Usefulness of three-dimensional transthoracic echocardiography for the classification of congenital bicuspid aortic valve in children

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Aims

Because the classification of congenital bicuspid aortic valve (BAV) is of importance to predict a possible valvular dysfunction, we sought to assess the feasibility, the reproducibility, and the accuracy of three-dimensional transthoracic echocardiography (3D-TTE) to accurately depict the morphology of the leaflets in a BAV.

Methods and results

Seventy-two consecutive children, who were suspected of having a BAV on two-dimensional transthoracic echocardiography (2D-TTE), were included in this prospective study. 2D-TTE and 3D-TTE views of a BAV were recorded by the same investigator, and then were analysed separately by two confirmed paediatric cardiologists. For each of these two imaging techniques, the spatial position of cusps and raphes was noted for each patient. Intra-observer concordance and inter-observer concordance were evaluated to assess the reproducibility of the techniques. Feasibility of 3D-TTE was 100%. Median acquisition time of 3D-TTE was 117 (98.5–176.8) s. Image quality seemed to be better with 3D-TTE compared with 2D-TTE. When using 3D-TTE, the diagnosis was reconsidered for 12 patients (17%). Only 44.4% of uncertain BAV cases identified by 2D-TTE were confirmed by 3D-TTE. Furthermore, 3D-TTE seems to provide a better visualization of the leaflet morphology, leading to reclassification for 34.4% (95% CI 22.9–47.3) of the patients. Agreement for the BAV classification between 2D-TTE and 3D-TTE was therefore moderate (κ = 0.46). Both inter-observer concordance and intra-observer concordance were good (κ = 0.91 and κ = 0.93, respectively) for 3D-TTE.

Conclusion

3D-TTE is feasible and provides accurate description of a BAV in children. Compared with 2D-TTE, 3D-TTE seems to enable a better visualization of the structural geometry of the leaflets.

Keywords

Congenital heart disease • Three-dimensional echocardiography • Bicuspid aortic valve

Introduction

Bicuspid aortic valve (BAV) is the most common congenital heart malformation, with an incidence among the newborn of 0.5–2%.1–6 Compared with a population with a normal tricuspid aortic valve, patients with a BAV have an increased risk of valvular dysfunction. Indeed, this malformation can lead to serious complications in at least one-third of cases.2–4,7–10 Consequently, compared with the general population, patients with a BAV may require earlier aortic valve surgery. A BAV stands for various morphological phenotypes4,10,11 that result in different haemodynamic and functional conditions. When necessary, both the time of the surgery and the type of surgical procedure directly depend on the morphological phenotype encountered.11,12 Thus, multiple morphological classifications have been proposed4,10,13–15 but the most used is that published in 2007 by Sievers.13 This classification is based both on the number and on the spatial position of the raphes. According to this

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classification, the functional status of the valve was proved to be correlated with the type of the BAV.\textsuperscript{11–13}

Two-dimensional transthoracic echocardiography (2D-TTE) is the easiest method to diagnose a BAV and determine its type. However, several studies tend to draw our attention on the imperfections of this technique. According to the authors, the sensitivity of 2D-TTE to diagnose a BAV ranges from 55 to 79%.\textsuperscript{1,2,16–18} Moreover, because the image quality is often impaired, determination of the type of the BAV is frequently not feasible. Indeed, using 2D-TTE, the number of cusps is unknown in 20–27% of cases.\textsuperscript{1,2,16–18} Although MRI and CT scans are more efficient to accurately depict the aortic valve, 2D-TTE remains widely used because of its large availability.\textsuperscript{17–21} Three-dimensional echocardiography (3DE) seems to provide a better image resolution to overcome this issue.\textsuperscript{22,23} Furthermore, a good correlation between surgical findings and transoesophageal 3DE was previously reported.\textsuperscript{24} Nevertheless, feasibility of three-dimensional transthoracic echocardiography (3D-TTE) to assess a BAV in children has never been studied so far. The aims of our study were to assess both the feasibility and the reproducibility of 3D-TTE in a paediatric population with a BAV and to compare 2D-TTE and 3D-TTE findings.

**Methods**

**Patients**

It was a prospective single-centre study conducted from November 2009 to October 2010. We consecutively enrolled all the children under 18 years who were referred to our Echolab (for heart murmur exploration or for the follow-up of an already known congenital heart disease) and who had a suspicion of a BAV on 2D-TTE. Exclusion criteria were previous aortic valve surgery and interventional catheterization because such interventions may modify both the anatomical and the functional status of the aortic valve.

This study was approved by our local Ethics Committee. For every patient, an informed verbal consent was obtained from the legal representatives. A written consent form was not required according to the French law since 3D-TTE was part of the regular management of the children. No exams were performed only for the purpose of the study.

**Definitions of raphe and BAV**

The term ‘raphe’ defines the conjoint or ‘fused’ area of two under-developed cusps turning into a malformed commissure between both cusps.\textsuperscript{8} Raphes can either develop partially or totally. Sievers\textsuperscript{13} defined a BAV as a deformed aortic valve with less than three zones of parallel apposition between the cusps. This definition includes both a ‘true’ BAV (with only two cusps and no raphe) and a ‘false’ BAV (with three cusps and one or two raphes).

**Echocardiographic acquisitions and data analysis**

When, using the short-axis view in systole and in diastole,\textsuperscript{25} a BAV was suspected on 2D-TTE, 3D-TTE was performed by the same investigator. 3D images were acquired using a high-quality commercially available ultrasound system (Philips iE33, Philips Medical Systems, Andover, MA, USA). X3-1 and X7-2 matrix probes (Philips Medical Systems) were used depending on the age of the patient. Real-time (RT) 3D-TTE images were acquired in parasternal short-axis views. The best short-axis section view was selected to see both cusps and commissures from a ventricular view. All data were stored digitally both on the hard disk of the ultrasound system and in a connected computer. The QLab software (Philips Medical Systems) was used for the off-line analysis. Images were assessed in a random order—in terms of patients and imaging modality (2D or 3D)—by two confirmed paediatric cardiologists who had same level of experience of the software. The 3DE acquisition time was measured for every patient.

Diagnosis of a BAV, previously stated by 2DE, was systematically re-evaluated using 3DE. For every patient, the spatial position of cusps and raphes was noted according to the classification of Sievers. The quality of the RT-3DE acquisitions was graded as high, average, and poor. Intra-observer variability and inter-observer variability were analysed by two confirmed cardiologists on the first 18 patients. To assess intra-observer variability, 2DE and 3DE acquisitions were repeated 1 month later by the first operator and analysed randomly. To assess inter-observer variability, 2DE and 3DE acquisitions were analysed in a random order, blindly and separately by the two observers.

**Statistical analysis**

Continuous variables are expressed as the median and first and third quartiles. Categorical variables are presented as percentages and absolute numbers. Image quality was compared using a \( \chi^2 \) test. Statistical significance was accepted for a \( p \)-value of \(<0.05\). The concordance between variables was measured using the percentage agreement between categories (with its 95% confidence interval calculated with the binomial exact method) and unweighted kappa coefficients (\( \kappa \)). Statistical analysis was performed using the Statistical Analyzing System software (Stata SE 11.1).

**Results**

**Population**

Eighty-three patients were suspected of having a BAV, using 2DE. Eleven of them were excluded from the study because they previously had either a commissurotomy (seven patients) or an aortic percutaneous dilatation (one patient) or because they were over 18 years (three patients). Thus, seventy-two patients were finally included in the study. The median age was 5 years (1.4–11.3), ranging from 0 to 17.8 years. Eight patients (11%) were <1 month and 58 (81%) patients were >3 months. The sex ratio was 1.88 (47 males/25 females). The median weight was 15.8 kg (10–31.7). No sedation was required to perform echocardiography in this population.

**Feasibility and reproducibility**

The median time for the 3DE data set acquisition was 117 (98.5–176.8) s. The feasibility of 3D-TTE was 100%. Intra-observer concordance of RT-3DE was good (\( \kappa = 0.91 \)), with an agreement in the phenotype classification observed for 17 of 18 patients (94% [73.7–100%]). The only disagreement concerned a vertical type 0, which was classified as type 1 L-R by the second observer. Inter-observer concordance was also good (\( \kappa = 0.93 \)), with an agreement in 94% (73.7–100%). The only discordant case was a horizontal type 0 considered a type 2 by the second observer.
As expressed by a kappa coefficient of 0.35, the inter-observer variability was high for 2DE. Indeed, agreement was obtained for only nine patients [50% (28.8–77.0)].

**Image quality**

As 9.7% of 3D-TTE images were considered of poor quality vs. 25.0% of 2D-TTE images ($P = 0.01$), the image quality seemed to be higher for 3D-TTE than for 2D-TTE (Table 1). It was also observed for children under 3 months (28% for 3D-TTE vs. 21% for 2D-TTE, $P = 0.03$). When considering the proportions of high-quality images, we noted a trend only in favour of 3D-TTE (47.2 vs. 33.3%, $P = 0.09$).

<table>
<thead>
<tr>
<th>Image quality</th>
<th>Overall population</th>
<th>&lt;3 months</th>
<th>&gt;3 months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2D-TTE</td>
<td>3D-TTE</td>
<td>P-value</td>
</tr>
<tr>
<td>Poor</td>
<td>18 (25.0%)</td>
<td>7 (9.7%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Medium</td>
<td>30 (41.7%)</td>
<td>31 (43.7%)</td>
<td>0.92</td>
</tr>
<tr>
<td>High</td>
<td>24 (33.3%)</td>
<td>34 (47.2%)</td>
<td>0.09</td>
</tr>
</tbody>
</table>

A $\chi^2$ test was used to compare the variables.

2D-TTE, two-dimensional transthoracic echocardiography; 3D-TTE, three-dimensional transthoracic echocardiography.

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**Comparison of 2DE and 3DE**

**Diagnosis of a BAV**

According to 3DE, a BAV was not observed in 8 of the 72 patients (11%) (Figure 1). Based on 2DE, the diagnosis was uncertain (indeterminate number of cusps) for 9 (12%) of the 72 children. A poor 2DE image quality was noted for eight of these nine (89%) children. Based on 3DE, four of these nine children were diagnosed as having a BAV, whereas five (56%) of them were considered having a normal tricuspid aortic valve. Thus, according to 3DE, three children were falsely classified as BAV, using 2DE. As a consequence, the diagnosis of 12 (17%) patients (9 children with an indeterminate number of cusps and 3 with a false diagnosis) was modified using 3DE. Among the 72 patients, 60 (83%) diagnoses were concordant between 2DE and 3DE ($\kappa = 0.43$).

**Classification of the BAV**

Proportions of the different types of the BAV according to 2DE and 3DE are reported in Table 2. Whereas all phenotypes of a BAV were noted using RT-3DE (Figure 2), type 1 L-N was not reported with 2DE. Agreement between 2DE and RT-3DE for the 72 children was moderate ($\kappa = 0.46$) and remained moderate ($\kappa = 0.57$) when considering only the 64 BAVs diagnosed by the two techniques. Among these 64 patients, 22 (34%) were reclassified using 3DE. For 18 (90%) of them, 3DE allowed the visualization of a raphe which was unseen with 2DE (Figure 3). The most reclassified type was type 0 (60% becoming horizontal type and 70% becoming vertical type). Three type 1 L-R and one type 1 R-N were also reclassified using 3DE.

**Discussion**

This study shows that 3D-TTE is a feasible (even in newborn babies) and reproducible method to assess a BAV in children. Indeed, both intra-observer concordance and inter-observer concordance are good ($\kappa = 0.91$ and $\kappa = 0.93$, respectively) using this technique. Although 3DE is now accepted as a complementary imaging technique to conventional cross-sectional echocardiography in congenital heart diseases, allowing both morphological and functional assessment of the heart structures, we found a poor agreement with 2DE both for the diagnosis and the description of a BAV in our population. A lack of precision of 2DE for the determination of the aortic valve structure was previously reported in a study of adult patients with aortic stenosis. In
our paediatric cohort, using 2DE, the precise determination of the number of cusps was also not possible for 12% of the patients, and agreement between observers was poor ($\kappa = 0.46$). Because some raphes were not seen on 2DE, 3DE seems to provide a better spatial visualization of the aortic valve. Our data are consistent with those of a recent study that demonstrated an incremental value of 3DE over 2DE for detecting both malformations of the atrioventricular valve leaflets and commissural abnormalities.28 This improvement of the valvular depiction is probably due to the fact that 3DE gives a visualization of the surface of the valve, whereas 2DE offers only a planar view. Thus, in our study, 90% of reclassified BAV gained a raphe on 3DE. Surprisingly, among the 22 reclassifications, 2D image quality was reported as poor for 5 (23%), as medium for 6 (27%), and as high for 11 (50%) of them. Thus, reclassification is possible even for high-quality 2DE images. Furthermore, with 3DE, the respective proportions of each subtype are quite similar to those previously reported.9,12–15 Thus, according to 3DE, the most common type of a BAV was type 1 L-R, followed by type 1 R-N and horizontal type 0. 2DE clearly overestimated type 0 (41.6%), whereas 3DE found a value (17.2%) closer to that previously published by Sievers13 (20%).

The major limitation of this study is due to the absence of a gold standard to compare with 2DE and 3DE findings. No children underwent surgery during the time of the study and because MRI and CT scans are more invasive than TTE—MRI frequently requiring sedation in young children and CT scan being irradiating—these examinations were not performed. Finally, compared with adults, children have a better echocardiographic window and the aortic valve is rarely calcified, making transoesophageal echocardiography unnecessary. For all of these reasons, it would not have been ethical to use MRI, CT scan, or transoesophageal echocardiography as a gold standard in our paediatric population. Consequently, we were not able to determine the sensitivity and the specificity of 3DE for the diagnosis of a BAV. We could only evaluate the concordance between 2DE and 3DE findings.

The fact that, in our study, the image quality was considered higher for 3DE than for 2DE is surprising. Indeed, it has been reported that 3DE seems to suffer more from suboptimal image quality compared with conventional 2DE.29 Our findings may reflect the bias of the operators towards the 3D modality. However, previous studies that compared 3DE with 2DE were conducted with large 3D transducers that provided poor resolution, especially in small children. The advent of smaller matrix probes resulted in optimized images. Thus, a recent study, conducted on healthy subjects, showed a comparable 2D image
quality with 3D transducer compared with 2D transducer. Furthermore, the 3D software allows modulating both the gain, the compression of the image and the smoothing, thus improving its quality.

A murine study showed that the two most frequent subtypes of a BAV result from two distinct embryological mechanisms. Indeed, it is now admitted that the different subtypes of a BAV result from different embryological pathways, thereby having distinct evolutions and prognoses. It was thus reported that type 1 R-N seems to be affected with early valve dysfunction and type 2 frequently requires early surgery. Type 1 L-R is still debated to develop aortic wall degeneration but is highly associated with aortic coarctation. Thus, the systematic classification of the BAV phenotype is beneficial to provide a more precise prognosis. Moreover, the difficulty and the outcome of surgery are different according to the phenotype. Indeed, the spatial arrangement of the coronary ostia is of importance when considering the possibility of an autograft. In some cases of type 0, where the aorta has only two sinuses of Valsalva, Ross surgery—by replacing the native BAV by a pulmonary valve autograft—is not advised. It is indeed more challenging, unlike types 1 or 2, which do not involve any major surgical concern. A recent adult study also recommends performing elective aortic valve repair surgery according to the anatomy, with good mid-term results. Finally, because, in case of aortic stenosis in young children, the decision of an intervention is sometimes difficult, it was suggested that 3DE could aid the patient selection for a surgical or catheter-based intervention. Further studies should analyse the outcome of both valve repair surgery and percutaneous dilatation according to each type of the BAV.

Figure 3 Examples of BAV reclassification by 3DE. (A) 2D-TTE short-axis view of a BAV. This valve seems to have only two cusps on this view and was therefore classified as type 0. (B) The same valve was reclassified as type 1 L-N, using 3D-TTE. Indeed, a raphe (star) is clearly seen with this echocardiographic mode. (C) Short-axis 2D-TTE view of a BAV first classified as type 0 and (D) secondly reclassified as type 1 L-R by 3DE. The arrow shows a raphe that was not seen by a classic cross-sectional view. (E) Two-dimensional view suggesting again a true BAV and (F) its visualization by 3DE that allows the depiction of a raphe (star).
Conclusion
Because children with a BAV may have severe aortic valve dysfunction, accurate description of the aortic valve is of interest to organize the follow-up and clarify the prognosis. We showed that 3D-TTE is feasible and reproducible for the accurate description of a BAV in children. This technique seems to provide incremental value for the morphological analysis of aortic leaflets. Further studies are needed to confirm these data and to assess the sensitivity of 3D-TTE for the diagnosis of a BAV.

Conflict of interest: None declared.

References