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Structure and Function of the Tricuspid and Bicuspid Regurgitant Aortic Valve - an echocardiographic study
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Abstract

Objectives:

The emerging new treatment options for aortic valve disease call for more sophisticated diagnostics. We aimed to describe the echocardiographic pathophysiology and characteristics of the purely regurgitant aortic valve in detail.

Methods:

Twenty-nine men, with chronic aortic regurgitation without concomitant heart disease referred for aortic valve intervention, underwent 2D transesophageal echocardiographic (TEE) examination prior to surgery according to a previously published matrix. Measurements of the aortic valve apparatus in long and short axis view were made in systole and diastole and analysed off-line. The valves were grouped as tricuspid (TAV) or bicuspid (BAV) and classified by regurgitation mechanism.

Results:

Twenty-four examinations were eligible for analysis of which 13 presented TAV and 11 BAV. The regurgitation mechanism was classified as dilatation of the aorta in 6 cases, as prolapse in 11 cases and as poor cusp tissue quality or quantity in 7 cases. The ventriculoaortic junction (VAJ) and valve opening were closely related (TAV r = 0.5, BAV r = 0.73) but no correlation was found between the VAJ and the maximal sinus diameter (maxSiD) or the sinotubular junction (STJ). However, the STJ and maxSiD were significantly related (TAV vs. BAV: systole r = 0.9, r = 0.8; diastole r = 0.9, r = 0.7) forming an entity. The conjoined BAV cusps were shorter than the anterior cusps when closed (p = 0.002); the inter-commissural distance of the cusps in the BAV group were significantly different (p = 0.001 resp. 0.03) in both systole and diastole.

Conclusions:
The VAJ was independent of other aortic dimensions and should thereby be considered as a separate entity with influence on valve opening. The detailed 2D TEE measurements of this study add further important information to our knowledge about the function and echocardiographic anatomy of the pathologic aortic valve and root either as a stand-alone examination or as a benchmark and complement to 3D echocardiography. This may have an impact on decisions regarding repairability of the native aortic valve.

**Key words:**
aortic valve insufficiency, transesophageal echocardiography, tricuspid valve, bicuspid valve, cardiac surgery
**Introduction**

The prevalence of aortic regurgitation (AR) is 13% in men and 8.5% in women reported by the Framingham Heart Study [1]. The aortic valve can be incompetent due to inflammatory process, tissue degeneration as in tricuspid aortic valve (TAV) or affected congenitally as in bicuspid aortic valve (BAV). The incidence of BAV is 0.9-1.36% [2] and the malformation usually does not affect hemodynamics in children. The turbulent flow characteristics and the tissue changes may result in both aortic stenosis (AS) and AR. Symptoms of chronic AR may occur first in the young adult or in the middle-aged individual [3]. In surgical series of patients with BAV 69% of the patients were men; 75% suffered from AS (mean age 65 years) and 13% had AR (mean age 46 years) and only 1% of the BAVs functioned normally [4]. In a study of patients with pure AR from the Mayo Clinic [2], 20% of the valves proved to be bicuspid.

Regurgitant aortic valves can be classified by echocardiography based on the mechanism causing regurgitation. Both LePolains de Waroux et al. and Lansac et al. have presented valid classifications. LePolain de Waroux et al. focused mainly on cusp morphology classifying enlargement of the aortic root with normal cusps as type 1, cusp prolapse or fenestration as type 2, and poor cusp tissue quality or quantity as type 3. Regurgitation mechanisms type 1 and 2 are generally considered to be candidates for aortic valve repair [5]. Lansac et al. had aortic root dilatation with (type I) or without (type II) cusp lesion as the starting point for their classification and defined subgroups Ia as dilatation of the sinotubular junction (STJ) and Ib as simultaneous dilatation of the ventriculoartic junction (VAJ) and the STJ. Subgroup IIa includes cusp prolapse, IIb cusp retraction and IIC tear or perforation of the cusp tissue [6]. Type I lesions are generally characterized by a central jet on echocardiography while type II lesions cause an eccentric jet.

According to current guidelines [7] aortic valve replacement (AVR) is the choice of treatment for patients suffering from AS. However, for patients with AR (especially in physically active young individuals) preservation of the native valve eliminates possible complication due to patient prosthesis mismatch and warfarin treatment [8, 9], thereby leading to improved morbidity measures.
and better quality of life for these patients. Regurgitant tricuspid aortic valves are reconstructed and preserved with good short and medium term results measured by grading residual and/or recurrent AR postoperatively [10, 11]. A few studies have been published on preserving BAV with promising initial results [12]. The pre- and intraoperative evaluation and the postoperative follow-up of the aortic valve were performed by echocardiography, preferably transesophageal echocardiography (TEE). Even though a complete echocardiographic TEE examination is performed pre-operatively the decision, whether or not the valve is possible to reconstruct, is made in the operating theatre by surgical visual examination. Therefore a more standardised approach to the preoperative examination could aid surgeons’ assessment and planning of the surgical intervention.

The clinical application of 3D TEE has been expanding. During only a decade the development went from early reports of simple examinations of the aortic valve apparatus [13] to high quality real-time examinations. Nevertheless, 2D TEE still forms the basis of clinical decisions and description concerning aortic valve morphology in most of the tertiary centres.

The aim of the present study is to describe the detailed echocardiographic pathophysiology and characteristics of the purely regurgitant aortic valve by 2D TEE.
Materials and Methods
A series of 29 patients referred to our centre for surgical interventions due to severe chronic aortic regurgitation were included in this study. Patients with concomitant coronary artery disease, other heart valve disease than chronic aortic regurgitation (aortic stenosis defined as aortic orifice area \( \leq 1.6 \text{ cm}^2 \); any history of active endocarditis) and with ascending aortic aneurysm were excluded. All the patients underwent transesophageal ultrasound scan at rest (Vivid 5 or Vivid 7 ultrasound system, GE Healthcare, Wauwatosa, WI) one day prior to the planned surgery. Images were recorded, stored digitally and analysed off-line. Measurements on the aortic root and the cusps were taken according to a previously published matrix [14], which was proved reliable and highly reproducible. The analyses of AR mechanisms were performed according to the classification presented by LePolain de Waroux et al. chosen for its versatility in clinical practice.

In absence of a comprehensive definition, including numerical cut-off for raphe, for echocardiographic classification of BAV a merger of different, although not comprehensive classifications eligible for echocardiographic use was constructed [15-17] to enable classification of valves with challenging echocardiographic image. The aortic valve was classified as TAV when having three visible cusps, three identifiable commissures as absolute criteria and a Y-shaped valve opening in systole with a raphe/fusion less than 10 mm as relative criteria. To be classified as BAV two visible cusps and two identifiable commissures were required as absolute criteria and a fish mouth shaped valve opening and a raphe/fusion longer than 10 mm as relative criteria.

In summary, 2D ECG-synchronized cine loops of the aortic root in the long and short axis views were recorded. Parameters (Fig.1.) were measured in end-diastole and end-systole using the inner edge technique. Each parameter was measured three times and the mean was entered into the statistical analysis. Systolic and diastolic parameters, as well as characteristics for tricuspid and bicuspid valves were analysed by Mann-Whitney and Sign test, Wilcoxon’s matched paired test or Friedman ANOVA, as appropriate, due to sample size and distribution pattern. Tree clustering (Ward’s method based on variance) was used to detect relationships among parameters. For further
specification of relationships of significance within a cluster, Spearman’s rank order correlation ($r$) was applied. Significance was set as $p \leq 0.05$ throughout the statistical analysis. All statistical analyses were performed by STATISTICA 10.0 Statsoft, Tulsa, Okla., USA. The Regional Ethical Review Board in Linköping, Sweden approved the study.
Results
All of the included patients happened to be men. The echocardiographic images were technically satisfactory and eligible for detailed analyses in 24 cases. Patients were grouped based on having tricuspid or bicuspid valve according to the above definition. The demographic characteristics of the two groups were comparable except that patients with BAV were significantly younger (Table 1). The echocardiographic measurements and a comparison between TAV and BAV are presented in Table 2. The opening of the valves was comparable for both BAV and TAV. Raphe was observed between the left and the right coronary cusp in all but one case and the two cusps were unequal [4], the conjoined cusp being bigger in all BAV cases. However, the inter-commissural distance of the non-coronary cusp of TAVs and the anterior cusp of the BAVs were comparable.

Long axis view
A close relationship between the VAJ and valve-opening both in tricuspid ($r = 0.5$) and bicuspid ($r = 0.73$) valves was verified. The VAJ, the STJ and the maximal sinus diameter (maxSiD) were found to be significantly related only in the BAV group in systole ($r = 0.6$ each). The STJ and the maxSiD were significantly related both in the TAV and the BAV groups in systole ($r = 0.9$, $r = 0.8$) and in diastole ($r = 0.9$, $r = 0.7$).

The height of cusps (TAV: $r = 0.9$ resp. 0.9; BAV: $r = 0.9$ resp. 0.8) and sinuses (TAV: $r = 0.9$ resp. 0.9; BAV systole: $r = 0.7$) in LAX were significantly correlated throughout the heart cycle with the exception of sinus height for BAV in diastole ($r = 0.6$), Fig.2. There was an indication of variation in aortic measurements between diastole and systole in BAV (VAJ $p = 0.09$, maxSiD $p = 0.02$, STJ $p = 0.15$).

Short axis view
The commissural distance of the TAV cusps were not significantly different ($p = 0.55$ resp. 0.23) from each other. However, the inter-commissural (IC) distance of the anterior and the posterior cusps in the BAV group were significantly different ($p = 0.001$ resp. 0.03) in both systole and diastole. The commissure-to-raphe distance was not significantly different from the raphe-to-
commissure distance (Fig.1.) but both were significantly less than the IC- distance of the anterior cusp when the valve was closed (p = 0.002 resp. 0.07).

Mechanisms of aortic regurgitation
All the patients had hemodynamically significant aortic regurgitation. The regurgitation mechanisms in the TAV group were classified as five type 1, four type 2 and four type 3. The distribution for the BAV group was one type 1, seven type 2 and three type 3.
Discussion
The main findings of the present study were that (A) the diameter of the ventriculoaortic junction proved to be significantly related to the opening of the valve both in TAV and BAV but (B) it was found to be a separate entity, not related to either the STJ or the maxSiD.

Both TAV and BAV have been studied previously in chronic aortic regurgitation but comparative data are scarce, mainly focusing on functional aspects. Thus, the novelty of the present study consists mainly of describing further complementing echocardiographic details and relations. The anatomy, in particular the echocardiographic anatomy of the aortic root and mechanism of regurgitation has an impact on planning aortic valve interventions, most specifically valve preserving surgery which is well-established and performed with good results in some centres [10-12] both on bicuspid and tricuspid valves but still not widely used in surgical practice. This is partly due to the complexity of the anatomy of the normal aortic root [18], partly because of the fully functional but anatomically basically different variations as in tricuspid and bicuspid valves. Furthermore, the different anatomy has apparent implications for tissue quality [19, 20].

The significant difference in the age of the patients between TAV and BAV in this study can be explained by the different etiology of the chronic aortic regurgitation [19], which is concordant with previous findings [4]. The comparison of the echocardiographic dimensions according to size showed that the majority of parameters were larger in TAV. This is, however, contradictory to previous knowledge which states that the aortic root containing a BAV is larger and more prone to dilatation, even more so in reguritant BAV [21]. Aortic dimensions for both TAV and BAV in this study were larger than diameters of the healthy aortic roots and most so in the TAV group. VAJ and maxSiD changed less than one mm between systole and diastole in healthy TAV and the difference was the same for STJ [14]. In this study of chronic aortic regurgitation there was a non-significant change in TAV for VAJ, maxSiD and STJ but noticeably larger aortic dimensions. The difference in diameters throughout the cardiac cycle was significant for maxSiD in BAV and a certain trend in
VAJ and STJ, indicating increased compliance in the aortic wall, was detected. Similar findings were described in a sample of mildly regurgitant bicuspid valves [22] but as our design did not include studies of elasticity or distensibility it does not allow any conclusions in this aspect. Since we did not find any general dilatation of the aorta in the BAV group the hemodynamically significant AR might be a forerunner and even the cause of imminent dilatation. The larger aortic dimension in AR TAV and the increased aortic wall compliance of the BAV compared with previously studied healthy valves are notable [14]. These two findings might indicate a selection bias due to exclusion of patients with ascending aortic aneurysm.

The diameter of the VAJ was found to be significantly related to the opening of the valve both in TAV and BAV but it was independent from both the STJ and the maxSiD. This is a finding which followed the pattern of normal aortic root previously studied by our group [14] and it supports previous findings made in healthy subjects stating that the VAJ is a separate entity not under the influence of the aorta and should be considered and treated as such. It seems logical to assume it to be under the influence of structures and physiological events in the left ventricle when it is not under aortic influence [6, 14, 23], but that is beyond the scope of this study.

The position of the observed raphe between the left and right coronary cusp and the disparity of the cusps in this study represented the most common pattern for BAV. This is in concordance with the findings of Sabet et al. [4], who have published the single largest material on BAV so far, the pattern of raphe location between the left and the right cusps with unequal cusp size could be seen in 86% respectively 92% of the cases in their surgical material. Despite our modest number of subjects this correlated well with the findings for the type of regurgitation. In our patients the most common type of regurgitation in BAV was type 2 leading us to the conclusion that the conjoined cusps in the posterior cusp in BAV usually have excessive leaflet tissue. The results of visual observation of unequal cusps in BAV were confirmed by the statistical comparison of inter-commissural distances.
LePolain de Waroux et al. showed that the echocardiographically classified type of regurgitation mechanism has prognostic value for the result of valve-sparing surgery. Enlargement of the aortic root with normal cusps (type 1) and excessive tissue, cusp prolapse or fenestration (type 2) are candidates for valve-sparing surgery while type 3 regurgitation due to poor cusp tissue quality or quantity is associated with adverse outcome and more often in need of re-operation resulting in aortic valve replacement [5]. In the same study there were a number of valves classified as repairable, type 1 or 2 regurgitations, which were operated on with valve-sparing techniques which needed re-operation. These valves were suspected of being actually type 3 regurgitations wrongfully classified visually as repairable by the surgeon. In our material too, there were a number of TAV classified as type 3 regurgitation due to stretched cusps though with normal VAJ. These valves may in the future be classified as probably unrepairable based on an extensive echocardiographic examination incorporated in the process of decision complementing the surgeons’ visual examination.

The regurgitation mechanisms in our study were evenly distributed in TAV, but with an overrepresentation of prolapsing valves in BAV corresponding well with our findings of excessive leaflet tissue in BAV. Our echocardiographic description has the potential to provide additional knowledge prior to intervention thereby increasing the understanding of both the echocardiographic anatomy of the regurgitant aortic valve and the possible mechanism of the regurgitation.

Although the clinical application of 3D TEE has been expanding during the last decade, making 3D TEE an integrated part of transcatheter valve implantation procedures, there is a sparse number of studies comparing 3D TEE to 2D TEE or validating 3D TEE for describing the morphology and structures of the aortic valve. Studies comparing 2D TEE and 3D TEE focusing on a few specific measurements are to be found [24]. Some measurements are not even possible to compare between the two modalities because of their built-in limitations. Concerning the regurgitant aortic valve, 3D TEE is validated as a superior method of measuring regurgitant volumes and effective regurgitant
orifice area [25]. 3D TEE has also brought new knowledge of the structures and physiology of the aortic valve and of the aortic root as a complex structure. Real-time 3D TEE examination can today be performed with an acceptable frame rate. However, although 3D visualization provides valuable information on spatial relationships and may aid in determination of regurgitation mechanisms, due to its even higher frame rate and spatial resolution, 2D TEE still has a place in the diagnostics of aortic valve pathology based on its accuracy, which is needed to expose delicate structures such as the aortic valve leaflets. Hence 2D TEE can form the basis of clinical decision making regarding morphology of the regurgitant aortic valve for some time yet and constitute a possible benchmark for future 3D studies.

The fact that all but one of the BAV showed the same raphe position and inter-commissural relations limits the generalizability of the findings in this study. However, the one presented here is still the most common pattern and only less frequent dispositions are absent. Thus, the conclusions still can be considered representative for the majority of the BAV population. All the patients in this study happened to be men, which consequently does not allow conclusions to be drawn for women though studying gender aspects of the morphology of the regurgitant aortic valve was not part of the study design and, therefore, beyond the scope of this study. The gender distribution in purely regurgitant BAV was described earlier as 17.3 : 1 [4]. Furthermore, the small number of patients in this study is balanced by non-parametric analyses of the data to enhance generalizability.

In conclusion, the detailed 2D TEE measurements of this study can add further important information to our knowledge about the function and echocardiographic anatomy of the pathologic aortic valve and root as a stand-alone examination or as a benchmark and complement to 3D echocardiography. This could have an impact on planning the type of aortic valve intervention.

**Fundings**
This work was supported by the Swedish Heart Lung Foundation [HLF 20120570] and ALF Grants from the County Council of Östergötland, Sweden [LIO-204141].
Conflicts of interest
Conflicts of interest: none to be declared
Figure 1  Echocardiographic parameters of the aortic root with a bicuspid valve
Figure 2  Tree cluster analyses for variables seen in the long axis view

TAV LAX systole

TAV LAX diastole

BAV LAX systole

BAV LAX diastole
Figure 3  Tree cluster analyses for variables seen in the short axis view
Table 1  Patient characteristics

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<th>Bicuspid</th>
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<tr>
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<td>N = 13</td>
<td>N = 11</td>
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<td>Age (yrs)</td>
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<td>42 ± 11</td>
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<td>Height (cm)</td>
<td>177 ± 4</td>
<td>181 ± 8</td>
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<tr>
<td>BSA (m²)</td>
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<td>BMI (kg/m²)</td>
<td>28 ± 3</td>
<td>27 ± 3</td>
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## Table 2  Tricuspid and bicuspid aortic valve parameters

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<th>Bicuspid (mm)</th>
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<tr>
<td></td>
<td>Systole</td>
<td>Diastole</td>
<td>p&lt;sub&gt;s&lt;/sub&gt;</td>
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<td>Diastole</td>
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<tr>
<td>Ventriculoaortic junction</td>
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<td>0.05</td>
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<td>27 ± 3</td>
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<tr>
<td>Maximal Sinus Diameter</td>
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<td>41 ± 6</td>
<td>0.07</td>
<td>38 ± 5</td>
<td>36 ± 6</td>
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<td>39 ± 9</td>
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<td>32 ± 6</td>
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<td>0.95</td>
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<td>12 ± 4</td>
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<td>Posterior Cusp Height</td>
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<tr>
<td>RC Cusp Height</td>
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<td>12 ± 3</td>
<td>6 ± 4</td>
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<tr>
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<td></td>
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<td></td>
<td>52 ± 6</td>
<td>49 ± 7</td>
<td>IC Distance</td>
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<tr>
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<td>28 ± 4</td>
<td>Posterior Sinus *</td>
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<tr>
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<td>10 ± 4</td>
<td>18 ± 4</td>
<td>Anterior Cusp Diameter</td>
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</table>
FIGURE LEGENDS

Figure 1

Aortic root and cusp parameters measured in diastole (A & C) and systole (B & D): 1, 2: ventriculaoortic junction diameter (VAJ); 3, 4: maximal sinus diameter; 5, 6: sinotubular junction (STJ); 7: valve opening; 9, 10: Posterior cusp height; 11, 12: Anterior cusp height; 13, 14: Posterior sinus height; 15, 16: Anterior sinus height; 17, 18: Comissure-to-raphe distance posterior cusp; 19, 20: Raphe-to-commissure distance posterior cusp; 21, 22: Inter-commissural distance non-coronary (NC) sinus; 23, 24: Posterior cusp diameter 1; 25, 26: Posterior cusp diameter 2; 27, 28: NC cusp diameter

Figure 2


Figure 3


Table 1

Patients with bicuspid and tricuspid aortic valve had comparable demographical parameters except age. BSA: body surface area, BMI: body mass index.
Table 2

STJ: Sinotubular junction; LC: left coronary; RC: Right coronary; NC: Non-coronary; IC: Inter-commissural. Measures in mm, mean ± SD. * calculated from commissure-to-raphe distance posterior cusp and raphe-to-commissure distance posterior cusp.
References


