Fate of the normal-sized ascending aorta after aortic valve replacement in bicuspid aortic valve disease

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Abstract

Background and Aims: Bicuspid aortic valve (BAV) related aortopathy has been a controversial issue in the past few years. Most of the researches focused on BAV with dilated ascending aorta after aortic valve replacement (AVR), but there were limited documents of patients with the normal-sized proximal aorta. We retrospectively analyzed the clinical data of patients undergoing AVR in our institution and evaluated the progression of the unreplaced ascending aorta in a relatively long term follow-up. Methods: In our institution, 165 patients were consecutively recruited from July 2004 to December 2017. Detailed perioperative information and follow-up data were comprehensively collected and quantitatively analyzed. Results: 48 patients (29.1%) had BAV, while TAV was found in 117 patients. A significant difference was observed in diameters of ascending aorta at baseline between BAV and TAV group (37.5 ±4.2mm vs 35.1 ±4.4mm; p=0.001). The overall survival rates were 89% and 95.8% at 10 years postoperatively in BAV versus TAV group (Plog rank=0.138). Only 1 patient suffered an aortic dissection and underwent proximal aortic surgery. No difference in the progression of ascending aorta (0.8±4.7mm vs 0.6±3.5mm, p=0.821) was observed. The diameter of ascending aorta at baseline was a significant predictor of progression in ascending aorta. Conclusions: BAV patients with a normal-sized ascending aorta have a considerable low incidence of late adverse aortic events after AVR. Meanwhile, the progression of the unreplaced ascending aorta in BAV patients is not different from that in TAV patients.

Introduction

Bicuspid aortic valve (BAV) is a very common congenital valvular malformation, with a prevalence of 0.9˜2% in general population.[1-3] Aortic valve degeneration is the main problem for these patients, approximately half of them requiring aortic valve replacement (AVR) because of valvular stenosis, regurgitation or infective endocarditis. Even in the absence of aortic valve dysfunction, they may be associated with a high risk of ascending aortic dilatation, which leads to aortic aneurysm and dissection.[4]

The ascending aorta of BAV may still dilate progressively after AVR, which leads to an increased risk of adverse aortic complication (ie., aortic dissection and rupture).[5] As a result , the recent American College of Cardiology/ American Heart Association guidelines indicated replacement of the moderately enlarged ascending aorta(>45mm) in case of concomitant surgery of valvular heart disease.[6] Some centers have even adopted a more aggressive surgical strategy, relaxing the indication for proximal aortic surgery to 40mm in diameter. Moreover, Russo and colleagues proposed a "prophylactic" replacement of the ascending aorta in young BAV patients regardless of its size.[7] This phenomenon was based on the hypothesis of genetic aortopathy in BAV. However, there were also some researchers questioning such an aggressive surgical approach.[8, 9]

The majority of researches focused on the dilated ascending aorta, there are few data on the progression of normal-sized ascending aorta after AVR in BAV population with respect to those with tricuspid aortic valve (TAV). Therefore, we retrospectively analyzed the clinical data of patients undergoing AVR in our institution, and evaluated the progression of unreplaced ascending aorta in a relatively long term follow-up.

Materials and Methods

From July 2004 to December 2017, three hundred and nine consecutive patients referred for elective surgery for aortic valve disease at our institution were retrospectively reviewed. Approval of the local Ethics Committee was obtained and individual patient consent was waived. Inclusion criteria were age[?]18y,the maximal diameters of ascending aorta¡45mm,BAV or TAV were diagnosed by preoperative echocardiography and confirmed by intraoperative direct inspection. Exclusions were previous history of cardiac surgery, acute and chronic aortic dissections, concomitant replacement of the proximal aorta, systemic syndromes (i.e., Marfan, Loeys-Dietz, Ehler-Danlos, Turner).

After exclusions, a total of 165 patients were included in the study. Standard demographic, clinical, and echocardiographic data were collected from the database and medical records. The diameters of aortic root and ascending aortic were determined from preoperative and the most recent echocardiograms. Long term follow-up was obtained by telephone interviews to the patients and/or their family members and by reviewing the resent outpatient medical files. The most recent echocardiograms were reviewed and compared with preoperative data for each patient, when available. Patients were considered lost to follow-up if their phone numbers were no longer valid, and their postal addresses were modified.

Statistical analysis

Analysis was performed using SPSS software, version 22(IBM Corp., Armonk, NY, USA). Descriptive statistics were presented as mean ± standard deviation for continuous variables and frequency and percentage for categorical variables. The X^2 and Fisher's test were used to compare subgroups. Kaplan- Meier method was applied to draw survival curves and calculate 10-year survival statistics. Linear regression analysis was used to analyze changes in the ascending aorta. Model selection was based on Akaike's information criterion. All statistical tests were 2 sided with the alpha level set at 0.05 for statistical significance.

Results

A total of 165 patients were included during the study period, 48 patients (29.1%) had BAV, while TAV was found in 117 patients (70.9%). The demographics, clinical characteristics and perioperative outcomes are summarized in Table1. The mean diameter of aortic root at baseline was comparable between the two groups (33.3±4mm vs 33.6±4.4mm, p=0.717), but the mean diameter of ascending aorta at baseline was larger in BAV group than in TAV group (38±4.1mm vs 35.6±4.5mm, p=0.001, Fig. 1).

Follow-up data was obtained on all 165 hospital survivors. The median follow-up was 7 years, up to a maximum of 15 years, with no difference between BAV group and TAV group (P=0.883). During the follow-up, a total of 10 patients(6.1%) died, including 5 in the BAV group while 5 in TAV group(p=0.439) . The causes of late deaths were listed in Table 2. In the BAV group, there were 2 cardiac related death, 1 patient died of congestive heart failure, and 1 patient died of sudden cardiac death. In the TAV-group, there were 2 cardiac related death, 1 patient died of congestive heart failure and 1 patients suffered sudden cardiac death. In both groups, there were no late deaths due to aortic dissection or aortic rupture. The overall survival rate was 89% and 95.8% at 10 years postoperatively in BAV versus TAV groups ($P_{\log\ rank}$=0.138, Fig. 2).

Only 1 patient suffered aortic dissection and underwent proximal aortic surgery during the follow up period. The patient, in the TAV-group, was diagnosed as ascending aortic dissection 5 years after the initial AVR procedure. The progression of the aortic root and ascending aorta between the initial AVR surgery and the proximal aortic surgery were 20mm and 18mm . No patient in the BAV-group required proximal aortic surgery.

During follow-up, there was no difference in progression of aortic root (1.3±4.7mm vs 0.3±4mm, p=0.225) and ascending aorta (0.8±4.7mm vs 0.6±3.5mm, p=0.821. Fig. 3). When demographic, clinical and echocardiographic variables were added to the unconditional model, The diameter of ascending aorta at baseline (p¡0.001) was a significant predictor of progression in ascending aorta.

Discussion

BAV related aortopathy has been a controversial issue in the past few years. Most of the researches focused on BAV with dilated ascending aorta, but there were limited documents of patients with normal-sized proximal aorta. In this current study, the following main findings were described: 1) ascending aortic dimensions at baseline were larger in BAV patients than in TAV patients, but growth rates of aortic size in a follow-up of 7 years were comparable between two groups after AVR ; 2) the incidence of adverse aortic events were very low in BAV patients with normal-sized proximal aorta after AVR, which was not different from TAV patients; 3) ascending aortic dimension at baseline was a significant predictor of progression of ascending aorta .

Although the exact pathogenesis of BAV related aortopathy is not yet well elucidated, there were two main hypotheses being widely accepted: hemodynamic and genetic causal factors. Robicsek and colleagues first described the patterns of transvalvular flow in BAV patients.[10] After that, many clinical and basic researches focused on the role of valve related hemodynamics and found consistently eccentric turbulent transvalvular flow in non-stenotic or regurgitated BAV patients.[11-14] BAV related hemodynamic factors, such as tensile and shear stresses, play an important role in dilation of ascending aorta. In an ex-vivo model, Juraszek and colleagues found significant pressure differences in various locations of ascending aorta in BAV compared with TAV, which may contribute to BAV related aortopathy.[15] On the other hand, some studies have found the ascending aortic wall of BAV patients is intrinsically different from that of TAV patients.[16-19] Due to significant lack of fibrillin-1, vascular smooth muscular cell would detach from elastin and collagen, leading to apoptosis and loss of structural integrity.[3] Several genes mutations have been reported in BAV patients, including that involved in cell growth, differentiation, and matrix deposition and apoptosis.[20, 21] There is still no consensus on the roles of these two factors. The two different hypothesis lead to different surgical strategies for the ascending aorta in BAV patients: the former may lead to a relatively conservative strategy, it's believed that the ascending aorta will not further progress after disappearance of hemodynamic factors due to AVR; however, the latter may bring out a more aggressive strategy.

In the present study, we found a larger ascending aorta at baseline in BAV patients compared to TAV patients. However, there was a comparable progression of ascending aortic dimension in both groups in a relatively long term follow up period. Most of the patients in our study groups didn't experience severe ascending aortic dilatation. In accordance with previous studies, there was a considerable low risk of adverse aortic events in our population.[9, 22, 23] Mayo published a large series of cases with an average follow up of 12 years after AVR, there was a very low rate (1.9%) of aortic events in BAV patients.[24] Meanwhile, many clinical basic studies have found that the transvalvular flow patterns are significantly abnormal in BAV patients, which is obviously related to ascending aortic dilation.[11-14] According to the present study and other literatures, we thought that the hemodynamic factor may be the main pathogenesis of BAV related aortopathy.

We didn't evaluate per year growth rate of the ascending aorta in BAV group, but it seems that there was no significant aortic dilation during follow-up in patients with normal ascending aorta at baseline after AVR. Valentina Agnese and colleagues found a growth rate of 0.5mm per year of ascending aorta in BAV patients, and the growth rate per year was high in the first two years then decreased steadily.[22]However, all included patients in their study didn't undergo AVR. A correlation between artery hypertension and aortic dilation was observed in some research,[9, 25] but the correlation was insignificant in our study, that perhaps due to a more precise control of artery hypertension after AVR in our patients. Notably, we found ascending aortic dimension at baseline was a significant predictor of progression in ascending aorta. Further prospective study should be conducted to confirm this finding.

Study limitations

There are several limitations in our study. The retrospective study represents the major limitation of our study. The number of patients in BAV group was limited, but the prevalence of BAV versus TAV patients is similar to previous studies. Aortic dimensions were measured and analyzed by echocardiography, either at baseline or at follow up. Another limitation is that we used a proximal aortic diameter of 45mm as our uniform cutoff value.

Conclusions

BAV patients with a normal-sized ascending aorta have a considerable low incidence of late adverse aortic events after AVR. Meanwhile, progression of unreplaced ascending aorta in BAV patients is not different from that in TAV patients.

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