Real-time three-dimensional transoesophageal echocardiography in the assessment of aortic valve stenosis

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Aims
To determine the feasibility of real-time three-dimensional transoesophageal echocardiography (3D-TOE) in the evaluation of aortic valve stenosis, to study its reliability, and to test the concordance of this new method when compared with transthoracic two-dimensional echocardiography (2D-TTE) as the diagnostic standard.

Methods and results
Fifty-nine consecutive patients with moderate-to-severe aortic valve stenosis were assessed by means of 2D-TTE and 3D-TOE by independent blinded observers. Aortic valve planimetry was possible in 94.9% of patients. Inter-observer intraclass correlation coefficients (ICC) were 0.892 (CI 95% 0.818–0.936; \( P < 0.001 \)), and 0.871 (CI 95% 0.780–0.925; \( P < 0.001 \)) for 2D-TTE and 3D-TOE, respectively. Bland-Altman plot showed a mean difference in aortic valve area (AVA) of 0.040 cm², with 2D-TTE yielding larger values than 3D-TOE. ICC of both methods was 0.724 (CI 95% 0.530–0.839; \( P < 0.001 \)).

Conclusion
Assessment of AVA by means of 3D-TOE is feasible in most patients with aortic valve stenosis. Reliability of the measurement is good. However, there is some disagreement with standard 2D-TTE that needs further investigation.

Keywords
Aortic valve stenosis • Diagnostic imaging • Ultrasonography • Validation studies • Reproducibility of results

Introduction
Aortic valve stenosis1 is the most frequent form of clinically significant valvular heart disease in aged populations.2,3 Echocardiography is the diagnostic method of choice in the evaluation and management of patients with aortic valve stenosis.4,5 Cardiac catheterization is no longer recommended on a routine basis, and is performed only in a limited subset of patients.1,4,5 Moreover, the prediction of clinical outcomes has been mainly studied using transthoracic echocardiographic techniques.5–8 Echocardiography is now considered the diagnostic standard for the evaluation of aortic stenosis severity.9

One of the most important advances in echocardiography during the last decade has been the development of matrix-array transducers able to perform volumetric imaging. Some studies suggest that adding three-dimensional imaging to standard two-dimensional transthoracic echocardiography (2D-TTE) could be helpful in the quantification of aortic valve area (AVA).10–15 Recent advances in miniaturization have made possible the incorporation of matrix-array transducers into the tip of a transoesophageal probe. Three-dimensional transoesophageal echocardiography (3D-TOE) allows real-time volume rendering images and off-line volumetric quantification techniques from three-dimensional data set obtained from a single heart beat.16 Its limitations include lower spatial and temporal resolution, among others.17 Although 3D-TOE is a promising tool with potential advantages over conventional 2D imaging, the value of information added by this new technology remains to be determined in several clinical settings.

We aimed (i) to determine the feasibility of 3D-TOE in the evaluation of aortic valve stenosis, (ii) to study its reliability, and (iii) to evaluate the concordance of this new method when compared with 2D echocardiography as the diagnostic standard.
Methods

Patients
We enrolled consecutive patients with moderate-to-severe aortic valve stenosis as assessed by transthoracic echocardiography. Patients were referred to our echo-lab from the outpatient clinic and the wards of our Cardiology Department from 1st December 2008 to 31st March 2009. Clinical data were obtained from the clinical chart. None of the patients were excluded despite of poor image quality. Informed consent was obtained from all patients.

Transthoracic echocardiography
Transthoracic echocardiography was performed using an iE33 ultrasound system (Philips Medical Systems, Andover, MA, USA) equipped with a 5S-2 phased array (5–1 MHz broadband) transducer (Philips Medical Systems, Andover, MA, USA). A systematic imaging protocol was performed by European Association of Echocardiography-accredited cardiologists (G.M., D.S., M.J.O., F.S.) closely following current guidelines. Image processing was performed off-line at an image management system (Xcelera, Philips Medical Systems, Andover, MA, USA). AVA calculated with the continuity equation by means of transthoracic echocardiography was considered the reference standard.

Three-dimensional transoesophageal echocardiography
On a different day (but within 1 week from the standard transthoracic echocardiogram), patients underwent transoesophageal echocardiography under sedation with intravenous propofol (1 mg/kg followed by 0.5 mg/kg every 3–5 min as needed for sedation). 3D-TOE was performed using the iE33 ultrasound system (Philips Medical Systems, Andover, MA, USA) equipped with a matrix-array X7-2t transducer (Philips Medical Systems, Andover, MA, USA). Settings were optimized using the narrow-angled acquisition mode, and real-time 3D imaging of a pyramidal volume (around 30° × 60°) of the aortic valve and left ventricular outflow tract was obtained. Frame rates were kept between 23 and 28 Hz and depth around 8 and 10 cm. Images were obtained from a mid-oesophageal short-axis view of the aortic valve from a single heart beat (Figure 1). A total of three different cycles were recorded in each patient. Studies were carried out by the same team as the transthoracic study, but by a different echocardiographer from the transthoracic study, who was unaware of the 2D study results. Image processing was performed off-line at the Xcelera workstation using the QLAB (3DQ module) software (Philips Medical Systems, Andover, MA, USA). This workstation software allows any-plane reconstruction from the original pyramidal data set. In a mid-systolic frame (as defined as maximal aortic valve opening at 3D-TOE volume rendered images), two orthogonal planes were set through aortic cusp tips, with their intersection line parallel to the aortic root. A third plane (perpendicular to the previous two planes) was set through the aortic cusp tips, and re-oriented as needed to ensure that the minimal orifice area was identified. Finally, AVA was planimetered at the cusp tips (Figure 2).

Data processing and statistical analysis
Calculations were averaged from three cycles (five non-extreme cycles in case of atrial fibrillation). Measurements and calculations were performed twice for each patient in a blind manner, once by each of two observers (D.S. and M.J.O. for transthoracic studies, and G.M. and F.S. for 3D-TOE studies).

Figure 1 Real-time three-dimensional transoesophageal echocardiogram (volume rendering image) displaying aortic valve short-axis view. Mid-systolic aortic opening is shown in a patient with degenerative valvular aortic stenosis.

Figure 2 Off-line processing of echocardiographic three-dimensional pyramidal data set. Any-plane reconstruction allowed to set a image plane through the cusp tips of aortic valve in a mid-systolic frame. Aortic valve area was planimetered as 1 cm² in this case.

Normal distribution of continuous variables was assessed with the Kolmogorov–Smirnov (Lilliefors correction) test. Variables are expressed as proportions, mean, and standard deviation (SD), or median and interquartile range (IQR) as appropriate. Reliability of measurements was tested with two-way mixed model intraclass correlation coefficient (ICC) for average measurements agreement. The
agreement between modalities was evaluated by means of ICC and Bland–Altman plots. Differences were considered statistically significant at the two-sided $P < 0.05$ level. All computations were carried out with the software SPSS 15.0 for Windows (SPSS Inc. Chicago, IL, USA).

**Results**

**Feasibility of 3D-TOE**

Characteristics of the 59 patients assessed during the study period are shown in Table 1. Quantification of AVA by 2D-TTE was possible in all but one of the patients due to poor visualization of the left ventricle outflow tract; however, aortic valve stenosis severity was assessed by means of gradient measurements. Quantification of AVA by 3D-TOE planimetry was possible in 56 (94.9%) of the patients. In two patients, AVA could not be determined because of massive degenerative calcification of the valve. In a third patient, the aortic cusp tips were not included in the acquired volume data set because of a too low position of the probe. An example of AVA planimetry by means of 3D-TOE is seen in Figure 2. Mean values of the parameters obtained by means of both methods are shown in Table 1.

**Reliability study**

Inter-observer ICC of 2D-TTE was 0.892 (CI 95% 0.818–0.936; $P < 0.001$). Similarly, the value obtained with 3D-TOE was 0.871 (CI 95% 0.780–0.925; $P < 0.001$). Scatter plots of AVA measurements obtained by two independent observers with both techniques are shown in Figure 3.

**Concordance study**

In 55 out of the 59 patients there were AVA calculations by both methods available for comparison. When measurements of AVA by 3D-TOE were compared with the reference standard by means of a Bland–Altman plot (Figure 4A), the mean difference in AVA was 0.040 cm$^2$, with AVA by 2D-TTE yielding larger values than 3D-TOE. Within two standard deviations of this mean, the differences between these two methods ranged between $-0.370$ and 0.452 cm$^2$. ICC of AVA measurements by

![Figure 3](https://academic.oup.com/ehjcimaging/article-abstract/11/1/9/2396734/2396734)  

**Table 1**  

<table>
<thead>
<tr>
<th>Patient characteristics ($n = 59$)</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>75 (68–81)</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>28 (47.5%)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>73.9 ± 16.3</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>160.2 ± 8.1</td>
</tr>
<tr>
<td>BSA (m$^2$)</td>
<td>1.8 ± 0.1</td>
</tr>
<tr>
<td>IVS (mm)</td>
<td>14.6 ± 2.9</td>
</tr>
<tr>
<td>LVPW (mm)</td>
<td>12.9 ± 2.1</td>
</tr>
<tr>
<td>LVEDD (mm)</td>
<td>44.0 ± 8.5</td>
</tr>
<tr>
<td>LVESD (mm)</td>
<td>28.5 ± 9.8</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>62.5 (50–70)</td>
</tr>
<tr>
<td>CHD</td>
<td>5 (8.6%)</td>
</tr>
<tr>
<td>AR</td>
<td>19 (32.2%)</td>
</tr>
<tr>
<td>MR</td>
<td>6 (8.6%)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>11 (15.7%)</td>
</tr>
<tr>
<td>Bicuspid aortic valve</td>
<td>11 (15.7%)</td>
</tr>
<tr>
<td>2D-TTE LVOT diameter (mm)</td>
<td>20.0 ± 0.2</td>
</tr>
<tr>
<td>2D-TTE VTI LVOT (cm)</td>
<td>21.1 ± 6.8</td>
</tr>
<tr>
<td>2D-TTE VTI AV (cm)</td>
<td>95.6 ± 6.1</td>
</tr>
<tr>
<td>2D-TTE AVA (cm$^2$)</td>
<td>0.72 ± 0.23</td>
</tr>
<tr>
<td>3D-TOE AVA (cm$^2$)</td>
<td>0.68 ± 0.21</td>
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</tbody>
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BSA, body surface area; IVS, interventricular septum thickness; LVPW, left ventricular posterior wall thickness; LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter; LVEF, left ventricular ejection fraction; CHD, coronary heart disease; AR, aortic regurgitation grade III/IV; MR, mitral regurgitation grade III/IV; 2D-TTE, two-dimensional transthoracic echocardiography; 3D-TOE, three-dimensional transoesophageal echocardiography; LVOT, left ventricle outflow tract; VTI, velocity-time integral from Doppler spectrum; AV, aortic valve; AHA, aortic valve area. Measures are expressed as mean, median, or absolute count, accompanied by standard deviation, interquartile range, or percent as appropriate, respectively.
Discussion

In this study, we have assessed for the first-time real-time 3D-TOE in the evaluation of AVA in patients with aortic stenosis. Although cut-off points to define aortic valve stenosis severity are somewhat arbitrary, accurate grading is still a challenge in clinical practice. Once considered a gold standard, invasive measurement of AVA with the Gorlin formula has demonstrated flaws and has been questioned as a clinical standard. Heart catheterization is now recommended only for a small subset of patients with non-diagnostic echocardiography or discrepancies with symptoms, a fact being reflected in current clinical practice. Echocardiography is now the method of choice for aortic valve stenosis quantification, albeit not free of problems in its definition or important technical issues. As new clinical developments (i.e. percutaneous aortic valve replacement) continue to demand an increasingly accurate anatomic characterization of the aortic valve and left ventricle outflow tract (LVOT), echo guidelines continue to state that 'standards still have to be defined'.

Studies of 3D-TTE have tried to improve characterization of the LVOT area aiming to improve accuracy of continuity-equation AVA calculations, while others have focused on strategies such as volumetric calculation of the stroke volume, or Doppler-derived LVOT stroke volume. Goland et al. showed that aortic valve planimetry from transthoracic electrocardiographic-gated 3D data set is feasible. Aortic valve planimetry has also been achieved with 3D-TOE, but with off-line reconstruction from multiple gated single views of conventional multipane transoesophageal probe. We aimed to directly measure anatomic AVA by means of real-time 3D-TOE planimetry with matrix-array transducer as a new method of aortic stenosis quantification.

Feasibility

3D-TOE allows AVA planimetry in most patients. Off-line image processing allows setting a mid-systolic image plane just at the cusp tips of the aortic valve, avoiding overestimation due to larger planes proximal to the cusp tips. Valve calcifications have been shown to limit aortic valve planimetry due to image artefacts. Degenerative calcification of the aortic valve progresses from the body towards the tips of the cusps. By setting an image plane just at the tips of the valve, most of calcium artefacts can be avoided when the 3D-TOE data set has been acquired from an aortic valve short-axis view. Only in two patients with massive calcification of the aortic valve AVA measurement could not be achieved. The feasibility of aortic valve planimetry by real-time 3D-TOE of our study compares favourably with previous data of 2D-TTE and is at least as good as the feasibility found in conventional multipane transoesophageal echocardiography, or offline three-dimensional reconstruction from multi-plane transoesophageal echocardiography, or 3D-TTE with matrix-array transducers.

Reliability and agreement with 2D-TTE

ICC is useful to assess the concordance between different methods of measure or different observers. ICC is based in the ANOVA model of repeated measures. In our study, both 2D-TTE and 3D-TOE have very good reliability after values obtained in inter-observer ICC according to Fleiss. However, concordance between 2D-TTE and 3D-TOE is somewhat worse, ranging from moderate to good. Bland–Altman plot shows a wide range of variation between methods, with 3D-TOE yielding slightly smaller valvular areas than Doppler-derived 2D-TTE calculation. Theoretically 2D-TTE should have shown smaller areas, since effective rather than anatomic AVA is calculated by means of continuity equation. Although the time during which the aortic valve remains opened is longer than the temporal resolution of 3D-TOE, relatively low frame rates of the technique could have contributed to discrepancies observed in comparison with Doppler-derived areas. 3D-TOE pyramidal volume data sets are manipulated off-line in order to obtain an image plane in any selected orientation. Such a plane is constituted by lines neither...
parallel nor perpendicular to the ultrasound beam. Thus spatial resolution is typically anisotropic, combining features of axial and lateral ultrasound resolution in variable grade at different points of the reconstructed imaging plane. Anisotropy in spatial resolution is a particular issue of concern in three-dimensional echocardiography that may account for the disagreement with the reference standard. Another possible factor contributing to differences in AVA measurements is sedation with propofol. Anatomic AVA in patients with aortic stenosis varies in response to haemodynamic changes,1,9 and propofol has demonstrated effects on myocardial contractility and blood pressure.31,32 However, the role of pharmacologic sedation in the observed differences remains speculative. Further investigations on these issues should clarify the reasons of limited agreement.

Limitations

There are limitations to this study that deserve consideration. First, patients were consecutively enrolled, but referral bias is possible and patients may not represent the whole population with significant aortic stenosis. Furthermore, patients with larger valve areas in the moderate range are poorly represented in our sample. Second, blood pressure monitoring during 2D-TTE and 3D-TOE are not available for comparison. Both studies were performed very closely in time, but changes related to haemodynamic variations could not be controlled.

Conclusion

Assessment of AVA by means of 3D-TOE is feasible in most patients with aortic valve stenosis. Reliability of the measurement is good. 3D-TOE could be an alternative method in the evaluation of aortic valve stenosis. However, we found some disagreement with standard 2D-TTE that needs further investigation.

Conflict of interest: none declared.

References