Value of anatomical aortic valve area using real-time three-dimensional transoesophageal echocardiography in patients with aortic stenosis: a comparison between tricuspid and bicuspid aortic valves

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Aims
Accurate assessment of disease severity is critical for appropriate treatment of patients with aortic stenosis (AS). This study investigated the influence of aortic-valve morphology on the determination of anatomical aortic-valve area (AVA) in patients with AS.

Methods and results
This prospective study included 126 patients with AS who underwent transoesophageal echocardiography (TEE). Aortic-valve area was measured using (i) planimetric two-dimensional (2D) TEE, (ii) volumetric three-dimensional (3D) TEE, and (iii) the continuity equation (CE) obtained with transthoracic echocardiography. Of these, 20 patients also underwent contrast-enhanced multidetector computed tomography (MDCT). Aortic-valve area was measured from multiplanar reconstruction of the MDCT images. Of the 126 patients, 20 (15.9%) were diagnosed with bicuspid AS and 106 were diagnosed with tricuspid AS. There was an excellent correlation between AVAADCT and AVA3DTEE (r = 0.83, P < 0.001) and a somewhat lower correlation between AVAADCT and AVA2DTEE (r = 0.63, P = 0.006). In the tricuspid AS group, both AVA2DTEE and AVA3DTEE significantly correlated with AVACE (r = 0.63, mean difference 0.13 ± 0.24 cm², and r = 0.83, mean difference 0.03 ± 0.12 cm², respectively, both P < 0.001). In contrast, in the bicuspid AS group, AVA3DTEE significantly correlated with AVACE (r = 0.83, mean difference 0.10 ± 0.18 cm², P < 0.001), whereas AVA2DTEE did not (r = 0.42, mean difference 0.48 ± 0.32 cm², P = 0.066).

Conclusion
Aortic-valve morphology influenced the assessment of anatomical AVA in patients with AS, and 3D TEE is useful for assessing anatomical AVA regardless of aortic-valve morphology.

Keywords
Aortic valve stenosis • Echocardiography • Three-dimensional echocardiography

Introduction
Aortic-valve stenosis (AS) is one of the most common valvular diseases and the third most common cardiovascular disease in developed countries.1–4 Aortic-valve stenosis is detected in 2–7% of adult aged 65 years and older and is characterized by degenerative calcification or congenital valvular defects, such as bicuspid aortic valve (AV).1,4 Accurate determination of the severity of AS is
crucial for timely and appropriate surgical and non-surgical interventions. The key diagnostic tools for the AS assessment are two-dimensional (2D) transthoracic echocardiography (TTE) and transoesophageal echocardiography (TEE) which is generally used for anatomical determination of aortic-valve area (AVA). Accuracy in measuring AVA is sometimes challenging because the oblique 2D short-axis views at the AV tips can result in overestimation of AVA in some patients. The recent development of real-time three-dimensional (3D) TEE allows volumetric data acquisition of the AV from which the true orthogonal 2D cut plane of the AV tips can be extracted for accurate determination of AVA. This study aimed to assess the influence of AV morphology on the determination of anatomical AVA and disease severity in patients with AS.

Methods

Study population
A total of 134 patients with moderate-to-severe AS (AVA < 1.2 cm²) who underwent TEE between November 2011 and April 2014 were prospectively enrolled. Patients with poor quality images (n = 8, 5.9%) were excluded from this study; ultimately, 126 patients were analysed. This study was approved by the institutional review board at St Marianna University Hospital.
University School of Medicine. All patients gave their written informed consent before study enrolment.

2D and 3D TEE
Transoesophageal echocardiography was performed using an iE33 ultrasound imaging system (Philips Medical Systems, Andover, MA, USA) equipped with a fully sampled matrix array TEE transducer which can display both 2D and live 3D images. After application of a topical anaesthesia in the pharynx and intravenous sedation (propofol), the probe was advanced into the oesophagus. From the mid-oesophageal position, in the zoomed 2D short-axis view (approximately 45° of the AV, AVA was traced from the middle-to-late systolic frames in which the AV opening was largest (Figure 1A and B). Planimetry was repeated three times and the values were averaged. A clear apical long-axis view (135° of the AV was obtained from the mid-oesophageal position with a slight anteroflexion of the probe. The 3D zoom mode, which displays a smaller magnified pyramidal volume, was subsequently activated to image the AV. The size of the pyramidal box was adjusted on the basis of the biplane images to ensure that the entire AV was included in the scan. Gain and compression as well as time-gain compensation were optimized. Zoomed 3D TEE images were acquired for two consecutive scans. Gain and compression as well as time-gain compensation were optimized. Digital acquisition was triggered by an electrocardiogram R-wave. The 3D TEE measurements of AVA in the multiplanar reconstruction mode and the two orthogonal long-axis views of the AV and the ascending aorta (antero-posterior and medio-lateral projections) were extracted from the zoomed 3D data sets. The third plane, which is perpendicular to the two long-axis planes, was shifted to adjust the orthogonal 2D cutting plane of the AV. After selecting one frame in which the largest AV opening was observed and finally adjusting the cutting plane to delineate the smallest AV orifice, the AVA was traced manually using magnified view mode (Figure 1C and D) (QLAB cardiac 3DQ, Philips Medical Systems, Andover, MA, USA).22

Transthoracic echocardiography
Comprehensive transthoracic echocardiography (TTE), including 2D and Doppler echocardiography, was performed using commercially available ultrasound equipment according to the American Society of Echocardiography guidelines within 1 week before and after TEE.23 Aortic-valve jet velocity was recorded from multiple acoustic windows with continuous Doppler to obtain the highest-velocity signal. Stroke volume was determined as time–velocity integral of pulsed wave Doppler echocardiography at the left-ventricular outflow tract x the left-ventricular outflow area. Aortic-valve area was calculated by using the time–velocity integral of the AV and left-ventricular outflow tract spectral curves in the standard continuity equation (CE). The biplane Simpson’s method was used to measure left-ventricular end-diastolic and end-systolic volume, stroke volume, and left-ventricular ejection fraction.24 Relative wall thickness was estimated as 2 x (diastolic left-ventricular posterior wall thickness)/left-ventricular end-diastolic diameter.25 Left-ventricular mass was calculated using Devereux’s formula.26 Maximum left-atrial volume was measured according to the biplane Simpson’s method and indexed to body surface area. The transmural flow velocity profile was assessed from the apical four-chamber view using pulsed wave Doppler echocardiography with a sample volume placed at the mitral leaflet tips. The early diastolic tissue velocity (E) on the septal corner of the mitral annulus was measured by tissue Doppler images in the same view.

Multidetector computed tomography
Of the 126 patients, 20 (14 with tricuspid AS and six with bicuspid AS) in our study population underwent retrospective ECG-gated conventional scans with tube current-dose modulation using a multidetector computed tomography (MDCT) (Aquilion ONE VISION Edition; Toshiba Medical Systems, Odawara, Japan). This system was equipped with 320-row detector arrays. Computed tomography was performed with a slice thickness of 0.5 mm, a tube voltage of 120 kV, and a maximum tube current of 580 mA with a gantry rotation time of 275 ms. We occasionally reduced voltage to 100 kV in patients with thin chests. All subjects with heart rates >65 bpm received 10 mg of propranolol hydrochloride or 0.125 mg/kg of ivabradine hydrochloride (Figure 2). Image reconstruction was performed in 5% intervals from R-wave to R-wave, and all 20 phases were loaded into an external workstation. The plane for AVA analysis was obtained using 20–30% of an RR interval on multi-planar reconstruction images by centring of the axis in the aorta on the level of the aortic leaflets in the coronal frame (Figure 2A) and then

Table 1 Baseline characteristics

<table>
<thead>
<tr>
<th>Variables Bicupid AS</th>
<th>Tricuspid AS</th>
<th>P-value</th>
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<tr>
<td>(n = 20)</td>
<td>(n = 106)</td>
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<tr>
<td>Age, years</td>
<td>71 ± 3</td>
<td>75 ± 1</td>
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<td>Male, n (%)</td>
<td>9 (45)</td>
<td>65 (61)</td>
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<td>BSA, m²</td>
<td>1.54 ± 0.13</td>
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<td>Systolic BP, mmHg</td>
<td>91 ± 26</td>
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<tr>
<td>Diastolic BP, mmHg</td>
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<td>HL, n (%)</td>
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<td>25 (23)</td>
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<tr>
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<td>6 (29)</td>
<td>37 (35)</td>
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<td>2 (12)</td>
<td>29 (27)</td>
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<tr>
<td>CKD, n (%)</td>
<td>3 (17)</td>
<td>36 (34)</td>
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<td>Transthoracic echocardiographic parameters</td>
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<tr>
<td>AVA, cm²</td>
<td>0.76 ± 0.30</td>
<td>0.79 ± 0.22</td>
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<tr>
<td>AVAI, cm²/m²</td>
<td>0.49 ± 0.17</td>
<td>0.51 ± 0.15</td>
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<td>Peak velocity, m/s</td>
<td>4.0 ± 1.4</td>
<td>3.7 ± 0.8</td>
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<td>Minimal PG, mmHg</td>
<td>70 ± 44</td>
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<td>Mean PG, mmHg</td>
<td>41 ± 27</td>
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<td>LVMI, g/m²</td>
<td>129 ± 30</td>
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<td>LVOT diameter, cm</td>
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<td>2.0 ± 0.2</td>
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<td>EDV, mL</td>
<td>102 ± 25</td>
<td>107 ± 40</td>
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<td>ESV, mL</td>
<td>43 ± 20</td>
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<td>SV, mL</td>
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<td>SVI, mL/m²</td>
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<td>LVEF, %</td>
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<td>RVSP, mmHg</td>
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<td>LAVI, mL/m³</td>
<td>42 ± 17</td>
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<td>E/A ratio</td>
<td>0.79 ± 0.33</td>
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<td>13 ± 3</td>
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<td>e′, cm/s</td>
<td>4.9 ± 1.6</td>
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</tbody>
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AS, aortic-valve stenosis; BSA, body surface area; BP, blood pressure; HT, hypertension; HL, hyperlipidaemia; DM, diabetes mellitus; CAD, coronary artery disease; CKD, chronic kidney disease; AVA, aortic-valve area; AVAI, indexed aortic-valve area; PG, pressure gradient; LVMI, left-ventricular mass index; LVOT, left-ventricular outflow tract; EDV, end-diastolic volume; ESV, end-systolic volume; SV, stroke volume; SVI, stroke volume index; RVSP, right-ventricular systolic pressure; LAVI, left-atrial volume index.  

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adjusting of the images to the plane perpendicular to the LVOT. In the sa-
gittal frame (Figure 2B), the plane was adjusted to achieve a circular shape
of the aorta in the axial frame. Finally, AVA was measured in the adjusted
axial frame (Figure 2C).

Statistical analysis
Results are expressed as mean ± standard deviation (SD) or percentage
unless otherwise specified. Data for the tricuspid AS and bicuspid AS
groups were compared using the Student’s t-test, χ² test, or Fisher
exact test as appropriate. Differences were considered significant if
P < 0.05. Pearson’s correlation coefficient was used to evaluate the
correlation between two parameters. Bland–Altman plots evaluated
differences in AVA measured using 2D TEE, 3D TEE, MDCT, and CE.

Results
Baseline characteristics
Baseline characteristics are summarized in Table 1. Of the 126
patients, 74 patients (58.7%) were men and the mean age was
74 ± 10 years (range 55–89 years). Twenty patients (15.9%) were

Figure 3  AVAs determined using MDCT, 2D and 3D TEE, and CE method. Comparisons of AVAs between MDCT and 2D TEE (A and B), MDCT
and 3D TEE (C and D), and MDCT and CE (E and F) are shown. AVAs were compared using linear regression and Bland–Altman analyses.
diagnosed with bicuspid AS and 106 patients (84.1%) with tricuspid AS. No differences in demographic and echocardiographic findings were found between the tricuspid and bicuspid AS groups.

**Comparisons between AVA determined by MDCT (AVA$_{MDCT}$), TEE (AVA$_{TEE}$), and TTE (AVA$_{CE}$)**

There was an excellent correlation between AVA$_{MDCT}$ and AVA$_{3DTEE}$ ($r = 0.83$, $P < 0.001$) and a somewhat lower, although still significant, correlation between AVA$_{MDCT}$ and AVA$_{2DTEE}$ ($r = 0.63$, $P = 0.006$). AVA$_{3DTEE}$ was slightly but significantly underestimated compared with AVA$_{MDCT}$ ($0.77 \pm 0.25$ vs. $0.86 \pm 0.26$ cm$^2$, mean difference $-0.09 \pm 0.11$ cm$^2$, $P = 0.010$), but AVA$_{2DTEE}$ was overestimated ($1.0 \pm 0.25$ vs. $0.86 \pm 0.26$ cm$^2$, mean difference $0.14 \pm 0.20$ cm$^2$, $P = 0.007$, Figure 3A–D). There was an excellent correlation between AVA$_{MDCT}$ and AVA$_{CE}$ ($r = 0.80$, $P < 0.001$) as well as AVA$_{3DTEE}$ with a mean difference of $0.11 \pm 0.11$ cm$^2$ (Figure 3E and F).

**Figure 4** AVAs determined using 2D and 3D TEE and the CE method. Data are shown for the bicuspid (A, C, and E) and tricuspid (B, D, and F) groups. AVAs were compared using linear regression analysis.
Comparisons between functional (CE) and anatomical (TEE) AVA

In the tricuspid AS group, both $AV_{A2\text{DTEE}}$ and $AV_{A3\text{DTEE}}$ were significantly correlated with $AV_{ACE}$ ($r = 0.63$, mean difference $0.13 \pm 0.24$ cm², and $r = 0.83$, mean difference $0.03 \pm 0.12$ cm², respectively, both $P < 0.001$). In contrast, in the bicuspid AS group, $AV_{A3\text{DTEE}}$ was significantly correlated with $AV_{ACE}$ ($r = 0.83$, mean difference $0.10 \pm 0.18$ cm², $P < 0.001$), whereas $AV_{A2\text{DTEE}}$ was not ($r = 0.42$, mean difference $0.48 \pm 0.32$ cm², $P = 0.066$). Figures 4A–D and 5A–D. When we assessed the correlation between $AV_{A2\text{DTEE}}$ and $AV_{A3\text{DTEE}}$, the tricuspid AS group had a stronger correlation than the bicuspid AS group (Figure 4E and F and 5E and F). The agreement in the different modalities assessed using ICCa was 0.60 [confidence interval (CI), 0.025–0.848; $P = 0.028$] for $AV_{ACE}$ vs. $AV_{A2\text{DTEE}}$, 0.83 (CI, 0.562–0.935; $P = 0.001$) for $AV_{ACE}$ vs. $AV_{A3\text{DTEE}}$, and 0.57 (CI, 0.137–0.831; $P = 0.034$) for $AV_{A3\text{DTEE}}$ vs. $AV_{A2\text{DTEE}}$ in the bicuspid AS group; 0.68 (CI, 0.386–0.787; $P < 0.001$) for $AV_{ACE}$ vs. $AV_{A2\text{DTEE}}$, 0.82 (CI, 0.629–0.929; $P < 0.001$) for $AV_{ACE}$ vs. $AV_{A3\text{DTEE}}$, and 0.80 (CI, 0.690–0.857; $P < 0.001$) for $AV_{A3\text{DTEE}}$ vs. $AV_{A2\text{DTEE}}$ in the tricuspid AS group.

Differences between the bicuspid and tricuspid AS groups

No significant differences in $AV_{A3\text{DTEE}}$ or $AV_{ACE}$ were found between the tricuspid AS and bicuspid AS groups ($AV_{A3\text{DTEE}}$, 0.78 ± 0.28 and 0.78 ± 0.26 cm², respectively; $AV_{ACE}$, 0.78 ± 0.23 and 0.70 ± 0.23 cm², respectively). $AV_{A2\text{DTEE}}$ was greater in the bicuspid than in the tricuspid AS group (1.0 ± 0.38 vs. $0.83 \pm 0.31$ cm², $P = 0.010$).

Reproducibility

The intraobserver variabilities assessed using the ICCa were 0.93 (95% CI, 0.81–0.98, n = 10) for $AV_{A2\text{DTEE}}$, 0.94 (95% CI, 0.77–0.97, n = 10) for $AV_{A3\text{DTEE}}$, and 0.91 (95% CI, 0.71–0.94, n = 10) for $AV_{ACE}$.

Figure 5  AVAs determined using 2D and 3D TEE and the CE method. Data are shown for the bicuspid (A, C, and E) and tricuspid (B, D, and F) groups. AVAs were compared using the Bland–Altman method.
for AVA_{MDCT}. The interobserver variabilities were 0.91 (95% CI, 0.78–0.95) for AVA_{2DTEE}, 0.93 (95% CI, 0.75–0.94) for AVA_{3DTEE}, and 0.90 (95% CI, 0.39–0.94) for AVA_{MDCT}. The Bland–Altman method showed that interobserver and intraobserver variabilities were 0.10 ± 0.09 and 0.06 ± 0.10 cm² for AVA_{2DTEE}, 0.10 ± 0.11 0.08 ± 0.06 cm² for AVA_{3DTEE}, and 0.12 ± 0.06 and 0.11 ± 0.08 cm² for AVA_{MDCT}, respectively.

Discussion

The main findings of the present study were (i) AVA_{3DTEE} had a stronger correlation than AVA_{2DTEE} with AVA_{MDCT}; and (ii) although AVA_{2DTEE}, AVA_{3DTEE}, and AVA_{CE} were significantly correlated in the tricuspid AS group, AVA_{2DTEE} was significantly larger than AVA_{3DTEE} and AVA_{CE} in the bicuspid AS group. These findings may be explained by the different morphologies of the dome-shaped valve leaflets associated with the bicuspid AV.

Analysis of AVA using 3D TEE

Determination of the severity of AS is generally accomplished by the CE and planimetric method with 2D TTE.21 Although semi-invasive, 2D TEE is more accurate than 2D TTE.13–15 Our study demonstrated a lower correlation between AVA_{CE} and AVA_{2DTEE} than earlier studies.13–15 This was due to the differences in patient characteristics between the earlier studies and our study: the earlier studies included patients with mild-to-severe AS (AVA < 1.5 cm²), whereas our study included patients with moderate-to-severe AS (AVA < 1.2 cm²). Accordingly, the patients in our study had more severe AS with heavily calcified aortic-valve cusps, and the planimetry of our patients was more challenging to assess than that of those in the earlier studies.13–15 Cormier et al.27 reported an excellent correlation in the mild-to-moderate calcified aortic cusps, although its correlation was very weak in the heavily calcified valves. The different patient backgrounds might lead to the differences in the study results.
between the earlier studies and our study. Also, the accuracy of 2D TEE is diluted by the difficulty obtaining the correct cross-sectional view at the level of the aortic cusp edges. Earlier studies demonstrated that 3D TEE with multi-gated acquisition of serial 2D images more accurately determines anatomicalAVA than 2D TEE.19–22 However, no studies have defined a gold standard for the accurate determination of AS severity or the influence of morphology onAVA determination.

In this study, we evaluated the accuracy of 2D TEE and 3D TEE using MDCT as a reference. AVA3DTEE correlated more closely with AVA3DMDCT than did AVA2DTEE. The technology of 3D TEE is similar to that of recently developed MDCT. 3D TEE, which is relatively new, allows detailed 3D assessment of cardiac structures. The multiplanar reconstruction mode of 3D TEE extracts short-axis views of the tips of the AV leaflets perpendicular to the two long-axis planes of the AV. For this reason, 3D TEE is a potentially useful clinical tool for evaluating anatomical AVA. In the present study, AVA3DTEE tended to be smaller than AVA3DMDCT perhaps because of the relatively lower spatial resolution of the 3D zoom mode or calcification of the AV. However, the absolute difference between AVA3DTEE and AVA3DMDCT was smaller than the difference between AVA2DTEE and AVA3DMDCT. Moreover, the excellent correlation of AVA3DTEE and AVA3DMDCT suggests that 3D TEE could be a viable alternative technique for assessing AVA. Thus, a multi-parametric approach including valve anatomy as well as function may aid in correctly identifying in patients with AS.

Comparisons of AVA between bicuspid and tricuspid AVs

In the present study, there were no significant differences between AVA2DTEE and AVA3DTEE or AVA2DMDCT in the tricuspid AS group, whereas 2D TEE (but not 3D TEE) overestimated AVA compared with CE in the bicuspid AS group. These findings suggest that 3D TEE may be more useful than 2D TEE. Earlier animal and human studies reported that the aortic annulus moves in the cranial direction during early systole and then moves back in the caudal direction for the remainder of systole and isovolumetric relaxation.19,20 Accordingly, we believe that the optimal 2D short-axis view of the aortic cusps for the calculation of anatomical AVA should be based on aortic cusps viewed during systole, not diastole. Even when we selected a subset of AS patients using optimal 2D image criteria, planimetric 2D TEE still showed a larger AVA than volumetric 3D TEE. In the present study, 3D TEE confirmed that aortic leaflets in tricuspid valves were flat and that aortic-valve leaflets in bicuspid valves were dome-shaped. The geometry of dome-shaped AV may contribute to erroneous measurements because small differences in through plane can lead to wide variations of AVA by 2D TEE as shown in Figure 6. Thus, we suggest that 3D TEE provide a more accurate assessment of AVA, particularly in patients with bicuspid AV.

Study limitations

Our study had several limitations. First, only 20 patients of this small subgroup (tricuspid AS, n = 14) underwent MDCT in this study. We used the CE method, which has an excellent correlation with MDCT, to compare AVA by using 2D and 3D TEE. Further prospective investigations with larger populations are warranted. Secondly, the anaesthetics used during TEE and the beta-blockers used during MDCT may have affected loading conditions. Finally, this prospective study included some patients who underwent a detailed TEE evaluation before surgery, which might have led to the higher prevalence of bicuspid AS than the earlier studies.13–18 Accordingly, the bias in the study population could not be completely ruled out.

Conclusions

Aortic-valve morphology influenced the assessment of anatomical AVA in patients with AS, and 3D TEE is useful for assessing anatomical AVA regardless of AV morphology.

Conflict of interest: none declared.

References


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Chronic total occlusion of abdominal aorta due to Takayasu’s arteritis: a noteworthy finding

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A 35-year-old man was diagnosed with Takayasu’s arteritis aged 11 years when he presented with hypertension. He had raised inflammatory markers, and computed tomography angiography (CTA) revealed narrowing of the thoracic aorta (TA). Drug therapy was recommended, which the family declined for personal reasons.

The patient led an active life and was asymptomatic until a year ago, when he presented with lower extremity claudication and fatigue on moderate exertion. Physical examination revealed reduced pulses in the lower extremities and hypertension in the upper extremities.

Transthoracic echocardiography demonstrated a preserved left ventricular systolic function and no significant valve abnormalities; negative inflammatory markers indicated disease inactivity.

CTA of the aorta revealed calcification and multiple aneurysms of the TA and abdominal aorta (AA). The largest aneurysm (71 mm in diameter) was located in the TA (Panel D, red arrow). There was significant AA dilatation, associated with dissection of the anterior portion and a probable saccular thrombus in the anterior wall (Panel D, yellow arrow).

Distal AA occlusion following the renal arteries origin (Panels A–D, green arrow) was associated with significant internal thoracic arteries (ITA) dilatation and collateral vessels (CV) directed to the iliac arteries (IAS) (Panels B and C, white arrows). The mesenteric artery (MA), right renal arteries (RRA), and left renal arteries (LRA) were spared (Panel A, blue arrows).

The patient declined surgical resection of the thoracic aneurysm and bypass grafts to the legs. He was discharged on beta-blockers and ACE inhibitors, with outpatient follow-up for close monitoring.

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