN valve | 8 (9) |
| Age, yrs | 77 ± 12 |
| Height, m | 1.6 ± 0.1 |
| Weight, kg | 71 ± 17 |
| Body surface area, m² | 1.8 ± 0.2 |
| Male | 114 (56) |
| Leaflets | Functionally bicuspid | 19 (9) |
| Tricuspid | 183 (91) |
| AV area, cm² | 0.76 ± 0.3 |
| AV peak velocity, m/s* | 3.9 ± 1.1 |
| LVEF, % | 59 ± 19 |

Values are n, n (%) or mean ± SD. *Aortic valve peak velocity measured by transthoracic echocardiography. AV = aortic valve; CCT = cardiac computed tomography; CMR = cardiovascular magnetic resonance; LVEF = left ventricular ejection fraction; TAVI = transcatheter aortic valve implantation; TTE = transthoracic echocardiography.

**Table 2**

Intraobserver and Interobserver Variability of Largest Aortic Root and Ascending Aorta Measurements in Patients With Severe Aortic Stenosis

<table>
<thead>
<tr>
<th>Measurement</th>
<th>CMR</th>
<th>CCT</th>
<th>TTE</th>
</tr>
</thead>
<tbody>
<tr>
<td>AV annulus</td>
<td>Intraobserver variability</td>
<td>1.7</td>
<td>3.6</td>
</tr>
<tr>
<td>Sinus of Valsalva</td>
<td>Intraobserver variability</td>
<td>0.6</td>
<td>2.7</td>
</tr>
<tr>
<td>Sinotubular Junction</td>
<td>Intraobserver variability</td>
<td>1.6</td>
<td>6.5</td>
</tr>
<tr>
<td>Ascending aorta</td>
<td>Intraobserver variability</td>
<td>1.4</td>
<td>4.5</td>
</tr>
</tbody>
</table>

Values are %. Intraobserver and interobserver variability of largest aortic root and ascending aorta measurements in patients with severe aortic stenosis. Values shown are coefficients of variation expressed as percentages. Abbreviations as in Table 1.

**Table 3**

Agreement Among CMR, CCT, and TTE

<table>
<thead>
<tr>
<th>Measurement (Diameter)</th>
<th>Bias, mm</th>
<th>SD of Bias, mm</th>
<th>95% Limits of Agreement</th>
</tr>
</thead>
<tbody>
<tr>
<td>CMR-CCT</td>
<td>Largest AV annulus</td>
<td>0.39</td>
<td>2.54</td>
</tr>
<tr>
<td></td>
<td>Smallest AV annulus</td>
<td>0.38</td>
<td>2.54</td>
</tr>
<tr>
<td></td>
<td>Average AV annulus</td>
<td>0.48</td>
<td>2.21</td>
</tr>
<tr>
<td></td>
<td>Largest sinus of Valsalva</td>
<td>−0.24</td>
<td>2.25</td>
</tr>
<tr>
<td></td>
<td>Smallest sinus of Valsalva</td>
<td>0.15</td>
<td>2.04</td>
</tr>
<tr>
<td></td>
<td>Average sinus of Valsalva</td>
<td>−0.10</td>
<td>1.43</td>
</tr>
<tr>
<td></td>
<td>Largest sinotubular junction</td>
<td>−0.81</td>
<td>2.01</td>
</tr>
<tr>
<td></td>
<td>Smallest sinotubular junction</td>
<td>−0.97</td>
<td>2.17</td>
</tr>
<tr>
<td></td>
<td>Average sinotubular junction</td>
<td>−0.82</td>
<td>1.87</td>
</tr>
<tr>
<td></td>
<td>Largest ascending aorta</td>
<td>−0.10</td>
<td>2.21</td>
</tr>
<tr>
<td></td>
<td>Smallest ascending aorta</td>
<td>−0.12</td>
<td>2.45</td>
</tr>
<tr>
<td></td>
<td>Average ascending aorta</td>
<td>−0.03</td>
<td>2.24</td>
</tr>
<tr>
<td>CCT-TTE</td>
<td>Largest AV annulus</td>
<td>4.52</td>
<td>3.25</td>
</tr>
<tr>
<td></td>
<td>Largest sinus of Valsalva</td>
<td>−0.45</td>
<td>3.45</td>
</tr>
<tr>
<td></td>
<td>Largest sinotubular junction</td>
<td>−0.70</td>
<td>3.94</td>
</tr>
<tr>
<td></td>
<td>Largest ascending aorta</td>
<td>1.78</td>
<td>4.21</td>
</tr>
<tr>
<td></td>
<td>Largest sinus of Valsalva</td>
<td>−0.33</td>
<td>3.43</td>
</tr>
<tr>
<td></td>
<td>Largest sinotubular junction</td>
<td>0.06</td>
<td>4.60</td>
</tr>
<tr>
<td></td>
<td>Largest ascending aorta</td>
<td>1.56</td>
<td>4.04</td>
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</tbody>
</table>

Bland-Altman agreement analyses of aortic root and ascending aorta measurements by CMR, CCT, and TTE. Abbreviations as in Table 1.
erable. In our study, the interobserver and intraobserver variability of CMR and CCT were both low and displayed lower variability than did TTE.

Although the variability of CMR was lowest, CCT measures had to be reconstructed from an axial dataset, whereas CMR measures were repeated on fixed images, thus confounding a direct comparison. To partially address this, the interstudy reproducibility of CMR was assessed and found to be similar to its intraobserver and interobserver variability, reinforcing the low variability of CMR-derived AV annulus measurements.

Echocardiography is widely used for AV annulus sizing but does not account for the ellipsoid nature of the annulus (7,17). This study demonstrates that TTE underestimates AV annulus diameter compared with CCT and CMR, modalities that allow 3-dimensional (3-D) imaging. Notably, close agreement and little systematic bias (difference) existed between CCT and CMR, both of which demonstrated similarly larger AV annulus measurements compared with TTE (Fig. 6).

TAVI planning strategy. Selection of the appropriate prosthetic valve size is crucial to preventing complications after TAVI including embolization and AR (6). Although TAVI strategies using TTE and transesophageal echocardiography (TEE) for prosthesis sizing are associated with good clinical results (4,5,17), data suggest that TEE also underestimates AV annulus size compared with intraoperative surgical caliper sizing and CCT (17,18).

The 3-D imaging capability of CMR and CCT highlights the issue of which AV annulus measure should be used for TAVI sizing. We believe that as a greater range of TAVI sizes becomes available, optimal coverage of the entire AV annulus is desirable to prevent AR. This is more likely to be achieved if the largest AV annulus diameter is used. Our study demonstrates quite poor agreement between CMR/CCT and TTE regarding TAVI size selection (CMR-TTE agree on same TAVI in 14% and CCT-TTE agree in 19%), a finding consistent with existing data on CCT and TTE (17). Given this poor agreement, we suggest a 3-D imaging modality be used to determine the largest annulus size and corresponding appropriate TAVI.

Impact on outcome: predicting AR. Significant post-procedural AR is a predictor of adverse outcome (3). In our study, the presence and severity of AR after TAVI were associated with increasing AV annulus dimensions by both

Figure 4
Bland-Altman Plots Comparing CMR- and CCT-Derived AV Annulus Measurements

Bland-Altman plots demonstrating close agreement between cardiovascular magnetic resonance (CMR)- and cardiac computed tomography (CCT)-derived aortic valve (AV) annulus diameters. The largest annulus diameter (A), smallest annulus diameter (B), and average annulus diameter (C) show similar agreement. Upper and lower dotted lines denote the 95% limits of agreement; the middle dotted line is the bias.

Figure 5
Bland-Altman Plots Comparing the Largest CMR-, CCT-, and TTE-Derived AV Annulus Measurements

Bland-Altman plots demonstrating closer agreement and lower bias for cardiovascular magnetic resonance (CMR)- and cardiac computed tomography (CCT)-derived aortic valve (AV) annulus diameters (A) compared with CMR-transthoracic echocardiography (TTE) (B) and CMR-CCT (C). Upper and lower dotted lines are the 95% limits of agreement; the middle dotted line is the bias.
CMR and CCT, but not TTE. The lack of association between the TTE-derived AV annulus diameter and AR after TAVI requires further investigation. It likely relates, in part, to the variability of TTE annulus measures. The lack of association is unlikely to be due solely to the single imaging plane of TTE because both the smallest and average AV annulus measures by CCT and CMR were also associated with AR after TAVI (all $p < 0.05$). In a group of 48 patients, Delgado et al. (5) also demonstrated increased CCT AV annulus diameters in 5 patients with moderate AR after TAVI. Our finding that increasing CMR-derived and CCT-derived AV annulus measures predict AR after TAVI adds weight to the importance of 3-D imaging.

**Study limitations.** Although TEE data were not available for our study, its comparison with CMR and CCT should be further investigated because TEE-based TAVI sizing is associated with good clinical results (18). Furthermore, 3-D and contrast-enhanced TTE are increasingly being used and may also provide a better assessment of AV annulus geometry and diameter.

Although feasibility was not the focus of this study, CCT provides a rapid assessment of aortic root morphology, coronary anatomy, and vascular access with the limitations of ionizing radiation exposure and potentially nephrotoxic contrast media. Given the advanced age of the current TAVI population, the amount of ionizing radiation exposure is unlikely to have a clinical impact. CMR overcomes these limitations but requires a significantly longer scan time and the patient to reliably breath hold. A separate feasibility study would ideally also investigate the number of patients who could not tolerate or were deemed unsuitable for each modality. Despite this, good agreement exists in our cohort of elderly, frail patients. Another limitation is the small proportion (9%) of ESVs included in our study. Given this, between-group differences were not assessed, and conclusions regarding AR prediction are restricted to the MCV prosthesis. A further dedicated study is required to determine whether any difference in AV annulus size and AR association exists between the MCV and ESV prostheses.

Finally, Dashkevich et al. (19) recently demonstrated that a calculated average diameter of a CCT-derived planimetric AV annulus area has a higher correlation with intraoperative measurements with a Hegar dilator than measurements obtained on oblique sagittal and oblique coronal images. CMR could produce similar images by using an electrocardiography- and respiratory-gated 3-D steady-state free precession sequence that can be reformatted in multiple planes and allow double oblique reformations. This sequence would also demonstrate the course of the aorta, which might also guide the TAVI approach. The correlation and impact of these measurements on outcome should be further explored.

**Conclusions**

This study demonstrates that in patients with severe AS undergoing assessment for TAVI, aortic root measurements made by both CMR and CCT are highly reproducible and show close agreement. TTE-derived measures, however, display higher variability and significantly underestimate AV annulus size compared with both CMR and CCT. This has clinical implications for predicting AR after TAVI. Using a TAVI selection strategy that involves multimodality imaging, the incidence and severity of significant AR after predominantly MCV TAVI are associated with larger AV annulus measures by both 3-D imaging modalities, CMR and CCT, but not TTE.

**Acknowledgments**

The authors thank Dr. Michael Mullen, Dr. Paul Yea, Nicola Delahunty, and Ricardo Wage for their academic input.

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Key Words: aortic stenosis • cardiac computed tomography • cardiovascular magnetic resonance • transcatheter aortic valve implantation • transthoracic echocardiography.