The Influence of Operative Techniques on the Outcomes of Bicuspid Aortic Valve Disease and Aortic Dilatation

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Background. Bicuspid aortic valve is associated with aortic aneurysm formation that may extend beyond the ascending aorta.

Methods. Between 1979 and 1997, 143 bicuspid aortic valve patients had aortic valve operations with replacement of an aneurysmal ascending aorta: 93 (65%) underwent full root replacement and 50 (35%) underwent separate valve and graft replacement. Distal aortic anastomosis was open in 42 patients (29%) and closed in 101 (71%). Late survival and complications were compared by surgical technique.

Results. Patients undergoing full root replacement tended to be younger (mean age 46 ± 16 vs 59 ± 13, p < 0.001) and presented with more aortic insufficiency (80% vs 35%, p < 0.001). Three (2.1%) hospital deaths occurred. Event-free survival was 82% (95% confidence interval, 75% to 88%) at 10 years and 41% (95% confidence interval, 11% to 71%) at 20 years. At a median follow-up of 11.5 years, the incidence of new aneurysms and late aortic complications were not significantly different among the procedure groups. Age at the time of operation was the only predictor of late survival (hazard ratio, 1.07; p = 0.007).

Conclusions. Aortic root replacement with distal aortic reconstruction can be achieved with very low operative mortality and excellent long-term outcomes in patients with bicuspid aortic valve and dilated ascending aorta. The type of surgical procedure done in the aortic root and in the distal ascending aorta does not influence late survival, subsequent operation, or aortic complications. This is likely influenced by our patient-specific strategy when replacing the aortic root and distal ascending aorta.

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Bicuspid aortic valve (BAV) has been linked to a spectrum of clinical conditions. Recognized as most common congenital heart anomaly, it is present in 0.5% to 2% of the general population [1, 2]. Despite the seemingly simple anatomic lesion, it is estimated that serious complications that require intervention will develop in one-third of BAV patients [3]. Surgical intervention is the mainstay treatment for BAV complications. Ascending aortic dilatation with subsequent aortic rupture and dissection poses a serious challenge [4].

Some reports have shown that the aorta continues to expand after valve replacement [5]. Because of this, reoperation for aortic aneurysm as well as late aortic dissection and sudden death are significantly higher in this group [6, 7]. Although the proximal ascending aorta is thought to be the most commonly affected segment [8, 9], recent imaging studies of the thoracic aorta using computed tomographic angiography (CTA) and magnetic resonance angiography (MRA) show more diffuse and distinctive patterns of aortopathy extending from the aortic root to the proximal aortic arch [10, 11]. Whether this phenomenon is due to intrinsic aortic wall abnormalities or just hemodynamic stress is still a matter of debate [12].

Over the years, surgical techniques have been devised to treat patients with BAV disease and dilated ascending aorta [4]. This is primarily done by replacing the ascending aorta with a tube graft. Some authors advocate a more radical resection because of the possible potential for late dilatation and dissection in the remaining distal ascending aorta and aortic root [13–15]. This involves replacing the aortic root, aortic arch, or both in conjunction with the ascending aorta.

This study reports our long-term results and experience with the different surgical techniques in patients with BAV disease and ascending aortic aneurysm who had concomitant replacement of the ascending aorta.

Patients and Methods

Approval for this study was granted by our institutional ethics board, and individual patient consent was waived. A computerized database was retrospectively examined to identify all patients with BAV who underwent aortic valve operations with concomitant replacement of the ascending aorta at the Toronto General Hospital. Our
database was queried from its starting date in January 1979 to December 1997, allowing a minimum of 10 years of follow-up. We identified 143 consecutive patients.

All patients were operated on by one surgeon, which reflected consistency in the operative approach and decision making. The aortic valve was documented as bicuspid by the operative note and pathology report. The mean ± standard deviation diameter of the ascending aorta measured 6.0 ± 1.6 cm. This was documented by intraoperative echo or by direct measurement. The operative technique for the distal aortic anastomosis and the decision to do a full root replacement was left to the operating surgeon.

Surgical Technique

The techniques for aortic valve replacement and the choice for valve prosthesis were previously described [16, 17]. The thoracic aorta was accessed through a median sternotomy. The arterial cannula was placed in the proximal aortic arch. Groin cannulation was used in aortic dissection. All patients underwent cardiopulmonary bypass with mild-to-moderate systemic hypothermia. A short period moderate hypothermic (25° to 28°C) circulatory arrest without adjunctive cerebral protection was performed in 32 patients in whom the ascending aorta was replaced up to the innominate artery trunk in an open distal fashion. Open distal anastomosis under deep hypothermic (18°C) circulatory arrest with retrograde or antegrade cerebral perfusion was used for hemiarch in 9 patients and for total arch replacement in 1 patient. Direct infusion of intermittent cold antegrade crystalloid cardioplegia was used until 1989, and cold blood cardioplegia was used thereafter.

The extent of aortic resection in our practice is patient-specific [17]. For young patients with dilated aortic roots (≥4.0 cm) who choose a mechanical prosthesis, we perform a composite replacement of the aortic valve, root, and ascending aorta up to the innominate artery. Alternatively, if the patient chooses a tissue valve and the coronary ostia are not displaced, we perform a supra-coronary replacement of the ascending aorta with a Dacron (DuPont, Wilmington, DE) tube graft. If the noncoronary sinus is dilated or thinned, the tube graft is tailored to create a neosinus secured to the aortic annulus. The aortic root is replaced with a tissue valve secured inside a Dacron tube, homograft, pulmonary autograft, or aortic valve-sparing, once the coronary ostia are displaced. Older patients receive a separate tissue valve and graft, provided that the root is not massively dilated. Figure 1 summarizes the different techniques.

Follow-Up

All demographic and perioperative outcomes were retrieved from medical records, operative notes, and the cardiac surgical database. Late follow-up was collected and documented in a separate database using mail questionnaire, direct communication with the patient or a close relative, and by contacting the referring physician. Follow-up was completed between July 1, 2008, and January 31, 2009. Death certificates and autopsy results were retrieved for patients who were thought to have died from cardiac causes or had sudden death. Follow-up

Fig 1. Schematic illustration shows techniques used after ascending aortic resection in bicuspid aortic valve, consisting of (A) closed distal anastomosis: aortic arch left intact (n = 101); (B) open distal anastomosis: aortic arch replaced (n = 42); (C) separate valve and supracoronary aorta replacement: aortic sinuses left intact (n = 50); and (D) full root replacement: all sinuses are resected and coronaries reimplanted (n = 93).
time was measured from the date of the operation to the earlier of morbid events, death, or last contact alive. In this study, the follow-up was 99% complete with a median of 11.5 years (range, 0 to 22 years; Q1 = 9.5, Q3 = 13.5). The total cumulative follow-up was 1595 patient-years.

Statistical Analysis
Statistical analysis was done using SPSS 15.0 software (SPSS Inc, Chicago, IL). Categoric data were tabulated in 2 × n tables and two-group comparisons were made using the χ² test or Fisher exact test. Continuous variables are expressed as means ± standard deviation. The t test was used to compare two-group continuous variables. The Mantel log-rank test determined difference in event-free survival. Variables deemed important by the univariable analysis or those clinically significant were entered into a multivariable Cox proportional hazards model. A propensity score predicting the probability for root replacement was created for each patient in the series. Independent predictors were compared before and after propensity adjustment. Multivariable analysis results were expressed as hazard ratios (HR) and p values. A two-tailed value of p < 0.05 was considered to be significant for all statistical tests.

Results

Study Population
Depending on the surgeon’s choice to preserve or replace the aortic root, patients were categorized into two broad groups: 93 patients had “full root” replacement and 50 patients designated the “no root” intervention group who had aortic valve replacement combined with suprakoronary replacement of the ascending aorta. The demographics for the two groups are reported in Table 1. Patients who had full root replacement were significantly younger and were more likely to have aortic regurgitation preoperatively. Except for more hypertension in the older no root group, comorbidities were similar.

Forty-two patients (29%) required hypothermic circulatory arrest to construct an open distal anastomosis. Because of the technical nature of aortic root replacements, the mean cardiopulmonary bypass and aortic cross clamp times were longer in this group. Table 2 summarizes some of the operative characteristics.

Early Outcome

There were 3 (2.1%) 30-day operative deaths; two died of cardiac related issues, and one died of sepsis at 15 days. Hospital stay was significantly longer for the full root group (Table 3). Although not significant, there seemed to be a trend for higher rates of insertion of intraaortic balloon pumps, low cardiac output syndrome, sepsis, and reexploration for bleeding in the full root group. Important perioperative outcomes are listed in Table 3.

Late Survival

During the course of follow-up, there were 10 late deaths in the full root replacement group and 23 deaths in the no root intervention group. The event-free survival in this series was 82% (95% confidence interval, 75% to 88%) at 10 years and 41% (95% confidence interval, 11% to 71%) at 20 years. Table 4 summarizes the major adverse cardiac events in each group. Kaplan-Meier analysis (Fig 2) showed superior survival among patients who under-
went full root replacement (p < 0.001). However, propensity-adjusted Cox regression identified the patient’s age at the time of operation as the only independent predictor of all-cause mortality (HR, 1.07; p < 0.007; Fig 3).

Late Distal Aortic Complications

Complications associated with the distal ascending aorta and aortic arch occurred in 6 patients, in whom an aneurysmal distal ascending aorta was documented on reoperation. No patient came back with aortic dissection. At the initial operation, all had “closed” distal anastomosis to a normal sized aortic arch (2.95 ± 0.42 cm) and a tissue valve separated from the ascending graft. It took an average of 11.4 ± 4.4 years for the distal ascending aorta to dilate. At 15 years, Kaplan-Meier curves (Fig 4) illustrating freedom from aortic complications or sudden death show no significant difference between the open and closed distal anastomosis patients (97% ± 3% vs 83% ± 7%; p = 0.22).

Cardiac Death

Death from cardiac-related conditions was more evident in the group with no root replacement. This was mostly attributed to fatal myocardial infarction, congestive heart failure, and sudden death (Table 4). All the risk factors were analyzed in a propensity-adjusted Cox regression model that included age at the time of the operation, tissue aortic valve prosthesis, functional class, ventricular function, presence of coronary artery disease, hyperlipidemia, and hypertension. Only the patient’s age predicted late cardiac death (HR, 1.07; p = 0.018).

Reoperation

Structural valve dysfunction was the most common indication for reoperation in the no root replacement group (Table 4). Aortic root aneurysm developed on follow-up in 3 patients in those with structural dysfunction. In those with full root replacement, prosthetic valve endocarditis was the most common indication for reoperation. Kaplan-Meier freedom from reoperation showed no difference between the two groups (p = 0.46). Propensity-
adjusted Cox regression revealed tissue aortic valve bioprosthesis as the only independent predictor for late reoperations (HR, 3.54; \( p < 0.028 \)).

Comment

BAV is inherently associated with valvular and vascular complications. Attention in recent years has focused on characterizing aortic dilatation and identifying the markers predicting aneurysm growth and risk of rupture and dissection in patients with BAV disease [18]. Davies and colleagues [19] documented the natural history of aortic dilatation in patients with unoperated-on BAV. For 2 decades, 514 patients with ascending aortic aneurysm were prospectively monitored, of which 70 (13.4%) were diagnosed to have BAV. Aneurysm growth rates in the BAV group were 0.19 cm/y compared with 0.13 cm/y in those with tricuspid aortic valves (TAV). A higher proportion of patients with BAV had operative repair of their aorta (72.8% vs 44.8%) and presented much younger than those with TAV (49.0 vs 64.2 years). Yasuda and coworkers [5] found aortic valve replacement in BAV disease to have no effect on the dilatation rate at all levels of the aorta. In comparison, no significant dilatation at any level of the aorta after aortic valve repair was observed in TAV patients. This suggests that progressive dilatation in BAV is more diffuse and independent of the hemodynamic effects of the valvular dysfunction.

Aortic dilatation typically affects the proximal aorta, whereby the ascending aorta is asymmetrically affected [20]. By using more advanced imaging modalities such as CTA or MRA, the extent of thoracic aortic involvement can be better characterized in patients with ascending aortic aneurysm. Fazel and colleagues [10], from Stanford University, used CTA and MRA to size the thoracic aorta at 10 different levels in a cohort of 64 consecutive patients with BAV. Hierarchic cluster analysis was used to identify specific patterns of aortic dilatation. Aortic root involvement was found in 58% of patients in their study and aortic arch involvement in 73%. This led the authors to recommend a custom-tailored approach to aortic replacement in patients with BAV disease depending on which cluster the patient was in.

All patients in the present study underwent ascending aorta replacement because of an ascending aortic aneurysm. Yet, given the propensity of the aortic root and the proximal aortic arch to continue growing after the initial operation, one might argue if a more extensive distal aortic resection and a full root replacement would be of long-term benefit. Such approach would seem attractive for a young patient who has evidence of aortic root dilatation and is agreeable to a mechanical aortic prosthesis to limit future reoperations. This approach is reflected in the series by Etz and colleagues [13] from the Mount Sinai Hospital in New York in which 206 BAV patients with aortic aneurysm (median aortic diameter, 5.5 cm) and a mean age of 53 years underwent full root replacement and an open distal anastomosis. A mechanical valve-conduit was used in 61%. Hospital mortality was 2.9%. During an 18-year interval, no patient required...
ascending aorta reoperation, and survival was comparable to an age- and sex-matched population. This led the authors to conclude that a Bentall root replacement with open distal anastomosis in patients with BAV and dilated ascending aorta has no worse operative mortality than with aortic valve replacement and showed superior long-term survival and lower rate of aortic reoperations.

The demographic findings in the current study reflect our previously stated strategy in managing the ascending aorta in patients with BAV [17]. The younger patients were selected for root replacements. An open distal technique was used whenever the aneurysm extended into the aortic arch. Two-thirds the BAV patients in our series with dilated ascending aorta received full root replacement and one-third received open arch repair with excellent perioperative results. This demonstrates the small influence the operative procedure exerts on the overall operative mortality in this subset of healthy patients.

Although BAV patients are estimated to have a nine-fold increased risk for type A aortic dissection [21], no patient in our series or in the series from Mount Sinai came back with type A aortic dissection. This stresses the important role of having the proximal ascending aorta replaced in the setting of bicuspid aortopathy. The consequence of keeping a pathologic ascending aorta after aortic valve replacement in BAV patients was first addressed by Russo and colleagues [6]. In their landmark study, 50 consecutive patients with BAV were matched with another 50 patients with TAV. Late follow-up revealed 5 deaths due to acute aortic dissection and 7 sudden deaths in the BAV group, with no events in the TAV group. Moreover, late echocardiography showed the sinuses of Valsalva and the ascending aorta were significantly more dilated in the BAV group. Three patients in the BAV group need reoperation for an ascending aorta of more than 6.0 cm. Our group has previously demonstrated that an ascending aorta of 4.5 cm or greater was associated with a higher incidence of late aortic complications and diminished survival at 15 years [7]. Although the present study failed to demonstrate a significant effect for extended aortic resection on subsequent aneurysm growth in the distal aorta, this lack of significance is likely a reflection of the small sample size, as no one in the open group developed distal aortic aneurysm. Except for aortic dissection situations, we believe that open arch repair should be custom tailored according to the extent of aortopathy and the potential for future aneurysm growth. Better imaging of the distal aorta and aortic arch with CTA or MRA can also be of great value when selecting patients for open arch repair.

Aortopathy in BAV disease has the greatest expression in the midascending aorta [22]. This addresses the actual merits of replacing the whole aortic root vs just replacing the grossly dilated ascending aorta in patients with BAV disease. Debate still exists for opting to replace an aortic root that is mildly dilated (4.0 to 4.5 cm) or choosing to go with the relatively easier and faster separate valve and graft replacement. The largest series addressing this issue came from Stanford University [23]. The authors conducted a 30-year review (1965 to 1995) of 390 consecutive patients treated for aortic valve disease and ascending aortic aneurysm or type A dissection. Of these, 135 patients had root replacement with a composite graft and 255 had separate graft and valve replacement. There was no significant difference in the operative mortality between the two groups. Survival at 15 years was better in the aortic root replacement group, who were significantly younger (42 vs 56 years). Multivariate analysis revealed age and coronary artery disease as predictors for late death. Seven patients in the supracoronary graft group required reoperation for aortic root aneurysm but were confirmed to have had preexisting annuloaortic ectasia at the initial operation. The type of root procedure in this subset of patients was not shown to be a predictor of any outcome variable, including reoperation for aortic root aneurysm.

Our current series identified 3 patients who had separate valve and graft replacement and returned with aortic root aneurysm at the time of reoperation. Aortic root dimensions were described as normal in all 3 at their first operation. Another patient from the same group had sudden death at age 50. His autopsy revealed a striking 8-cm aortic root aneurysm, although his aortic root was described as being mildly dilated at his first operation 12 years earlier.

In a series similar to ours, Sundt and colleagues [24] analyzed perioperative and late results among 45 patients with BAV and ascending aortic aneurysm, 27 with separate valve and graft procedures and 18 with composite valve graft. The demographic findings were quite similar to those in this current report. Patients who had no root intervention were older (60 years) and more likely to present with aortic stenosis, whereas the composite valve graft group was younger (42 years) and had valvular regurgitation. At a mean follow-up, which was 50% less than in our current report, survival was significantly better in the full root replacement group. Patient age—not the procedure—was the only significant predictor for late death. Their results are strikingly similar to our own findings, except they had no late reoperations in the remaining aorta or new aneurysms in the aortic root.

Our series identified 6 patients who presented with distal thoracic aortic aneurysms and at least 3 other patients who required reoperations because of aortic root aneurysms. This difference is likely the result of the longer mean follow-up in our series, because the rate of dilatation in patients with dysfunctional BAVs varies from 0.04 to 0.5 mm/y in the aortic root and from 0.2 to 1.9 mm/y in the ascending aorta [18].

This study reinforces our patient-specific strategy in managing the dilated thoracic aorta in patients with BAV disease. The extent of aortopathy on CTA or MRA and the diameter of the different segments of the aorta largely dictate the need for distal aortic resection and root replacement. We also incorporate the patient’s age and the choice of aortic valve prosthesis in our decision-making process. This allows us to custom-tailor our surgical approach and minimizes the added risk of replacing the aortic root and aortic arch. Conversely, re-
secting more of the aorta in patients who are young theoretically minimizes the need for future redo operations because of new aortic aneurysms. As in the earlier studies, this study failed to link the operative techniques with late survival, redo operations, or thoracic aortic complications. This demonstrates the proper role of patient-specific procedure selection.

As this study sheds light on some of the controversial aspects of the surgical management of BAV aortopathy, it has several limitations that temper the inferences drawn from its present findings. The retrospective nature of this study imposes all the limitations inherent in retrospective data analysis. To allow for at least 10 years of follow-up, the sample size of this cohort is much smaller than what it would have been if the series were extended to more recent years. Accordingly, this limits the generalization of some of its findings.

The decision to replace the aortic root or perform an open distal procedure, or both, was exclusively based on the subjective assessment and experience of the operating surgeon. This inherently introduces bias when the surgical techniques are compared. The degree of sinus dilatation and coronary displacement in each case is not known. Because of the long time span of this study, newer surgical techniques, such as open distal anastomosis, stentless aortic bioprostheses, and aortic valve sparing were introduced in the more recent years. This could have affected some of the final results.

Aortopathy in BAV is usually asymmetric and has multiple patterns. Until genetic testing or other biomarkers are developed to identify those at greatest risk for future aneurysm growth and subsequent dissection and rupture, a patient-specific approach seems to be a reasonable option. This takes into account the extent and the size of aortic dilatation as well as the patient’s age and choice of aortic valve prosthesis.

References