Should the proximal arch be routinely replaced in patients with bicuspid aortic valve disease and ascending aortic aneurysm?

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Objectives: Bicuspid aortic valve is frequently associated with underlying aortopathy. Data support an aggressive approach to replacement of the ascending aorta. However, the natural history of the unreplaced aortic arch is unknown, and some have advocated routine replacement of the proximal arch in this setting.

Methods: We identified patients with bicuspid aortic valve undergoing repair or replacement of the ascending aorta with or without aortic valve replacement or root replacement between January 1988 and December 2007 at our institution. Follow-up was by review of clinical records and postal questionnaire.

Results: Of 470 patients identified, 48 patients had hemiarch or total arch replacement and were excluded. Of the remaining 422 patients, 227 had separate aortic valve replacement or repair and ascending aortoplasty (76) or ascending aortic graft replacement (175), 107 a valved conduit, 40 a homograft root, and 21 a valve-sparing root replacement. The mean age was 56 ± 15 years, and 80% were male. Follow-up was up to 17 (median 4.2) years. There were 23 (5.5%) late reoperations, of which none were for arch dilatation. Survival at 1, 5, 10, and 12 years was 96.5%, 89.6%, 77.7%, and 74.0%. Freedom from late reoperation was 98.7%, 94.1%, 81.0%, and 81.0%. Paired echocardiographic measurements of aortic arch diameter ($n = 58$) were 33.3 mm preoperatively versus 31.9 mm postoperatively ($P = .135$) at a mean 4 years.

Conclusions: Progressive dilatation of the aortic arch leading to reoperation after repair of ascending aortic aneurysm in patients with bicuspid aortic valve is uncommon. A selective approach to transverse aortic arch replacement is appropriate. (J Thorac Cardiovasc Surg 2011;142:602-7)

Bicuspid aortic valve (BAV) is the most common congenital cardiac malformation, occurring in 1% to 2% of the population.¹ BAV is associated with a variety of vascular abnormalities, such as aortic dilatation, coarctation of the aorta, interrupted aortic arch, anomalous coronary ostium, and patent ductus arteriosus, of which enlargement of the ascending aorta is the most common.²⁻⁵ These observations support the concept of an inherited, generalized aortopathy.⁶ Furthermore, an increasingly aggressive approach to ascending aortic replacement is advocated given clinical evidence of significant need for reoperation when even an only moderately dilated ascending aorta is left behind at the time of aortic valve replacement (AVR).^{1,7,8}

On the basis of these observations, as well as imaging analyses that suggest extension of the enlargement into the aortic arch in up to 73% of patients, some have argued

for almost routine hemiarch replacement in the setting of BAV.⁹ Despite improvements in techniques for aortic arch procedures with low operative morbidity and mortality in the current era, the operative risk remains higher than that of isolated ascending aortic surgery.¹⁰ The added complexity and risk associated with arch replacement is only justifiable if the incidence of clinically relevant progressive aortic arch dilatation leads to reoperation, however. We therefore examined our experience with the treatment of aneurysmal disease of the ascending aorta without arch replacement to determine the late incidence of reoperation for arch disease.

METHODS

After approval by the Mayo Clinic Rochester Institutional Review Board with waiver of study-specific consent, we searched our computerized Society of Thoracic Surgeons-compliant clinical database for patients who had undergone intervention on an aneurysmal ascending aorta associated with a BAV between January 1, 1988, and December 31, 2007. Patients denying consent for inclusion in research studies were excluded, as were those with known Marfan syndrome or Ehlers-Danlos syndrome. We reviewed the electronic medical record including echocardiographic reports, pathologic reports, and all operative records. Among those with paired studies, aortic arch dimensions were determined from preoperative and most recent (>3 months) postoperative echocardiography.

Follow-up

Follow-up information was obtained by chart review and cardiothoracic questionnaire survey. Maximum follow-up period was extended to 17.2 years and median was 4.2 years.

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Abbreviations and Acronyms

BAV = bicuspid aortic valve
 AVR = aortic valve replacement
 HR = hazard ratio

Statistical Analysis

Continuous variables were described as mean $\pm$ standard deviation and categorical variables were expressed as percentage and frequency. Preoperative and postoperative aortic arch dimension was compared by paired *t* test. Long-term survival and freedom from reoperation were studied by the Kaplan–Meier method. Log–rank test was used for comparison between groups according to surgical procedure or risk factor. Cox regression models were used to identify the univariate and multivariate predictors of overall survival. The SAS system (SAS Institute Inc, Cary, NC) was used for all analyses.

RESULTS**Patient Demographics**

A total of 470 patients undergoing ascending aortic replacement for BAV-associated aneurysms were identified during the study interval. Of these, 48 patients underwent hemiarch or total arch replacement and were excluded. Among the 422 patients included in this study, men predominated (79.6%) and the mean age of the patients at the initial operation was 55.8 ± 14.9 years, with a range from 20 to 86 years (Table 1). Of these, 30 (7%) patients had a history of aortic coarctation. The dominant functional aortic valve disease was stenosis in 49.5% and insufficiency in 43.6% (Table 2). The mean ascending aortic diameter was only 50.6 ± 8.1 mm at the time of surgery; however, the majority of patients (374/422, 89%) had concomitant valve repair or replacement, making it difficult to tell in retrospect which pathologic condition was considered by the surgeon to be the primary driver for intervention. Five patients had acute dissection as their primary indication for surgery.

Operative Characteristics

Separate AVR and graft replacement of the ascending aorta or aortoplasty was performed in 227 (54%) patients and composite valve graft replacement in 107 (25%) patients (Table 3). The most common concomitant procedure was coronary artery bypass grafting (15%). In 33 (7.8%) patients, at the preference of the operating surgeon, the distal anastomosis was performed open under circulatory arrest at the level of innominate artery origin to achieve complete ascending aortic replacement without true hemiarch replacement. Among those 33 undergoing the distal anastomosis open under circulatory arrest, the mean aortic arch diameter was slightly larger at 36.3 ± 8.0 mm than that for the 389 in whom the distal anastomosis was performed with a crossclamp in place at 33.7 ± 6.0 mm. The corresponding ascending aortic diameters were

55.2 ± 6.6 mm and 50.2 ± 8.1 mm for open versus cross-clamp technique.

There were 7 (1.7%) perioperative deaths and operative mortality was similar regardless of the procedure ($P = .42$). In 5 cases the indication for surgery was acute dissection; 3 of these patients did not survive their hospitalization. Thirty-two (7.8%) patients underwent reoperation for bleeding. Postoperative intra-aortic balloon pump support was used in 12 (2.9%) patients, and 31 (8.2%) patients required prolonged ventilation. Three (0.7%) patients had transient ischemic attacks and 7 (1.7%) permanent stroke. Seven (1.9%) patients had postoperative renal failure, 3 (0.7%) had sepsis, and 1 (0.2%) had multiorgan failure.

Late Outcomes

During follow-up, 52 patients died. There were no deaths known to be due to aortic dissection or rupture, although the cause of death was unknown in 28 patients. The causes of death were cardiac in 15.4%, noncardiac in 30.8%, and unknown in 53.8%. Cox regression model analysis showed age (hazard ratio [HR], 1.1; $P < .001$), diabetes mellitus (HR, 4.2; $P < .001$), preoperative renal failure (HR, 7.9; $P < .001$), and New York Heart Association functional class III/IV (HR, 2.6; $P < .003$) as independent predictors for overall death. Overall survival at 1, 5, 10, and 12 years was 96.5%, 89.6%, 77.7%, and 74%, respectively (Figure 1). Predictors of late death by multivariate analysis included age, diabetes mellitus, preoperative renal failure, New York Heart Association functional class III or IV, and acute dissection (Table 4).

Reoperations occurred in 23 (5.5%) patients, none of whom had had arch surgery (Table 5). The average interval between the first operation and reoperation was 5.8 years, and the most common indication for reoperative surgery was endocarditis (7 patients). Four patients underwent reoperation for ascending aortic dilatation at a mean of 9.7 years (range, 8.1–12.3 years) after ascending aortic aortoplasty. A 67-year-old man who had undergone AVR for aortic stenosis, ascending reduction aortoplasty, and coronary artery bypass grafting underwent graft replacement of the ascending aorta and root 9 years later for enlargement of the aortic root and ascending aorta. A 53-year-old male patient who had undergone aortic valve repair and aortoplasty required first reoperation for AVR 1 year later for aortic regurgitation and again 11 years later for aortic root and ascending aorta replacement. A 40-year-old man who had undergone AVR and ascending aortoplasty required AVR and graft replacement of the ascending aorta 9 years later because of patient–prosthesis mismatch with redilation of the ascending aorta incidentally noted. A 24-year-old woman who had undergone homograft AVR required reoperation for dilated distal native ascending aorta 8 years later. In summary, 4 (17%) of 23 reoperations were primarily for aorta-related problems, including 4 (5.3%) ascending aortic reoperations among

TABLE 1. Preoperative data

Variable	Frequency
Age (y)	55.8 ± 14.9
Sex (male), no.	336 (79.6%)
Tobacco abuse, no.	194 (50.3%)
Diabetes mellitus, no.	35 (9.0%)
Hypercholesterolemia, no.	213 (55.5%)
Renal failure, no.	8 (1.9%)
Hypertension, no.	205 (53.2%)
Cerebrovascular accident, no.	12 (2.9%)
Peripheral vascular disease, no.	37 (9.7%)
NYHA (III/IV), no.	134 (35.7%)
Coronary artery disease, no.	99 (23.7%)
History of coarctation of aorta, no.	30 (7.3%)

NYHA, New York Heart Association.

76 patients undergoing aortoplasty. When considered conversely, among the 23 patients undergoing reoperation, 7 (30%) had undergone aortoplasty at their initial operation, although not all were for aortic complications. The probability of freedom from late reoperation at 1, 5, 10, and 12 years was 98.7%, 94.1%, 81.0%, and 81.0%, respectively (Figure 2).

Comparison of Aortic Arch Dimensions

Preoperatively, the dimensions of the aortic root were 26.3 mm at the annulus, 42.7 mm at the sinuses of Valsalva, and 36.8 mm at the sinotubular junction; dimension of the ascending aorta was 50.6 mm. Perioperative measures of the aortic arch diameter were available in 199 (47.2%) patients. The median diameter was 33.9 mm with a range from 19 to 51 mm. As shown in Figure 3, 58% of these were between 30 and 39 mm and 18% were 40 mm or larger. Among 395 patients having postoperative echocardiograms, 58 patients had data sufficient for paired measurement of aortic arch dimensions. The average dimension of

TABLE 3. Operative characteristics

Variable	Frequency
ACC time (min)	78.5 ± 33.8
CPB time (min)	107.3 ± 48.9
Circulatory arrest time (min)	18.6 ± 10.8
Operative procedures	
Separate AVR/graft replacement, no.	156 (37.0%)
Separate AVR/aortoplasty, no.	71 (16.8%)
Valved conduit, no.	107 (25.4%)
Homograft, no.	40 (9.5%)
Valve-sparing root replacement, no.	21 (5.0%)
AV repair/graft replacement, no.	19 (4.5%)
AV repair/aortoplasty, no.	5 (1.2%)
Concomitant procedure	
CABG, no.	64 (15.2%)
MV procedure, no.	8 (1.9%)
TV procedure, no.	6 (1.4%)
PV procedure, no.	3 (0.7%)
Type of valve	
Mechanical, no.	209 (55.9%)
Bioprosthetic, no.	125 (33.4%)
Homograft, no.	40 (10.7%)

ACC, Aortic crossclamp; CPB, cardiopulmonary bypass; AVR, aortic valve replacement; AV, aortic valve; CABG, coronary artery bypass grafting; MV, mitral valve; TV, tricuspid valve; PV, pulmonary valve.

the aortic arch (Figure 4) was unchanged at 4 years postoperatively (mean, 31.9 ± 5.4 mm) compared with preoperatively (mean, 33.3 ± 6.2 mm). Among 8 patients whose aortic arch was measured at 4 cm or greater (42.6 ± 2.3 mm), at a mean follow-up of 4.6 ± 2.9 years the mean arch diameter was actually reduced at 35.6 ± 6.4 mm ($P = .027$), perhaps secondary to changes in proximal arch geometry owing to the distal anastomosis. None of these arches reached threshold for reoperation.

DISCUSSION

The findings of this study demonstrate that, despite concerns about a generalized aortopathy associated with BAV, reoperation for aortic arch dilatation after replacement or repair of the ascending aorta alone is uncommon. This is not to say that arch replacement is never necessary, inasmuch as arch replacement was undertaken in approximately 10% of patients during the study interval. It may well be that our observation that late reoperation for arch replacement is, at a minimum, uncommonly necessary is a reflection of accurate identification of the patients at risk by the operating surgeon, and that progressive dilatation was obviated by appropriate surgical intervention. The data suggest, however, that if the arch does not meet clinical threshold for replacement at the time of ascending aortic replacement, it is unlikely to progressively dilate to a point requiring reoperation. Furthermore, although serial arch measurements are available only in a small percentage of cases, and some instances of dilatation may have gone unrecognized,

TABLE 2. Preoperative echocardiographic findings

Variable	Frequency
Dominance of AV disease	
Aortic stenosis, no.	209 (49.5%)
Aortic insufficiency, no.	184 (43.6%)
Mixed, no.	29 (6.9%)
EF (%)	59.8 ± 11.0
Sizes of aortic root	
Annulus (mm)	26.3 ± 4.4
Sinuses of Valsalva (mm)	42.7 ± 7.6
Sinotubular junction (mm)	36.8 ± 6.5
Sizes of aorta	
Ascending aorta (mm)	50.6 ± 8.1
Arch (mm)	33.9 ± 6.2
Descending aorta (mm)	23.5 ± 6.4

AV, Aortic valve; EF, ejection fraction.

FIGURE 1. Overall survival of 422 patients undergoing repair or replacement of the ascending aorta for bicuspid aortic valve disease and ascending aortic aneurysm.

the late survival data suggest that there is no excess mortality associated with the condition. Finally, aortoplasty as opposed to graft replacement of the aorta appears to leave patients at risk for reoperation; this procedure is rarely practiced in our institution currently.

Previous clinical studies have focused principally on dilatation of the ascending aorta in association with BAV²⁻⁵ even independent of functional valve pathology¹¹⁻¹³ and the risk of reoperation, dissection, or sudden death.^{7,8,14,15} Inasmuch as there is ample evidence from pedigree studies of a genetic basis to BAV, and histologic abnormalities have been identified in the media of the ascending aorta in patients with BAV, it is reasonable to suspect that, at least in a subset of patients, aortic dilatation or aneurysm formation may also extend to the transverse aortic arch.⁹ Magnetic resonance angiography has suggested associated dilatation of the entire thoracic aorta in patients with BAV,⁴ and cluster analysis has demonstrated involvement of the proximal aortic arch in 73% of individuals with BAV with extension into the mid-arch in 35%.⁹ Evidence of the clinical relevance of this finding

as manifest by surgically relevant late aneurysm formation, however, is not clear. In our patients with BAV and ascending aortic aneurysm, only 10% of patients underwent arch intervention, and another 18% of patients showed dilated aortic arch (≥ 40 mm). In contrast to findings reported previously by others pertinent to the unreplaced ascending aorta,^{8,16} however, reoperation was not observed.

Our findings are consistent with a prior community-based study reporting no significant difference between the BAV and control groups with respect to dimensions of the aortic arch,¹⁴ and another recent magnetic resonance imaging study that revealed no differences in the mean diameters of the aortic arch.¹⁷ Correlation between age and the dimension of the aortic arch was suggested by Cecconi and associates,¹⁸ and significant increases in the dimensions of the aortic arch were predominantly found in patients over 40 years of age. Admittedly, these are cross-sectional studies, and not longitudinal.

It is likely that the aortopathy associated with BAV is heterogeneous as suggested by Della Corte and colleagues¹⁹ and that aneurysm formation is multifactorial, with hemodynamic effects superimposed on underlying abnormality of the connective tissue leading to phenotypic variability. Accordingly, it would not be surprising if the arch behaved differently from the ascending aorta given differences in hemodynamic forces. Dissection tears less often begin in the arch, and arch aneurysms of all etiologies are less common than aneurysms of either the ascending or descending thoracic aorta. Among patients with BAV, the largest aortic diameter is in the ascending segment. With a baseline smaller diameter, the aortic arch might be expected to dilate less rapidly given lower wall tension by the law of LaPlace and clinical evidence from patients with ascending aortic dilatation of a lower incidence of late aortic dilation among those without baseline dilatation than those with larger diameter.^{19,20}

We do not advocate ignoring arch dilatation that exists at the time of ascending aortic replacement. In the study of

TABLE 4. Univariate and multivariate analysis for overall survival

	Univariate			Multivariate		
	HR	CI	P value	HR	CI	P value
Age	1.1	1.04–1.1	<.001	1.1	1.03–1.09	<.001
DM	4.4	2.29–8.55	<.001	3.8	1.87–7.89	<.001
Preop RF	5.2	1.86–14.51	.002	8.3	2.85–23.78	<.001
History of CVA	3.5	1.4–8.96	.008			
PVD	2.2	1.16–4.26	.016			
NYHA (III/IV)	3.2	1.76–5.87	<.001	2.3	1.25–4.35	.008
CAD	3.3	1.86–5.68	<.001			
Current CABG	3.1	1.75–5.43	<.001			
LV dysfunction (EF $\leq$ 40%)	2.6	1.17–5.89	.019			
Acute dissection	21	7.29–59.52	<.001	6.9	2–23.60	.002

HR, Hazard ratio; CI, confidence interval; DM, diabetes mellitus; RF, renal failure; CVA, cerebrovascular accident; PVD, peripheral vascular disease; NYHA, New York Heart Association; CAD, coronary artery disease; CABG, coronary artery bypass grafting; LV, left ventricle; EF, ejection fraction.

TABLE 5. Indications for reoperations

Indication	No.
Aorta related	
Aortic root/ascending aortic dilatation	2
Ascending aortic dilatation	2
AV related	
Endocarditis	7
Prosthetic valve	5
Homograft	1
Native valve	1
PPM	2
Native AV disease	2
Periprosthetic leakage	1
Other	3

AV, Aortic valve; PPM, patient-prosthesis mismatching.

206 patients with BAV undergoing root replacement reported by Etz and associates,²¹ 38% of patients underwent concomitant arch surgery, including hemiarch and total arch replacement. Three patients required late reoperation for aortic arch surgery, including 1 patient who had progressive arch dilation 6 years after hemiarch replacement. There were no late reoperations for the arch among the patients undergoing isolated ascending aortic surgery, perhaps demonstrating good clinical judgment with regard to who might progress. They also found that there were no significant increases in the growth rates of the distal aortic arch during 5 years' follow-up. In their study of BAV disease with longer follow-up to a mean of 20 years, Russo and associates¹⁷ found 3 reoperations for late ascending aortic aneurysm but no late procedures involving the aortic arch. Although total arch replacement is performed with low morbidity and mortality in experienced centers²²⁻²³ and some groups recommend extensive aortic arch replacement in BAV patients with ascending aortic dilatation,⁹ in most centers aortic arch surgery still carries some increment of excess risk of morbidity and mortality (3% vs 9%).¹⁰ Therefore, replacement of the aortic arch should not be undertaken lightly.

FIGURE 2. Freedom from late reoperation after repair of ascending aortic aneurysm and bicuspid aortic valve disease.

FIGURE 3. Distribution of aortic arch size at the time of operation.

Our study has limitations. It is a retrospective study heavily dependent on the details provided in the medical record. Paired comparisons of aortic arch size were available in only 14% of patients, inasmuch as aortic measurements were not performed routinely in the past in our echocardiography laboratory. Inconsistency in criteria for arch replacement among the numerous surgeons involved in the study may also be cited as a weakness and certainly makes it difficult to establish threshold criteria for arch surgery. Conversely, we would argue that this diversity also supports the generalizability of the results.

In conclusion, hemiarch or total arch replacement need not be performed routinely when replacing the ascending aorta for BAV-associated ascending aortic dilatation. To do so would potentially expose a large percentage of patients unnecessarily to a more extensive procedure with associated perfusion complexity required for arch intervention. It is our current practice to tailor the procedure to the patient, being more aggressive in those patients younger than 50 years of age and more conservative in those over

FIGURE 4. Change of size in aortic arch at a mean of 4 years postoperatively.

the age of 70, but generally performing hemiarch replacement if the proximal arch exceeds 4 cm in diameter.

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