Valve Configuration Determines Long-Term Results After Repair of the Bicuspid Aortic Valve

Diana Aicher, MD; Takashi Kunihara, MD; Omar Abou Issa, MD; Brigitte Brittnier, MD; Stefan Gräber, MD; Hans-Joachim Schäfers, MD

**Background**—Reconstruction of the regurgitant bicuspid aortic valve has been performed for >10 years, but there is limited information on long-term results. We analyzed our results to determine the predictors of suboptimal outcome.

**Methods and Results**—Between November 1995 and December 2008, 316 patients (age, 49±14 years; male, 268) underwent reconstruction of a regurgitant bicuspid aortic valve. Intraoperative assessment included extent of fusion, root dimensions, circumferential orientation of the 2 normal commissures (≥160°, ≤160°), and effective height after repair. Cusp pathology was treated by central plication (n=277), triangular resection (n=138), or pericardial patch (n=94). Root dilatation was treated by subcommissural plication (n=100), root remodeling (n=122), or valve reimplantation (n=2). All patients were followed up echocardiographically (cumulative follow-up, 1253 years; mean, 4±3.1 years). Clinical and morphological parameters were analyzed for correlation with 10-year freedom from reoperation with the Cox proportional hazards model. Hospital mortality was 0.63%; survival was 92% at 10 years. Freedom from reoperation at 5 and 10 years was 88% and 81%; freedom from valve replacement, 95% and 84%. By univariable analysis, statistically significant predictors of reoperation were age (hazard ratio [HR]=0.97), aortoventricular diameter (HR=1.24), effective height (HR=0.76), commissural orientation (HR=0.95), use of a pericardial patch (HR=7.63), no root replacement (HR=3.80), subcommissural plication (HR=2.07), and preoperative aortic regurgitation grade 3 or greater. By multivariable analysis, statistically significant predictors for reoperation were age (HR=0.96), aortoventricular diameter (HR=1.30), effective height (HR=0.74), commissural orientation (HR=0.96), and use of a pericardial patch (HR=5.16).

**Conclusions**—Reconstruction of bicuspid aortic valve can be performed reproducibly with good early results. Recurrence and progression of regurgitation, however, may occur, depending primarily on anatomic features of the valve. *(Circulation. 2011;123:178-185.)*

**Key Words:** aortic valve ▪ regurgitation, aortic valve ▪ bicuspid valve

Bicuspid aortic valve (BAV) anatomy is the most common congenital cardiovascular malformation. Relevant aortic stenosis occurs at a mean age of ≈60 years or relevant regurgitation at a mean age of ≈30 years.1,2 Aortic dilatation may be associated with bicuspid valve anatomy in 50% to 60% of individuals. The exact mechanism of proximal aortic dilatation has not been clarified, but there is increasing evidence of inherent aortic wall abnormality leading to dilatation and dissection.3,4 Reconstruction of the regurgitant BAV was proposed as early as 1992.5 Others, including our group, have been able to reproduce reconstructive surgery for this setting with good early results.6 Valve-preserving aortic replacement has been performed in those patients who require aortic replacement for prognostic reasons.4 So far, only a few mid- to long-term results have been published for reconstruction of a BAV.7,8 Repair failures have been observed and related to secondary aortic dilatation7 or the need for triangular resection.8 The number of patients studied, however, has been limited, and as yet there is no information on 10-year results of reconstruction of BAVs.

**Clinical Perspective on p 185**

The anatomy of the BAV is less uniform than generally believed. It is recognized as normally consisting of 2 rudimentary cusps that are fused, and the commissure between these 2 cusps is of subnormal height. The “normal” nonfused cusp is commonly larger and has 2 commissures of normal height. There are different anatomic variants of cusp fusion, with fusion of the right and left cusps being the most frequent.9 The degree of fusion may vary from complete to minimal (ie, only a few millimeters).10 Less recognized is
the fact that there is also variability in the circumferential orientation of the commissures of the normal cusp not involved in fusion. These commissures rarely exhibit a 180° orientation as a naturally symmetrical bicuspid valve. It has also been shown that the commissures may be close to a 120° orientation.11

Although we have generally been impressed with the reproducibility of the standard repair approach,12 we have also encountered midterm repair failures related to the geometric alterations associated with aortic replacement.12 With a follow-up now reaching up to 13 years and a larger patient cohort, we decided to analyze long-term results of BAV repair to determine the predictors of good long-term functional outcome.

Methods

Between November 1995 and December 2008, 316 patients (268 male; age, 49±14 years; age range, 3 to 79 years; 0 to 19 years, n=6; 20 to 29 years, n=17; 30 to 39 years, n=53; 40 to 49 years, n=93; 50 to 59 years, n=73; 60 to 69 years, n=56; 70 to 79 years, n=18) underwent surgery with repair or preservation of a BAV. The primary indication for surgery was severe aortic regurgitation (n=201), ascending aeurysm (n=89), aortic valve endocarditis (n=11), acute dissection (n=8), coronary artery disease (n=5), or severe mitral regurgitation (n=2). The preoperative degree of aortic regurgitation ranged from mild to severe (mean, 3.1±0.4; mild, n=31; moderate, n=55; severe, n=230). Mean preoperative left ventricular end-diastolic diameter was 60±9 mm (range, 46 to 86 mm); mean aortoventricular diameter (AVD) was 27±5 mm (range, 21 to 35 mm); mean sinutubular diameter was 32±9 mm (range, 20 to 50 mm; Table 1).

Informed consent was obtained from all patients. The institutional ethics committee agreed to the analysis and publication of the data in anonymized form.

Operative Technique

In all patients, the chest was opened by a median sternotomy, and aortic and right atrial cannulation was used in most instances. After aortic cross-clamping, the ascending aorta was opened by a transverse incision 5 to 10 mm above the sinutubular junction, and blood cardioplegia was administered into the coronary ostia.

Aortic root dimensions were determined by intraoperative transesophageal echocardiography in 299 patients; in addition, sinutubular and aortoventricular dimensions were assessed in all patients by intubation with a valve sizer or Hegar dilator after induction of cardioplegia. The valve anatomy was studied for the presence of partial or complete fusion of 2 cusps, and the circumferential orientation of the 2 true commissures was recorded.

Stay sutures were placed under tension in the 2 commissures of the nonfused cusp (mostly noncoronary). Additional stay sutures were placed as needed for stable exposure to expand the aortic root.

In the last 129 patients, the geometric height of the nonfused cusp was measured to rule out retraction. Effective height (eH) of this cusp13 was measured and corrected by plicating the free margin if <9 mm.

Two 5-0 Prolene sutures were placed into the corresponding parts of the free cusp margin, ascertaining that equidistant parts were aligned as measured from the corresponding commissure. Central plicating sutures were then placed on the free margin of the fused cusp until both free margins were at an identical height. If extensive tissue redundancy or limited fibrosis was encountered, triangular excision of cusp tissue with direct approximation of cusp tissue was chosen. In the presence of more extensive pathology (ie, calcification in the raphe), the pathological tissue was excised and the cusp was reconstructed by implantation of an autologous pericardial patch.

Figure 1. BAV with a commissural orientation of 125°.

Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n</th>
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<tbody>
<tr>
<td>Age, n</td>
<td></td>
</tr>
<tr>
<td>0–19 y</td>
<td>6</td>
</tr>
<tr>
<td>20–29 y</td>
<td>17</td>
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<tr>
<td>30–39 y</td>
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<td>56</td>
</tr>
<tr>
<td>70–79 y</td>
<td>18</td>
</tr>
<tr>
<td>Sex, F/M</td>
<td>48/268</td>
</tr>
</tbody>
</table>

AR indicates aortic regurgitation; LVEDD, left ventricular end-diastolic diameter; and STD, sinutubular diameter.

The pericardium was preserved in 1.5% glutaraldehyde for 3 minutes and rinsed for 2 minutes. Limited calcific plaques were merely debrided in 6 instances. If aortoventricular junction exceeded 29 mm, subcommisural plication sutures14 were placed under the commissures of the nonfused cusp.

In the presence of aortic aneurysm not involving the root (sinus diameter <43 mm; n=75), ascending aortic replacement was performed. In the first 36 patients, this was done after cusp repair; in the subsequent 39 patients, this was done before cusp repair to minimize...
the risk of induced symmetrical prolapse.\textsuperscript{12} If dilatation also involved the root (sinus diameter $>$43 mm; $n=122$), root remodeling was performed with the technique published previously.\textsuperscript{12} In the first 77 individuals, this was done after valve repair; in the subsequent 45 patients, it was done before valve repair.

All patients were studied intraoperatively with transesophageal echocardiography. The degree of aortic regurgitation was determined primarily by the size of the regurgitant jet determined by color Doppler and the downward slope of the continuous-wave Doppler.\textsuperscript{15} All patients were studied at least once before discharge (ie, between postoperative days 5 and 7). Further transthoracic echocardiography was performed at 6 and 12 months and yearly thereafter. Follow-up was complete in 97% of patients and ranged from 1 to 163 months for a cumulative follow-up of 1253 patient-years (mean, 4.0±3.1 years). Follow-up was actual as of June 2009. Freedom from aortic regurgitation grade 2 or greater was defined by the event, which was occurrence of aortic regurgitation grade 2 or greater, and the time, which was the date of first diagnosis of aortic regurgitation grade 2 or greater. The time of first diagnosis of aortic regurgitation grade 2 or greater was recorded and incorporated into the actuarial analysis.

Parameters analyzed were age, sex, presence of comorbidity, and preoperative degree of aortic regurgitation. Intraoperative parameters were prerepair root dimensions (AVD, sinutubular diameter), commissural orientation, site and extent of cusp fusion, and postrepair eH. Operative aspects were use of subcommissural plication, use of a pericardial patch, root replacement, cusp plication, or triangular resection.

All data are presented as mean±SD. Receiver-operating characteristics analysis was used to determine thresholds of specific predictors for reoperation (ie, eH, AVD, and commissural orientation). Kaplan-Meier curves were calculated for freedom from relevant regurgitation, from reoperation, and from valve replacement with a commercially available software package (Prism, GraphPad Inc, San Diego, CA). Group differences were tested by a log-rank test. Factors influencing freedom from reoperation on the aortic valve were analyzed in multivariable analysis with the Cox proportional hazards model. To study the dependency of AVD on the degree of preoperative aortic regurgitation, we used ANOVA with the Bonferroni posthoc test. This analysis was performed with the statistical package SPSS version 17 (SPSS Inc, Chicago, IL). A value of $P<0.05$ was considered statistically significant.

### Results

Cusp fusion was seen mostly between the right and left coronary cusps ($n=281$, 89%), less often between the right coronary and noncoronary cusps ($n=30$, 9%), and very rarely between the left coronary and noncoronary cusps ($n=5$, 1%). We found partial ($n=122$) or complete ($n=194$) fusion of the 2 involved cusps. The orientation of the 2 normal commissures varied. We divided the patients into 2 groups; the first group had almost symmetrical orientation of the commissures ($\leq160^\circ$; $n=51$), and the second had an orientation of $\leq160^\circ$ ($n=265$; Figure 1).

Concomitant procedures were aortic arch replacement (partial, $n=35$; total, $n=2$), mitral valve repair ($n=12$), and coronary artery bypass grafting ($n=28$). Extracorporeal circulation was 80±30 minutes; myocardial ischemia was 57±23 minutes; and circulatory arrest lasted 7±6 minutes.

In-hospital mortality was 0.63% ($n=2$). No patient died after emergency surgery. No patient underwent intraoperative conversion to replacement for immediate valve failure. Two patients died after elective surgery ($2$ of 297, 0.67%). The causes of death were mesenteric ischemia ($n=1$) and malignant ventricular arrhythmia ($n=1$). Five patients died during the follow-up period (6 to 64 months postoperatively). Survival was 99% at 5 years and 92% at 10 years. Four patients had thromboembolic events (ie, transitory ischemic attacks in conjunction with atrial fibrillation). Actuarial
freedom from aortic regurgitation grade 2 or higher was 81% at 10 years.

Reoperation was necessary for repair failure \((n=30)\), endocarditis \((n=2)\), or calcific stenosis \((n=1)\) between 4 hours and 10 years postoperatively. Freedom from reoperation at 5 and 10 years was 88% and 81%. In 14 of 33 patients, the valve was rerepaired; freedom from valve replacement was 95% and 84% at 5 and 10 years.

Univariable analysis revealed significant clinical, anatomic, and operative predictors of need for reoperation; patients <40 years of age \((P=0.021)\) and patients with a higher degree of preoperative aortic regurgitation \((P=0.0029)\) had a higher risk for reoperation. Patients with a commissural orientation \(<160^\circ\) \((P=0.000;\) Figure 2) and an aortoventricular junction of \(>28\) mm \((P=0.009;\) Figure 3) required reoperation significantly more often. Interestingly, ANOVA with the posthoc Bonferroni test showed a significant increase in aortoventricular size with higher degrees of preoperative aortic regurgitation \((P<0.0001)\). The absence of root replacement \((P=0.002;\) Figure 4), the use of subcommissural plication \((P=0.04)\), and the use of a pericardial patch \((P=0.000)\) had a negative effect on repair durability \((P=0.038;\) Figure 7).

A postrepair eH \(<9\) mm had also a negative effect on repair results \((P=0.003;\) Figure 8). Receiver-operating characteristics analysis revealed an eH of \(\geq9\) mm as a positive factor for valve stability \((\text{area under the curve, 0.635};\) sensitivity, 0.797; specificity, 0.42). An AVD of \(\geq29\) mm showed similar results \((\text{area under the curve, 0.620};\) sensitivity, 0.45; specificity, 0.778), as did commissural orientation \(<160^\circ\) \((\text{area under the curve, 0.630};\) sensitivity, 0.81; specificity, 0.62).

The number of cusps corrected \((P=0.12)\), different cusp fusion patterns \((\text{right/left, noncoronary/left, noncoronary/right}; P=0.36)\), and extent of fusion \((\text{partial or complete}; P=0.1147)\) did not have an influence on freedom from reoperation. Repair results were not influenced by cusp margin plication \((P=0.60)\) or triangular resection \((P=0.52)\).

Multivariable analysis with continuous \((\text{age, AVD, eH, commissural orientation})\) and dichotomous variables \((\text{pericardial patch, subcommissural plication, root replacement})\) revealed age \((\text{HR}=0.96; P=0.001)\), commissural orientation \(<160^\circ\) \((\text{HR}=0.96; P=0.002)\), use of a pericardial patch \((\text{HR}=5.16; P=0.000)\), AVD \(>28\) mm \((\text{HR}=1.30; P=0.007)\), and eH \(<9\) mm \((\text{HR}=0.74; P=0.002)\) as statistically significant risk factors for reoperation \((\text{Table 2})\).

**Discussion**

In the past 15 years, reconstruction of the aortic valve has become an increasingly attractive alternative to replacement.\(^{16–18}\) Because the bicuspid valve affects young individuals and has only 1 coaptation line, cusp repair techniques have dealt mainly with bicuspid rather than tricuspid aortic valves.\(^{7,12,19–23}\) Initial attention has focused primarily on the fused cusp. Cosgrove and coworkers\(^5\)
published a technique for correcting prolapse of the fused cusp. In addition, triangular resection of abnormal cusp tissue and/or insertion of a pericardial patch have been shown to be feasible and to produce good early results.8,23,24 The application of valve-preserving aortic replacement has been published using both root remodeling and valve reimplantation.6,20,25 In the meantime, it has become evident that reconstruction of the aortic valve is associated with fewer valve-related complications than reported previously for valve replacement.16,26 The present results principally confirm the positive early results published previously in patients with BAVs. Hospital mortality was low despite the cardiovascular comorbidity, and no intraoperative conversions to replacement were necessary. Long-term survival was good, even though there is currently no control group with valve replacement for direct comparison. The incidence of valve-related complications was low, with recurrent aortic regurgitation being the most frequent late complication of repair. Overall freedom from reoperation at 10 years was only 81%, which is not ideal. On the other hand, 7% of patients were <30 years of age and 54% were <50 years of age. In these age groups, 10-year freedom from reoperation after biological aortic valve replacement has been reported to be between 33% and 68%,27–29

Although it is well known that BAVs have a tendency to develop regurgitation, the exact factors (ie, the mechanism[s] leading to regurgitation) have not been clearly defined. This becomes important in the context of repair, when the goal is to eliminate the exact pathomechanism of aortic regurgitation. Stress distribution of the BAV has been studied previously; however, that publication contains limited data.30 Initial observations indicate that the fused cusp is exposed to abnormally high stress in both diastole and systole. This was thought to be the explanation for progressive distortion of the fused cusp with elongation of the free margin and was considered to be the reason for early calcification and development of calcific aortic stenosis. In the previous analysis, however, only 3 bicuspid valves were studied, and the authors found marked differences between the 3 valves.30 Thus, the published data do not cover the wide spectrum of anatomic variants of BAVs. So far, the clinically and echocardiographically apparent prolapse of the fused cusp has been considered the main pathomechanism of aortic regurgitation in BAVs.19,31

The first repair approaches focused on correcting the prolapse of the fused cusp by shortening its free margin. The prolapse, however, was defined by visual inspection (ie, the fact that the fused free margin was apparently longer than that of the “normal” cusp). We initially assumed this definition, and it became obvious to us only later that this definition did not include all possible valve pathologies. With the introduction of eH,13 we found that in many patients not only the fused cusp but also the nonfused cusp exhibited prolapse, most likely as a result of pathological flow with chronic regurgitation. This is reflected by the fact that 68% of our patients required correction of prolapse on both cusps. The extension of prolapse correction to both cusps in BAVs did not have a negative influence on valve stability.

Progressive dilatation of the aorta has been documented in patients with BAVs and is a known pathomechanism leading to aortic regurgitation. On the other hand, we have seen marked root dilatation in the presence of minimal regurgitation. Interestingly, we have observed a correlation between the degree of preoperative aortic regurgitation and size of the aortoventricular junction, indicating that this structure may be an important determinant of valve competence. The size of the aortoventricular junction was also an independent risk factor for recurrence of regurgitation after repair. These observations underscore the finding that dilatation of the
The aortoventricular junction seems to play an important role in the pathomechanism of aortic regurgitation in BAVs. Thus, our findings are in concordance with those of Lansac and coworkers.\textsuperscript{32}

In our series, the dilatation of the aortoventricular junction could not be neutralized by the addition of subcommissural plication; durability was actually somewhat worse with the use of sutures. It is unclear whether this finding is due to the fact that this form of root plication carries a particular risk with local damage to the cusps, as we have seen in some patients, or rather is the result of suboptimal correction of aortoventricular dilatation. This brings up the question of optimal stabilization of the aortoventricular junction. Reimplantation of the aortic valve leads to unphysiological valve opening and closing with loss of aortic wall distensibility.\textsuperscript{33} Moreover, as a result of contact between the aortic cusps and the aortic graft, damage of the aortic cusps has been observed.\textsuperscript{34}

Interestingly, we have seen significant improvement in valve stability with the use of root remodeling, even though this technique does not specifically address the aortoventricular junction. A new technique of aortoventricular stabilization has been proposed by Lansac et al.\textsuperscript{35} They added an external subvalvular prosthetic ring to the remodeling technique and found improved short-term results with regard to freedom from reoperation compared with isolated remodeling.\textsuperscript{35} In the last few months, we have used a similar approach with circular stabilization of the aortoventricular junction by a circular external suture, either alone or in combination with root remodeling. Short-term results are encouraging; however, long-term results are necessary for evaluation of that technique.

In the present series, we have observed a pattern of anatomic variability similar to that published previously.\textsuperscript{9} Right/left fusion was the most frequent (89%). Complete fusion was seen in 61%, and the distribution of commissural orientation was identical to the data published previously. The consistency in anatomic pattern between the 2 different series despite differences in approach (autopsy versus surgery for valve dysfunction, all valves versus regurgitant valves) indicates that these anatomic variations do not differ in their tendency to develop dysfunction. Aortic dilatation was present in 65% of the individuals, similar to the prevalence published previously for bicuspid anatomy.

Interestingly, we saw an influence of anatomy with a constant repair approach (ie, leaving the BAV in a bicuspid design). Although the different cusp fusion patterns (right/left, noncoronary/left, noncoronary/right) and extent of cusp fusion (partial or complete) had no influence on repair results, the different orientation of the commissures led to different long-term results. Therefore, a possible explanation is an increased stress in certain patterns of bicuspid anatomy, as suggested previously.\textsuperscript{30} Whether it is reasonable to preserve the bicuspid design may be argued. Tricuspidization of the BAV has been proposed by some groups\textsuperscript{22,23,36} but was obviously possible in only a limited proportion of patients. There were intraoperative conversions to valve replacement for repair failure.\textsuperscript{22} This is a geometrically challenging procedure in most instances. Only in patients having an orientation of the normal commissures close to 120°, characterized by suboptimal durability in our series, could tricuspidization be a better option than preserving the bicuspid design. Alternatively, root replacement (ie, remodeling) could primarily be chosen in these instances. It allows better orientation of the commissures (>150°), and the superior results achieved in our series may have been due to this geometric result. In addition, root remodeling also partially neutralized the negative effect of the enlarged aortoventricular junction and may thus be seen as a means of stabilizing the valve repair.

Table 2. Results of Multivariable Analysis of Predictors for Reoperation

<table>
<thead>
<tr>
<th>HR</th>
<th>95% Confidence Interval</th>
<th>P</th>
</tr>
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<tbody>
<tr>
<td>Age</td>
<td>0.955</td>
<td>0.928–0.982</td>
</tr>
<tr>
<td>eH</td>
<td>0.740</td>
<td>0.612–0.894</td>
</tr>
<tr>
<td>AVD</td>
<td>1.302</td>
<td>1.076–1.575</td>
</tr>
<tr>
<td>Commisural orientation</td>
<td>0.961</td>
<td>0.938–0.985</td>
</tr>
<tr>
<td>Pericardial patch</td>
<td>5.175</td>
<td>2.100–12.753</td>
</tr>
<tr>
<td>Subcommissural plication</td>
<td>0.699</td>
<td>0.299–1.633</td>
</tr>
<tr>
<td>Root repair</td>
<td>2.354</td>
<td>0.770–7.192</td>
</tr>
</tbody>
</table>
The findings of the present analysis have an important impact on decision making in favor of or against repair. Considering the prognostic criteria of our analysis, one should be hesitant to repair a BAV if the AVD is $\geq 29$ mm, if commissural orientation is $< 160^\circ$, and if a pericardial patch is required for partial cusp replacement. On the other hand, we have started to reduce AVD systematically, and we have become more liberal with the use of root remodeling to change the position of the commissures. Further follow-up is necessary to define whether these technical modifications will actually improve long-term results in these high-risk morphologies.

Conclusions

The present analysis confirms previous data showing a low incidence of valve-related complications after reconstruction of the regurgitant BAV. Stenosis is very infrequent up to 14 years after surgery. Repair failure is the most frequent complication, and it is influenced by such anatomic characteristics of the valves as commissural orientation or AVD. Specific strategies still have to be developed and proven for the subtypes of bicuspid valves with these risk factors.

Disclosures

None.

References

Valve replacement has been a reliable therapy for bicuspid aortic valve dysfunction for decades. To minimize valve-related complications, repair techniques have been developed in the last 2 decades. Repair of the bicuspid valve has been less challenging geometrically because only 1 coaptation line has to be corrected. Different publications, however, have given a puzzling view of the functional results of reconstruction with generally excellent early results and a worrisome rate of midterm failures. In the present study, we have found answers and new questions. The positive message is that reconstruction of bicuspid aortic valves is worthwhile for the low prevalence of valve-related complications. Repair works well with excellent durability in certain anatomical situations but should be avoided, at least with current reconstructive techniques, in others. A strong influence of anatomical characteristics on long-term durability of repair was found, with commissural orientation and degree of annular dilatation as the 2 most important predictors. Repair also had to normalize cusp configuration to achieve a good long-term result. On the other hand, the findings also emphasize the fact that bicuspid anatomy is not constant but rather includes a wide spectrum of anatomic variations. It is unclear whether annular dilatation is determined by anatomy or the duration of regurgitation. Thus, we need to define whether it can be neutralized by earlier repair. Surgeons will have to develop new strategies to ultimately allow durable reconstructive surgery in a larger proportion of patients with this anomaly.
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