Feasibility and accuracy of three-dimensional transthoracic echocardiography vs. multidetector computed tomography in the evaluation of aortic valve annulus in patient candidates to transcatheter aortic valve implantation

Gloria Tamborini1*, Laura Fusini1, Manuela Muratori1, Claudia Cefalù1, Paola Gripari1, Sarah Ghulam Ali1, Gianluca Pontone1, Daniele Andreini1,2, Antonio L. Bartorelli1,2, Francesco Alamanni1,2, Cesare Fiorentini1,2, and Mauro Pepi1

1Centro Cardiologico Monzino IRCCS, Via Parea 4, Milan 20138, Italy; and 2Department of Clinical Sciences and Community Health, Cardiovascular Section, University of Milan, Milan, Italy

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Aims
Proper measurement of the aortic annulus (AoA) is crucial for the success of transcatheter aortic valve implantation (TAVI). Transthoracic echocardiography (TTE) is the first step to assess AoA diameter, but a two-dimensional TTE (2DTTE) measurement is no longer accepted as the sole determinant of prosthetic size. The aims of the study were to evaluate feasibility and accuracy of three-dimensional TTE (3DTTE) estimation of AoA dimensions in comparison with multidetector computer tomography (MDCT).

Methods and results
We enrolled 100 consecutive patients referred for TAVI. Feasibility of AoA evaluation was 91% for 3DTTE and in 90% for MDCT. In 81 of 100 patients, AoA maximum diameter (max-D), minimum diameter (min-D), and area were measured and compared using 2DTTE, 3DTTE, and MDCT. Image quality of 3DTTE was sufficient in 47, good in 46 and optimal in 7%. High correlations ($r$, $P < 0.001$) were found between MDCT and 3DTTE (max-D: $r = 0.89$; min-D: $r = 0.86$; area: $r = 0.93$), and between MDCT and 2DTTE (min-D: $r = 0.81$; area: 0.78). The 3DTTE measurements were found to be highly reproducible on intra- and interobserver variability analyses. Regarding the choice of prosthesis size, agreement between 3DTTE and MDCT was very good ($k = 0.84$, $P < 0.001$) while it was poor between 2DTTE and MDCT ($k = 0.36$, $P < 0.001$).

Conclusions
3DTTE may be a valid imaging alternative in patients unsuitable for MDCT during the preoperative evaluation for TAVI. Evaluation of AoA through 3DTTE is feasible, and measurements closely approximate those of MDCT thus improving TTE accuracy in identifying the correct prosthesis size.

Keywords
Three-dimensional transthoracic echocardiography • Transcatheter aortic valve implantation • Aortic valve stenosis • Multidetector computer tomography

Introduction
Transcatheter aortic valve implantation (TAVI) has become a valid alternative to conventional surgery in selected high-risk patients. However, a post-procedural paravalvular aortic regurgitation (PAR) has been frequently described. In the majority of patients, PAR after TAVI is mild grade, while the incidence of moderate or severe PAR is low. Although a mild PAR is known to be not...
associated with a dismal impact on left ventricular (LV) function and patient survival over the first year; recent reports have suggested that even a mild PAR could negatively impact mid- and long-term prognosis.8,9 Valve sizing has been shown to be one of the strongest predictors of PAR, and then an accurate pre-procedural evaluation of patient candidates for TAVI is mandatory to select the prosthesis size.10–13

Measurement of aortic annulus (AoA) dimension before TAVI has been traditionally and most commonly performed using transthoracic echocardiography (TTE) and/or multidetector computed tomography (MDCT), whereas transoesophageal echocardiographic (TEE) imaging (2D and 3D) is usually restricted to the intraoperative evaluation14–22 and magnetic resonance imaging (MRI) is not a standard perioperative procedure even though is an accurate method.23–25 However, up to 20% of patients undergoing TAVI cannot undergo MDCT due to various contraindications. The accuracy of two-dimensional TTE (2DTTE) in defining AoA dimensions is lower in comparison with MDCT and three-dimensional TEE (3DTTE).25–27 Recently, 3DTTE has been demonstrated to overcome 2D echo imaging limitations in different clinical settings.26,27 The aim of this study was two-fold: to assess the feasibility and accuracy of 3DTTE compared with 2DTTE and MDCT for the measurement of AoA dimensions in the preoperative evaluation of patient candidates to TAVI; to evaluate whether the three imaging methods impact differently on the choice of the prosthesis size.

**Methods**

**Study population**

From February 2013 to February 2014, 100 consecutive patients with severe symptomatic aortic valve stenosis were referred to our Institute for TAVI. Inclusion criteria were the presence of severe aortic valve stenosis (mean trans-aortic pressure gradient, >40 mmHg or an aortic valve area <1 cm²) in cases with a very high or prohibitive risk for surgical aortic valve replacement and a predicted post-implantation survival >12 months. Exclusion criteria were the presence of a bicuspid aortic valve.

After a complete pre-procedural imaging (2DTTE, 3DTTE, MDCT, and, when necessary, angiography to assess coronary, and aorto-iliac-femoral system) and clinical evaluation (assessment of operative risk, comorbidities, previous thoracic surgery, or radiation and physical frailty), all the patients were evaluated by a multidisciplinary heart team including cardiologist, cardiac surgeon, interventional cardiologist, imaging specialist, and cardiac anaesthesiologist to be finally admitted to the procedure.

In all patients, 2DTTE, 3DTTE, and MDCT were performed within 48 h each other and TTE preceded MDCT. The operators (echocardiographers and radiologists) were blinded to measure the other two modalities. TEE was performed only in cases undergoing TAVI.

**Transthoracic echocardiography**

TTE was obtained with patients in the left lateral decubitus position using a commercially available system (iE33 system, Philips Medical System, Andover, MA, USA with a S5-1 sector array probe). Real-time 3DTTE was performed immediately after the 2D examination, with the same ultrasound unit, using an X3-1 matrix array probe. For each patient, measurement of AoA diameter with 2DTTE (2DTTE min-D) was performed in systole in a parasternal long-axis view on the LV outflow tract at the points of insertion of the right and non-coronary aortic leaflets (Figure 1). The 2DTTE AoA area was than calculated using the formula: 

\[
AoA = (2DTTE \text{ min} \cdot -D/2)^2 \pi 
\]

with the assumption that the AoA had a circular configuration.

Moreover, real-time zoomed 3D or full volume images containing the whole aortic apparatus were acquired for quantitative analysis. Measurements on 3D datasets were obtained off-line with a commercially available software package (3DQ, Q-Lab version 7.0, Philips Medical Systems).

The 3D dataset was analysed moving three different orthogonal cut planes similarly to the published TEE recommendation method.27 The final cut plane was transversal, oriented to visualize a short-axis view of the AoA, and on this plane the maximum diameter (max-D), the minimum diameter (min-D) were measured and AoA area were traced in systole (Figure 1).

The quality of 3DTTE AoA reconstruction was graded as: (0) inadequate (these patients were not analysed and excluded from the study), (1) sufficient (sufficient quality with rare artefacts), (2) good (good images without artefacts), and (3) optimal (optimal images without artefacts).

**Transoesophageal echocardiography**

Patients were imaged during TAVI procedure using a commercially available echocardiographic system (iE33, Philips Medical System) equipped with a X7-2t probe, allowing 2D multiplane, real-time 3D, and full volume TEE acquisitions. According to the current clinical practice, a 2D acquisition in a zoom mode of the LV outflow tract from the midoesophageal parasternal position with scanning planes from 115° to 160° was performed in order to assess precise measurements of AoA. Moreover, real-time zoomed 3D or full volume images containing the whole aortic apparatus were acquired. The 3D dataset was analysed with the same modality used for 3DTTE for AoA evaluation and previously described.

**Multidetector computed tomography**

All examinations were performed with a Discovery HD750 scanner (GE Healthcare, Milwaukee, WI, USA). Scanning parameters were: slice configuration, 64 × 0.625 mm; gantry rotation time, 35 ms; tube voltage, 120 kVp; and effective tube current, 650 mA. Contrast enhancement was enhanced with a triphasic injection of an 80 mL bolus of iomeron 400 mg/mL (Bracco Imaging S.p.A., Milan, Italy) through an antecubital vein at a 5 mL/s infusion rate, followed by 50 mL of saline solution, and a further 50 mL bolus of contrast at 3.5 mL/s. After the threshold level of 200 Hounsfield units (HU) in the right ventricle was achieved, patients were instructed to hold a deep breath, and the scan was started when a threshold of 200 HU was reached in the left atrium, allowing the synchronization of the arrival of the contrast media and the scan. Data acquisition was performed with retrospective electrocardiogram triggering. Image analysis was performed on a separate computer workstation. AoA was defined as a virtual ring formed by joining the basal attachments of the aortic leaflets, max-D, min-D, and the area of AoA were measured in an orthogonal plane on the centre line of the aorta in systole.

**Prosthetic valve sizing**

To evaluate the difference in TAVI strategy, we indicated the theoretical prosthesis size based on 2D and 3D AoA measurements compared with MDCT values as the gold standard. The SAPIEN XT valve (Edwards Lifesciences, Inc., Irvine, CA, USA) in three different sizes (23-, 26-, and 29 mm expanded diameter) was considered. Currently, there is no consensus regarding the gold standard imaging technique for AoA sizing. From a practical perspective, the choice of the prosthesis size was made according to the guidelines.18–20 In particular the size was
primary chosen depending of AoA diameters and, secondary, in the uncertain cases, on the base of AoA area. Our current practice was to use both MDCT and echocardiographic data for sizing and the interventionist/surgeon in the event of discrepancy decided on the basis (i) of her/his experience related to the specific prosthetic model, (ii) of the method that provided the best image, and (iii) of other technical details (vascular accesses, coronary-AoA distance, and angiography).

Statistical analysis
Data are presented as mean and standard deviation for continuous variables, whereas categorical variables are presented with frequencies and relevant percentages. Normality of distributions for continuous variables was tested using the Kolmogorov–Smirnov test. Linear regression analysis with Pearson correlation coefficient was used to evaluate the relationship between 3DTTE and MDCT AoA measurements. Bland–Altman analysis was used to assess the intertechnique agreement by calculating the bias (mean difference) and the 95% limits of agreement (defined as 1.96 SD around the mean difference). To assess the reproducibility of the 3DTTE measurements, intra- and interobserver variability were evaluated in a subset of 25 randomly selected patients. Each parameter was re-evaluated ≥ 2 weeks later on the same 3DTTE dataset by the main investigator and by a second investigator who was blinded to the results obtained by the main investigator. Both intra- and interobserver variability are reported in terms of intraclass correlation coefficients (ICCs) and coefficients of variation (CV, percentages). Moreover, Bland–Altman analysis was applied to evaluate the limits of intra- and interobserver agreement. The Cohen k statistic was used to assess agreement between 2DTTE, 3DTTE, and MDCT prosthesis size indication. All statistical analyses were carried out with SPSS 20.0 (SPSS, Inc., Chicago, IL, USA).

Results
Clinical and echocardiographic characteristics of the study population are summarized in Table 1. Of the 100 consecutive patients enrolled, 19 were excluded from the study for inadequate echocardiographic window (9 patients) or inability to obtain MDCT data for renal impairment or tomographic poor image quality due to atrial fibrillation, arrhythmias, or tachycardia (10 patients). Therefore, feasibility of AoA measurements was 90% for MDCT and 91% for 3DTTE, and finally 81 patients constituted our study population.
Feasibility and accuracy of 3DTTE vs. MDCT

The quality of 3DTTE AoA imaging was sufficient in 38 cases (46.9%), good in 37 cases (45.6%), and optimal in 6 cases (7.5%).

### Evaluation of AoA dimensions

The mean value of AoA measurements and correlation between each method are presented in Table 2. Significant correlations were found both between 3DTTE and MDCT and between 2DTTE and MDCT. A significant correlation was also found between 3DTTE and MDCT AoA max-D measurements. In the evaluation of AoA area, an excellent correlation was demonstrated between 3DTTE and MDCT. Besides 2DTTE underestimation of AoA area in comparison with MDCT, a good correlation between the two methods was observed. Figure 2 shows correlations between 3DTTE and MDCT AoA measurements together with the results of Bland–Altman analysis. The quality of 3DTTE imaging did not affect these correlations.

3DTTE was performed in 43 of 52 patients who underwent TAVI (9 cases were excluded for contraindications to TEE or because the procedure was performed without TEE monitoring). A significant correlation was found between 3DTTE and MDCT AoA measurements (3DTTE max-D 25.3 ± 2.7 mm, r = 0.78, P < 0.001; min-D 21.5 ± 2.3 mm, r = 0.86, P < 0.001; area 440.1 ± 98 mm², r = 0.91, P < 0.001) and between 3DTTE and 3DTEE (max-D: r = 0.82, P < 0.001; min-D: r = 0.83, P < 0.01; area: r = 0.90, P < 0.001).

### Intra- and interobserver variability

The 3DTTE measurements was found to be highly reproducible in terms of intraobserver variability both using ICCs (min-D, 0.83; max-D, 0.81; area, 0.91) and CV (min-D, 2.8%; max-D, 3.2%; area, 3.3%). Similar results were obtained for the interobserver variability analysis (ICCs: min-D, 0.85; max-D, 0.81; area, 0.91; CV: min-D, 3.3%; max-D, 3.0%; area, 3.8%). The results of Bland–Altman analysis of the agreement between repeated measurements of min-D, max-D, and area are depicted in Figure 3.

### Choice of prosthetic size and clinical outcomes in patients undergoing TAVI

Of the 81 patients included in the study, 52 underwent TAVI. For clinical or anatomical contraindications, TAVI procedure was denied in 29 cases: in 13 a surgical prosthesis was implanted, in 3 a percutaneous balloon valvuloplasty was performed, and in 13 medical therapy was maintained.

In 45 of 52 cases, the implanted prosthesis size was concordant with MDCT and 3DTTE data. In one case, the interventionist/surgeon based the decision on measurements suggested by MDCT (29 mm), while 3DTTE indicated a lower size (26 mm). In five cases, the implanted prosthesis was oversized in comparison with MDCT data, while in one case it was undersized (a 23 mm prosthesis was implanted despite both MDCT and 3DTTE suggested a 26 mm model). Successful TAVI was reached in all patients. No in-hospital death was observed.

After the procedure, PAR was absent or trivial in 26 cases (50%), mild in 15 (29%), and mild/moderate in 11 (21.2%). No patient had moderate/severe regurgitation. The incidence and degree of severity of PAR were not different in cases in whom the interventionist/surgeon decided in accordance or discordance with 3DTTE or MDCT data, but this analysis was limited by the small sample size.

### Discussion

Accumulating data have reported promising results concerning procedural success, quality-of-life improvement, and short-, mid-, and more recently long-term outcomes after TAVI in high-risk patients with severe aortic stenosis. However, aortic regurgitation, mainly paravalvular, has been described in a relatively large number of patients after TAVI. The presence of significant, or even mild PAR is an independent risk factor for mortality at short- and mid-term follow-up. Incorrect valve sizing (together with commissural calcifications) has been proved to be the principal cause for postoperative PAR as well as it is known to be the principal guilty for severe complications such as annular ruptures. Thus, an accurate anatomical evaluation and correct sizing of the AoA are mandatory for patient selection and choice of prosthetic size.

| Table 1 Clinical and echocardiographic characteristics of the study population (n = 81) |
|---------------------------------|-----------------|
| Male, n (%)                    | 38 (47%)        |
| Age (years)                    | 81 ± 7          |
| Body surface area (m²)         | 1.75 ± 0.20     |
| Logistic EuroSCORE (%)         | 20.8 ± 12.1     |
| Aortic valve area index (cm²/m²)| 0.69 ± 0.13     |
| Aortic peak systolic gradient (mmHg) | 81 ± 24      |
| Aortic mean systolic gradient (mmHg) | 49 ± 16        |
| Left ventricular diastolic volume index (mL/m²) | 56 ± 22 |
| Left ventricular systolic volume index (mL/m²) | 26 ± 22 |
| Left ventricular ejection fraction (%) | 59.9 ± 11.9   |
| Left ventricular mass index (g/m²) | 151 ± 46     |
| Aortic regurgitation (1–4)     | 1.7 ± 0.8       |
| Systolic pulmonary pressure (mmHg) | 41 ± 12        |
Even though there are large series of cases with different imaging modalities, there is no consensus regarding the ideal imaging method for AoA sizing and preoperatively a multimodal assessment is suggested. Besides in guidelines18 –20 TTE, TEE and MDCT are all imaging modalities recommended as work-up study before TAVI, TEE in a conscious, or mildly sedated, patient may be frequently poorly tolerate in more critically cases and should be performed very carefully. For this reason in the preoperative phase, 2DTTE and MDCT are routinely used, while TEE with fluoroscopy and angiography are generally reserved to the perioperative phase in the procedural setting.

Moreover, AoA is not a circular ring but is a complex structure with an oval cross-sectional shape. A 2D evaluation of AoA dimensions through 2DTTE or 2DTEE diameters fails to appreciate its elliptical geometry, whereas 3D imaging methods as MDCT or 3DTEE can overcome this limitation.25

The accuracy of MDCT in identifying the correct prosthesis size has been well demonstrated and this is one of the most important reasons why MCDT may be considered the reference method, allowing a comprehensive evaluation not only of AoA morphology, but also of peripheral, carotid, and coronary circulation.15,18,21

The higher accuracy of 3DTEE in comparison with 2DTEE in the analysis of the AoA (using MDCT as the gold standard) has been extensively proved18,29,30 A previous research of our group17 showed that 3DTEE was a valid modality for the measurement not only of AoA dimensions but also of left coronary cusp length and of the distances from left main coronary ostium to the AoA, in a large TAVI population. Recently in a 'in vitro' model, MRI was also demonstrated to be the most accurate method for assessing the dimensions of the ring models.31 In a clinical setting, Pontone et al.24 confirmed that aortic root assessment with MRI including

### Table 2  Mean values of AoA measurements

<table>
<thead>
<tr>
<th>Measurement</th>
<th>3DTTE</th>
<th>MDCT</th>
<th>2DTTE</th>
<th>r₁</th>
<th>P₁ value</th>
<th>r₂</th>
<th>P₂ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Min-D (mm)</td>
<td>21.5 ± 2.3</td>
<td>21.4 ± 2.4</td>
<td>21.5 ± 2.2</td>
<td>0.86</td>
<td>&lt;0.001</td>
<td>0.81</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Max-D (mm)</td>
<td>25.5 ± 3.0</td>
<td>26.5 ± 3.1</td>
<td>26.5 ± 2.1</td>
<td>0.89</td>
<td>&lt;0.001</td>
<td>0.78</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Area (mm²)</td>
<td>443.2 ± 97.0</td>
<td>442.5 ± 94.8</td>
<td>456.3 ± 76.2</td>
<td>0.93</td>
<td>&lt;0.001</td>
<td>0.78</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Figure 2:* 3DTEE and MDCT correlations and agreements. Results of linear regression (top panels) and Bland–Altman analysis (bottom panels) for, from left to right, minimum AoA diameter (min-D), maximum AoA diameter (max-D), and AoA area measured by 3DTEE and MDCT. The dashed lines represent bias and the solid lines ± 1.96 standard deviation. LOA, limits of agreement.
AoA size, aortic leaflet length, and coronary artery ostia height is accurate compared with MDCT.

To the best of our knowledge, data on 3DTTE in this field are lacking. Doddamani et al. compared 3DTTE and 2DTTE in the evaluation of LV out flow tract anatomy and dimensions in 53 normal subjects, and demonstrated that 3DTTE reconstruction of LV outflow tract is feasible and discussed the addition value of 3DTTE in aortic valve area estimation due to the use of LV outflow tract planimetric area in continuity equation.

This is the first study aimed at the evaluation of 3DTTE analysis of AoA in patients with severe aortic stenosis undergoing a screening evaluation for TAVI. The main findings of our study are: (i) 3DTTE evaluation of AoA is feasible in the majority of the patients with low intra- and interobserver variability; (ii) 3DTTE and MDCT measurements did not differ significantly, with excellent agreement in the selection of cases with too small or too large AoA (exclusion criteria for TAVI) and a good agreement in the choice of prosthetic size in cases scheduled for the procedure.

In our study population, feasibility of MDCT and 3DTTE was similar (89 vs. 90%, respectively) and 3DTTE images were good or optimal for AoA measurement in 43 of 81 cases. In the remaining 38 cases, despite suboptimal resolution of 3DTTE, AoA planimetric area and diameters outline were possible in all of them.

Even though it is well known that MDCT provides precise information about the AoA anatomy and it is considered the gold standard for the preoperative assessment of TAVI candidates, not all the patients can be studied by MDCT for several reasons such as impaired renal function, severe breathlessness, and arrhythmias. MRI has been demonstrated to be a valid alternative in these cases; however, in a recent series from the original population of 80 consecutive TAVI patients, 30 were excluded being unsuitable candidates for one or both the procedures (MDCT and MRI).

3DTTE does not require breath-old and contrast infusion, may be obtained at the bedside, in more critical cases, and also in the presence of arrhythmias. In fact, the area of interest is limited to the aortic apparatus and can be completely contained in a 3D live format avoiding multibeat full volume acquisition. The most important limit of the method is the dependency to the acoustic window of the patient. In our population, an inadequate acoustic window was found in 9 of 90 cases. In the 10 of 100 cases who could not undergo MDCT (three for renal impairment and seven for arrhythmias), the preoperative AoA evaluation was obtained through 2D and 3DTTE and the correct prosthesis size was confirmed intraoperatively by 2D and 3DTEE.

In the present study, no significant differences have been observed between 3DTTE and MDCT AoA measurements. On the contrary,
while no significant differences were present between all the three methods in the evaluation of AoA min-D, the 2DTTE AoA area, geometrically derived from 2DTTE diameter, was considerably lower in comparison both with 3DTTE and MDCT planimetric surface area. These results may be expected due to the oval shape of AoA, with significant differences between maximum and minimum diameter that is generally observed in an antero-posterior position corresponding to the 2DTTE estimated diameter. Thus, the geometrical derived 2D area (derived from AoA min-D) amplifies the difference between 2D and 3D modalities. Moreover, in a minority of cases of our series (this was behind the scope of this study), measurements with 3DTEE were reported.

**Clinical implications**

Accurate AoA measurements are critical for patient selection and successful valve implantation. While 2DTTE and 2DTEE have been the primary methods for AoA measurements, nowadays MDCT is considered as the reference standard. The ability to manipulate imaging planes for AoA measurements is the main reason of MDCT accuracy. In this regard, the potential of 3DTTE has been underappreciated. Our data demonstrate that 3DTTE (confirming 3DTEE data) may easily allow AoA measurements. It may be proposed as a screening test not only for aortic valve stenosis diagnosis (inside a comprehensive 2D and Doppler examination), but also to identify too small or too large AoA and to indicate the presumable size of the different TAVI models. This is particularly useful in cases in whom MDCT or MRI are not suitable. Therefore, 3DTTE may be a gatekeeper to the procedure and in the different settings MDCT, MRI, and 3DTTE may be utilized depending on the local strategies. Moreover, the simplest method (2DTTE and 3DTTE) may be utilized in centres which do not perform TAVI and in which more advanced methodologies are not present to preselect candidates with severe aortic stenosis and high risk for surgery.

All these data are in agreement with previous studies on 3DTEE vs. 2DTEE, showing that 3DTEE provide more accurate information than 2DTEE with superior discrimination of post-TAVI regurgitation.

**Study limitations**

This study is not a randomized one; however, it includes a consecutive series of patients undergoing a multimodality imaging screening before TAVI. Only 52 of 81 cases underwent the procedure. Therefore, imaging measurements allowed us to compare values of the different modalities in all cases evaluating the theoretical impact on the choice of prosthetic size and clinical outcomes and choice of the implanted prosthetic size in only 52 patients undergoing TAVI.

3DTEE was performed in a subgroup of patients. Despite we could not perform a complete analysis and head-to-head comparison in all our cases (this was behind the scope of this study), measurements with 3DTEE showed an high correlation with both 3DTTE and MDCT values.

**Conflict of interest:** none declared.

**References**

Feasibility and accuracy of 3DTTE vs. MDCT


