Bicuspid pulmonary valve in transposition of the great arteries: impact on outcome†

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Received 1 September 2010; received in revised form 27 February 2011; accepted 7 March 2011

Abstract

OBJECTIVE: Long-term evaluation of the impact of bicuspid pulmonary valve on neoaortic valve regurgitation and aortic root dilatation (ARD) after arterial switch operation (ASO) for transposition of the great arteries (TGA).

METHODS: Between January 1987 and March 2010, 980 neonates underwent ASO for TGA. A total of 40 patients (4.0%) had a pulmonary bicuspid valve with no significant left ventricular outflow tract obstruction. In this group, 11 patients (28%) had associated ventricular septal defect, three hypoplastic aortic arch, and three had a right ventricular hypoplasia. No pulmonary valvuloplasty was attempted. Mean follow-up was 7.7 ± 5.5 years. Echocardiography evaluations of neoaortic valve function and morphology and aortic root dimensions were performed.

RESULTS: There were two hospital deaths (5%) related to hypoplastic right ventricle and left ventricular dysfunction, and no late death yielding an actuarial survival to 95% SD at 1, 5, and 10 years. At last follow-up, five patients (12%) had mild-to-moderate aortic regurgitation (AR). ARD was noted in 28% of the patients (Z-score up to +3). One patient needed a Bentall procedure for significant AR and severe dilatation of the ascending aorta at 11 years of age. As many as four patients underwent reoperation (10%) for stenosis of the left coronary artery. Freedom from reoperation was 95% SD, 88% SD, and 75% SD at 1, 5, and 10 years, respectively.

CONCLUSIONS: ASO is a safe option for TGA associated with a well-functioning bicuspid pulmonary valve with low morbidity and mortality. Prevalence of AR was not particularly high. Even though ARD was frequent, neoaortic bicuspid valve did not represent a high risk for aortic reoperation. Long-term individual follow-up is mandatory to observe the potential risk of root dilatation and AR.

Keywords: Congenital heart disease • Transposition of the great arteries • Bicuspid neoaortic valve

INTRODUCTION

The outstanding results of arterial switch operation (ASO), even in the presence of complex coronary artery patterns and associated cardiac defects, have left no doubt that this is one of the most successful achievements in the history of congenital heart surgery. However, some concerns regarding the long-term performance of the native pulmonary valve have led to the identification of potential risk factors associated with the development of neoaortic root dilatation and neoaortic valve regurgitation.

After ASO, anatomical and hemodynamic variables can be associated with the development of significant neoaortic regurgitation and neoaortic root dilatation. Previous pulmonary artery banding, ventricular septal defect (VSD) closure [1,2], and coronary arteries reimplantation techniques [3] play a crucial role in the fate of the neoaortic root and valve function. A well-functioning pulmonary bicuspid valve, with no left ventricular outflow tract obstruction, should not represent a contraindication to ASO but can contribute to a multifactorial process that leads to neoaortic valve incompetence and aortic root dilatation (ARD) [4,5].

We describe a single-center experience with long-term follow-up of patients operated on for transposition of the great arteries (TGA) with bicuspid pulmonary valve, with respect to long-term neoaortic valve competence and neoaortic root enlargement.

MATERIALS AND METHODS

Patient population

From January 1987 to March 2010, 980 patients presented with TGA underwent ASO at our institution. Among these, 40 (4%) had a bicuspid pulmonary valve diagnosed preoperatively by
echocardiography, without left ventricular outflow tract obstruction. Patients with any type of subvalvular obstruction (mitral or tricuspid accessory tissues, other endocardial cushion or fibromuscular tissue, and anomalous muscular bar) [6] were excluded from this study. There were 11 females and 29 males. The mean age at operation was 8 ± 0.8 days (median: 6 days, range: 2–21 days). Mean weight was 3.1 ± 0.06 kg. Antenatal echocardiographic diagnosis of TGA had been made for 65% of the patients. At surgery, all patients but two were stable after Rashkind procedure and infusion of prostaglandins based on the arterial saturation. Planned surgery was undertaken in all except for these two unstable patients.

Preoperative morphologic cardiac assessment was based on echocardiography with a diagnosis of bicuspid pulmonary valve made on the opening shape of the valve. Patients with greater than trivial pulmonary regurgitation or any grade of pulmonary stenosis were excluded. Five patients (12%) had a commissural mismatch between the pulmonary and the aortic valves, all in the context of an anterior posterior relationship of the great vessels. Eight patients (20%) had a non-restrictive VSD, two muscular, one infundibular and five perimembranous, and three patients (7%) had a restrictive VSD. All of them had a moderate-to-severe aorto-pulmonary diameter mismatch. Sixteen patients (42%) with intact ventricular septum also had a dilated pulmonary root. Aortic arch obstruction was noted in three patients (7%), and three patients (7%) had moderate-to-severe hypoplasia of the right ventricle. Arrangement of the great vessels was directly anterior to the pulmonary artery in 33 patients (82%), rightward in six patients (16%), and side-by-side orientation in one patient (2%).

Coronary pattern was confirmed at operation with a high proportion of intramural coronaries (10%) and retro-pulmonary loop (20%). Characteristics of patients with bicuspid pulmonary valve in TGA are illustrated in Table 1.

### Surgical management

All patients were operated upon by two surgeons. The ASO was performed with standard aortic and bicaval venous cannulation, and normothermic cardiopulmonary bypass (CPB; 37 °C) except for patients who needed an aortic arch repair (cerebral perfusion with moderate hypothermia). Antegrade normothermic blood cardioplegia was delivered via the aortic root and subsequently the coronary ostia, every 10 min during cross-clamp time. The pulmonary valve was assessed after transection of the pulmonary trunk and the valve was described: confirmation of bicuspid pulmonary valve and aspect of the leaflets were considered to be dysplastic (thickness and the mobility of the leaflet) in 11 patients (27%). No pulmonary valve procedures were attempted during the ASO for the entire cohort.

The strategy for coronary transfer was left to the discretion of the individual surgeon but was based on general principles. When TGA was associated with a VSD, the aorta was reconstructed prior to coronary reimplantation and the button technique was applied to minimize aorto-pulmonary mismatch and excessive aortic root enlargement [3]. In the case of a posterior loop (type D or E), the trap door technique was used preferentially to reimplant the right ostium to avoid any stretching.

In the case of TGA with VSD (5%) and a posterior loop, both techniques (trap door and button techniques) have been applied. If the trap door technique was used for one ostium, the patient was included in the trap door group.

![Table 1: Preoperative, operative and postoperative data of patients with TGA and bicuspid pulmonary valve.](Image)

When a mild commissural orientation mismatch was present, realignment was achieved by extensive dissection of any adhesion between aortic and pulmonary roots, and a mild rotation of the aortic root was applied while performing the aortic ascending anastomosis to obtain adequate orientation of the facing commissure, allowing optimal coronary reimplantation.

For major commissural orientation mismatch, realignment was partial, just enough to allow comfortable reimplantation of the left coronary in the sinus of Valsalva.

If the right ostium faced a commissure, high reimplantation above the commissure could be undertaken, excluding a trap door option. Finally if the commissural orientation was totally discordant, right and left ostia were eventually reimplanted in the same facing sinus.
 Closure of the VSD was undertaken either through the right atrium or by pulmonary valve before the ASO, depending on the type of VSD.

Data collection and statistical analysis

The health database records were reviewed in a retrospective study for the diagnosis, preoperative, operative and post-operative data, and follow-up. Permission to undertake this study was obtained from Paris V University Ethics Committee. The need for individual consent was waived. Follow-up data were obtained during a 5-month period (March 2010 and July 2010). Information was obtained for all patients.

Analysis of the aortic valve morphology and aortic valve incompetence or stenosis was achieved with transthoracic echocardiographic examination dimensions of the aortic root (aortic annulus, sinus of Valsalva, sinotubular junction (STJ)), and ascending aorta were evaluated as well). Aortic regurgitation (AR) was classified as absent, trivial, mild, moderate, and severe [4]. The vena contracta jet width was used to define the severity of AR, defined as the narrowest diameter of the AR jet directly beneath the aortic annulus in parasternal long-axis view [1]. AR was considered as significant for all patients with mild, moderate, or severe regurgitation.

Standardization of root dimensions was expressed by Z-score value calculated on the body surface area [7,8]. The ARD population was defined when Z-score for aortic annulus diameter, sinus of Valsalva, sinotubular junction, or ascending aorta was +3 or above [1].

Descriptive statistics were summarized as the mean and SD or median for continuous variables and were tested for normality by the Kolmogorov-Smirnov statistic and as frequencies and percentages for categorical variables. Univariate analysis was performed with the $\chi^2$ or Fischer exact test for categorical variables, when appropriate, and the Mann–Whitney U test was used in the case of continuous variables. The covariates tested included age at operation, sex, weight at operation, presence of non-restrictive VSD, aortic arch obstruction, position of the great arteries (antero-posterior, other), coronary artery pattern (usual, complex), commissural orientation mismatch, aorto-pulmonary diameter mismatch, neoaortic leaflet dysplasia, ‘trap door technique’ for coronary artery reimplantation, cardiopulmonary bypass (CPB) time, aortic cross-clamp time, intensive care unit stay, Z-score of the aortic root, aortic annulus, sinus of Valsalva, STJ, and ascending aorta, and aortic leaflet coaptation. Pearson’s correlation coefficients were used to assess for relations between aortic annulus Z-score and age of patients after ASO. Actuarial survival and freedom from reoperation, freedom from AR, and freedom from ARD were calculated by the Kaplan–Meier method [9]. Statistical analysis was performed with SPSS (version 17.0).

RESULTS

Early results

Hospital mortality. There were two hospital deaths (5%; defined as death within 30 days of operation) which occurred in 1992 and 1994. These deaths occurred at 4 h and 8 days after ASO. One patient died of left ventricular dysfunction probably from failure of adequate coronary reimplantation. The second patient died of acute right ventricular failure due to underestimated right ventricle and tricuspid valve hypoplasia associated with severely hypoplastic aortic arch.

Operative data. The mean CPB times and cardioplegic cardiac arrest times were 138 ± 12 min (range, 107–500 min) and 76 ± 2 min (range, 50–115 min) for ASO with intact ventricular septum and 150 ± 7 min (range, 128–200 min) and 94 ± 3 min (range, 75–105 min) for complex transpositions of the great vessels. The bicuspid pulmonary valve was dysplastic in 11 patients (27%) at operation. A total of eight (20%) patients underwent concurrent VSD repair. VSD closure was achieved through the right atrium in seven (18%) cases and through the pulmonary valve in one case (2%) with an infundibular VSD.

The sternum was left open in seven cases (18%) to allow hemodynamic stability. One patient required coronary revision after the primary operation, as perfusion of the left coronary artery was suboptimal following reimplantation with the trap door technique. The left ostium was enlarged with a large button of autologous pericardium. Operative data are reported in Table 1.

Early morbidity. The median stay in the intensive care unit was 6.6 ± 0.7 days (range, 0–19 days) after ASO with intact ventricular septum and 8.5 ± 1.7 days (range, 2–15 days) for complex transposition of the great vessels. The mean duration of ventilatory support was 75 ± 11.6 h (range, 8–240 h) for ASO with intact ventricular septum and 146 ± 34.6 h (range, 22–312 h) for complex transpositions of the great vessels. Two patients underwent reoperation for mediastinitis, respectively, at 6 and 8 days after ASO. One patient had pacemaker implantation for postoperative atrioventricular block. One patient (2%) required diaphragm plication 8 days after surgery.

Inotropic support was used in all patients, with a mean duration of 4 ± 0.4 days (range, 0–10 days) for ASO with intact ventricular septum and 5 ± 0.9 days (range, 2–9 days) for complex transposition of the great vessels. In patients with delayed sternal closure, the sternum was closed in the intensive care unit after a mean duration of 3.5 ± 0.7 days (range, 2–6 days). Data are shown in Table 1.

Early postoperative neoaortic regurgitation. Early postoperative AR was estimated to be absent or trivial in 36 patients, and mild in two patients (5%). Neither moderate nor severe AR was diagnosed. The two patients with mild AR had significant pulmonary valve dysplasia and size mismatch of the great vessels, but none required VSD closure. Commisural mismatch orientation was described in one patient.

Late results

Late survival and functional status. The mean duration of follow-up was 7.7 ± 5.5 years (range, 1–19 years). One patient was lost to follow-up after 3 years. There were no late deaths. The survival rate estimated by Kaplan–Meier was 95 ± 3.4% at 1, 5, and 10 years.

Last clinical follow-up was complete. Last echocardiographic evaluation was considered to be satisfactory for 36 out of 38 patients (95%).

Late reoperations. Five patients (13%) underwent reoperation for either coronary stenosis or root dilatation. No catheter reintervention was needed.

Four patients underwent reoperation (10%) for stenosis of the left coronary artery. As usual in our practice, angiographic evaluation was performed in the case of difficult coronary artery
transfer, clinical or electrocardiographic signs of coronary ischemia, mitral regurgitation, and papillary muscle hyperechogenicity. Mean age at coronary reoperation was 1.5 ± 0.7 years (range, 3 months to 3.5 years). One patient (3%) underwent mammary artery bypass graft for complete obstruction of the left coronary ostium at the age of 5 months. Surgical coronary angioplasty of the left main coronary stem was achieved using a saphenous vein patch in three patients. Initial diagnosis was simple TGA in three patients and TGA with VSD and aortic arch obstruction in one patient. One of these four reoperated patients had an intramural course of the left coronary artery and two had a commissural mismatch between the pulmonary and the aortic valves. The coronary arteries were reimplanted with trap door technique in all patients except one (3/4) at first operation.

A single patient in our cohort, with initial diagnosis of TGA and VSD, underwent reoperation for severe ARD and moderate AR, at the age of 11.5 years. Progressive increasing of the ascending aorta ( > 0.5 mm year$^{-1}$) with significant AR led to aortic root and valve replacement. Due to neoaortic valve morphology, aortic valve sparing operation was not considered and a Bentall operation was undertaken. At histological examination, medial aortic wall lesions consistent with a diffuse inflammatory process were found.

Kaplan–Meier estimated that the freedom from reintervention rates for all patients, excluding the two operative deaths, was 95% ± 3.6% at 1 year, 88% ± 6% at 5 years, and 75% ± 1.3% at 10 years (Fig. 1). Cross-clamp time was the only significant independent risk factor associated with reintervention in univariable analysis ($P = 0.02$).

**Late echocardiographic results.** The echocardiographic data were completed for AR evaluation and were undertaken in 36 patients (95%) for aortic root Z-score evaluation. All patients were reviewed during a 3-week interval.

**Fate of the neoaortic valve.** At last echo, performed by the same operator and following a predetermined schema, no patient had aortic stenosis. There was no AR in 21 cases, and only trivial AR in 12. AR was significant in five patients (13%). It was mild in three (8%) and moderate in two (5%) patients. No severe AR was noted. Patients with mild early postoperative AR showed a decrease of AR from mild to trivial in one case, and an increase from mild to moderate in the other. Of the five patients with significant AR, the initial diagnosis was simple TGA in three and TGA with VSD in two. Only one patient required transatrial VSD closure at ASO.

The mean age at occurrence of AR was 2.8 ± 1.3 years (range, immediate after surgery to 7.6 years) after ASO. The median leaflet height of coaptation of patients with significant AR and those without AR was 3 mm (range, 0.5-4.6 mm) and 3.5 mm (range, 1.5-9.5 mm), respectively. This was not statistically different ($P = 0.12$). Kaplan–Meier estimated that the freedom from AR rates for all patients, excluding the two operative deaths, was 95% ± 3.6% at 1 year, 88% ± 6% at 5 years, and 82% ± 8% at 10 years (Figs. 2A and 3).
In univariate analysis, weight at operation was the only independent variable that predicted increased AR (P = 0.02).

**Fate of the aortic root.** At last echocardiographic evaluation, ARD with a Z-score >3 was identified in 10 patients (28%). Dilatation of aortic annulus was diagnosed in six patients (16%), sinus of Valsava in eight (22%), STJ in three (8%), and ascending aorta in five patients (14%). Six patients (16%) had concomitant dilatation of the aortic annulus, sinus of Valsava, and ascending aorta. Four patients (10%) had isolated dilatation of the sinus of Valsava. Data are reported in Table 2. Fig. 4A and B illustrates the Z-scores of the neoaortic annulus and sinus of Valsava at the time of follow-up. The linear relation for sinus of Valsava

Z-score and age of patient suggested a tendency to dilatation over time (r = 0.81, P < 0.01).

Kaplan–Meier estimated that the freedom from ARD rates for all patients was 92% ± 5% at 1 year, 72% ± 8% at 5 years, and 64% ± 10% at 10 years (Figs. 2B and 3).

The mean age at diagnosis of ARD was 2.9 ± 0.9 years (range, 0.4–10 years). Of the 10 patients with ARD, two patients (20%) had early postoperative trivial AR and five patients (50%) had significant aorto-pulmonary diameter mismatch at ASO. Position of the great vessels was not antero-posterior (anterior rightward and side by side) in four of 10 patients (40%).

**Table 2:** Echocardiographic data at last follow-up; patient population: all survivors (n = 38)

<table>
<thead>
<tr>
<th>Echocardiographic characteristics</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic regurgitation</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>21 (55)</td>
</tr>
<tr>
<td>Trivial</td>
<td>12 (32)</td>
</tr>
<tr>
<td>Mild</td>
<td>3 (8)</td>
</tr>
<tr>
<td>Moderate</td>
<td>2 (5)</td>
</tr>
<tr>
<td>Severe</td>
<td>0</td>
</tr>
<tr>
<td>Significant aortic regurgitation (mild to severe)</td>
<td>5 (13)</td>
</tr>
<tr>
<td>Leaflet height coaptation</td>
<td></td>
</tr>
<tr>
<td>Absent or trivial AR</td>
<td>3.5 mm (1.5)</td>
</tr>
<tr>
<td>Significant AR</td>
<td>3 mm (1.7)</td>
</tr>
<tr>
<td>Dilated aortic root: Z-score &gt;3</td>
<td></td>
</tr>
<tr>
<td>Aortic annulus</td>
<td>6 (16)</td>
</tr>
<tr>
<td>Sinus of Valsava</td>
<td>8 (22)</td>
</tr>
<tr>
<td>Sino-tubular junction</td>
<td>3 (8)</td>
</tr>
<tr>
<td>Ascending aorta</td>
<td>5 (14)</td>
</tr>
<tr>
<td>Patients with any dilated segment of the aortic root</td>
<td>10 (28)</td>
</tr>
<tr>
<td>Leaflet height coaptation</td>
<td></td>
</tr>
<tr>
<td>Standard aortic root</td>
<td>3.4 mm (1.5)</td>
</tr>
<tr>
<td>ARD</td>
<td>3.5 mm (4.5)</td>
</tr>
</tbody>
</table>

AR: aortic regurgitation; ARD: aortic root dilatation.

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**Figure 3:** (A) Neoaortic annulus diameter (Z-score over time) in patients that underwent ASO with bicuspid aortic valve. Pearson’s correlation coefficients, \( r = 0.13 \) no significant; (B) neoaortic sinus of Valsava diameter (Z-score over time) in patients that underwent ASO with bicuspid aortic valve. Pearson’s correlation coefficients, \( r = 0.81; P < 0.01 \).

**Figure 4:** Kaplan–Meier estimated freedom from ARD and significant AR at 15 years follow-up after ASO. Number of patients at risk are indicated in parentheses.
Table 3: Risk factors for reintervention, aortic regurgitation and aortic root dilatation (univariate analysis)

<table>
<thead>
<tr>
<th>Independent variables</th>
<th>Univariable analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reintervention</td>
<td></td>
</tr>
<tr>
<td>Commissural orientation mismatch</td>
<td>0.12</td>
</tr>
<tr>
<td>Operative weight</td>
<td>0.08</td>
</tr>
<tr>
<td>CPB time</td>
<td>0.06</td>
</tr>
<tr>
<td>Cross-clamp time</td>
<td>0.02</td>
</tr>
<tr>
<td>Aortic regurgitation</td>
<td></td>
</tr>
<tr>
<td>Z-score annulus dimension</td>
<td>0.15</td>
</tr>
<tr>
<td>Operative weight</td>
<td>0.02</td>
</tr>
<tr>
<td>Aortic root dilatation</td>
<td></td>
</tr>
<tr>
<td>Trap door technique</td>
<td>0.15</td>
</tr>
<tr>
<td>Age at operation</td>
<td>0.13</td>
</tr>
<tr>
<td>Position of great arteries</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Table 4: Aortic regurgitation and Z-score dimensions of the neoaortic root

<table>
<thead>
<tr>
<th>Z-score</th>
<th>Aortic regurgitation (AR)</th>
<th>Univariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Significant AR</td>
<td>Absent or trivial AR</td>
</tr>
<tr>
<td>Annulus</td>
<td>2.5 (1.9)</td>
<td>1.7 (1.5)</td>
</tr>
<tr>
<td>Sinus of Valsalva</td>
<td>1 (4.3)</td>
<td>1.4 (2.2)</td>
</tr>
<tr>
<td>Sino-tubular junction</td>
<td>0.9 (2.5)</td>
<td>0.8 (2.6)</td>
</tr>
<tr>
<td>Ascending aorta</td>
<td>1.3 (4.2)</td>
<td>1.4 (2.5)</td>
</tr>
</tbody>
</table>

All the patients had trap door technique for coronary artery transfer. One patient with diagnosis of Duchenne syndrome and early postoperative mild AR developed ARD and moderate AR during follow-up.

Risks factors for ARD are shown in Table 3. Only the position of the great vessels (antero-posterior vs other position) was a higher risk of ARD for side-by-side or rightwarded position of the great arteries (univariate analysis: \( P = 0.03 \)). No other variable was associated with ARD in the univariate analyses.

Aortic root Z-scores for AR and non-ARD populations are listed in Table 4, with no statistical difference between the two groups.

The only patient with ARD and significant AR had a decreased leaflet coaptation height of the bicuspid neoaortic valve (<1 mm), whereas nine patients with ARD without significant AR had a preserved coaptation height.

DISCUSSION

The ASO is currently the standard surgical option in the management of TGA with excellent long-term survival and low reoperation rate [10]. The presence of a bicuspid pulmonary valve that remains in the systemic circulation after ASO is not uncommon with a prevalence of 4% in this large series.

In this retrospective study, we aimed to establish if the presence of a preoperatively well-functioning bicuspid pulmonary valve without left ventricular outflow tract obstruction (LVOTO) would alter the early and long-term results of ASO.

Technical considerations

The presence of a bicuspid pulmonary valve might increase difficulties during coronary transfer and aortic root reconstruction.

First, important dilatation of the pulmonary root (67% of aorto-pulmonary mismatch in this series) needs to be perfectly evaluated while coronary reimplantation is achieved. To minimize the impact of excessive neoaortic root diameter during coronary transfer, the optimal site of reimplantation is often higher than usual, thus avoiding kinking due to a shorter distance between the proximal coronary arteries and the aortic wall.

Second, discordant commissure orientation, often associated with bicuspid pulmonary valve in this series, can make coronary reimplantation slightly more challenging. Technically, in the presence of moderate discordant commissure orientation, correct realignment can be achieved by mild rotation of the root during the ascending aortic anastomosis. This technique, commonly used in our practice, may be criticized as it can affect the root itself, leading to aortic incompetence. We have not observed aortic incompetence in this setting and are unable to formally examine if the degree of rotation applied to the aortic root cannot be measured in a retrospective study.

With severe mismatch of commissure orientation only partial realignment was achieved, just enough to allow a comfortable reimplantation of the left coronary in the sinus of Valsalva. The right ostium, facing a commissure, was reimplanted above the commissure itself, in a high position, but without using the trap door technique. For complete discordance between the two commissures (horizontal bicuspid valve), right and left ostia are reimplanted in the same facing sinus, leading to an enlargement of this sinus and possible compression by the anterior pulmonary trunk.

These situations associated with TGA and bicuspid pulmonary valve may make surgical correction slightly more challenging and alter the long-term anatomical result.

Limits of the echocardiographic data

During the study period, the follow-up was essentially based on echocardiographic evaluation of the heart. The echocardiography was useful to describe neoaortic regurgitation, and the degree of severity was based on the vena contracta jet width. The valvular coaptation height evaluated at follow-up was a difficult parameter to obtain in infants, and the results must be interpreted with caution.

It was not possible to define commissural orientation (horizontal or vertical) as for a standard aortic bicuspid valve due to the relative position of the great arteries (antero-posterior to side by side). This may be achieved by tracing a reference line between the aortic and pulmonary root centers, defining the phenotype of the bicuspid valve by the angle made between the reference line and the intercommissural axis. These data could be readily obtained from computed tomography (CT) or magnetic resonance imaging (MRI) studies and would permit evaluation of the potential impact of the neoaortic bicuspid valve phenotype on aortic diameter and elastic properties as has been suggested [11] for standard aortic bicuspid valve.
Reinterventions

In this series the incidence of coronary stenosis (10%) is significantly higher if compared with the results of our total experience with ASO (5%) [12]. The technique of coronary artery reimplantation (button or trap door technique) was not a risk factor for the development of late coronary artery stenosis similarly to the entire series of ASO. One hypothesis is that in the case of commissural orientation mismatch, the coronary ostia are transferred to a suboptimal site due to the presence of a commissure at the optimal site of reimplantation. Second, the higher risk of coronary stenosis can be explained with the neo-aortic root dilatation observed for some patients that will change the take-off angle of the reimplemented coronary arteries, particularly at the sinus of Valsalva level.

One patient developed progressive ARD and mild AR and required a Bentall procedure, suggesting that ARD might have been responsible for the development of AR [13]. The Marfan-like histology of the aortic wall is something that has been described for conotruncal defects with a high prevalence of great arterial medial abnormalities of smooth muscle, elastic fibers, collagen, and ground substance [14]. Aortic medial abnormalities may be associated with or predispose to dilatation. Indeed, the presence of a bicuspid valve, known for its relationship with root dilatation, may contribute to root dilatation irrespective of the functional state of the valve [15].

ARD

Unfortunately, in our retrospective review, we were unable to analyze the exact dimensions of the aortic root over the time as description and measurements were inconsistent. Only measurements taken at last follow-up were considered for the study.

We aimed to detect ARD, particularly at the annulus and sinus of Valsalva levels and also at the sinotubular junction and ascending aorta. We found that the root dilatation was observed early during the follow-up with a mean time of diagnosis around 3 ± 1 years. Freedom from root dilatation was 80 ± 7% at 3 years, 72 ± 8% at 5 years, and 65 ± 10% at 10 years, suggesting that if the root dilated, it did so early after surgery. In this population, root dilatation was particularly observed at the annulus and sinus levels (in terms of prevalence), rather than the distal root and ascending aorta. Our hypothesis (not validated statistically in this small population) is that the annulus and sinus dilatations were the consequence of the preoperative aorto-pulmonary mismatch (bicuspid pulmonary valve and presence of VSD) and, to the ASO itself (root enlargement due to coronary reimplantation [3]), something well established even for TGA with intact septum [1]. Using button technique or even resection of a portion of the dilated sinus at the site of coronary reimplantation may present a potential option to decrease initial aortic root enlargement.

After this initial root dilatation, there is a mild and progressive dilatation of the sinus of Valsalva (Fig. 4B), but even strong speculations must be omitted in the absence of serial measurements. The progressive dilatation could be the consequence of medial histological abnormalities and the presence of the bicuspid valve, both known as risk factors for root and ascending aorta dilatation [14,15]. This hypothesis needs further studies with regular monitoring of individual patient.

Interestingly, the relative position of the great arteries seemed to play a role in root dilatation, with a tendency to dilatation for side-by-side and rightward orientation of the great vessels. All patients who had a root Z-score up to 3 underwent a trap door technique at coronary reimplantation. Even if not statistically significant, this finding should be borne in mind when faced with a severely dilated root at surgery.

No progressive increase of the neo-aortic annulus was observed during this midterm follow-up, despite the findings of Khan et al. [4]. Our findings suggest that the neo-aortic annuli were larger but stayed stable during the study period.

Fate of the neo-aortic valve

In this series, five patients had mild-to-moderate AR at last follow-up, despite only one patient demonstrated to have mild AR in the immediate postoperative period. For the two patients with mild AR, one worsened and the other one decreased. These data suggest that it is really not possible to predict the evolution of postoperative AR, neither to define patients who are at risk of developing AR, but only that the prevalence had increased over time. The same conclusions have been made by others for TGA with tricuspid pulmonary valve, with an increased incidence of AR over the years (30% in at 15 years follow-up), but a tendency to decreasing degree of AR degree [5].

Interestingly, all patients with late AR underwent ASO with the use of trap door technique, although this was not statistically significant. This correlation between AR and trap door has been extensively demonstrated for simple TGA [3,16] and might be observed for TGA with bicuspid pulmonary valve too. Only one patient with AR had a non-restrictive VSD closure through the right atrium. While we did not experience AR after trans-aortic VSD closure (only one patient), we do not recommend VSD closure through the neo-aortic valve, known as a risk factor for AR [16]. We suggest that the same approach is taken for neo-aortic bicuspid valve, and this approach should be used only if the VSD cannot be closed transatrially.

No correlation was found between AR and ARD, probably because the mechanisms of AR are multifactorial (dysplastic valve or root, commissure distortion, consequences of aortic reconstruction, and coronary reimplantation). Root dilatation might be a late risk factor for AR, but was not significant in this series, even though a tendency was noted for dilated aortic annulus (P = 0.15). Patients with ARD and no AR had a preserved leaflet coaptation height compared to patients with no AR and no root dilatation (although leaflet coaptation height was indexed to standard dimensions).

Although the finding of AR was not infrequent for this specific population of TGA, the incidence of reoperation rate for AR was low, as described by others for TGA without neo-aortic bicuspid valve [17].

CONCLUSION

The present study shows that ASO in the presence of a well-functioning bicuspid pulmonary valve can be performed in neonates with low morbidity and mortality. Our data have demonstrated that the presence of a bicuspid pulmonary valve does not represent a high risk for aortic reoperation, but increases the risk but for coronary reinterventions in this series.
Longer individual follow-up is mandatory and would provide further useful data on the evolution of root dilatation and AR.

LIMITATIONS OF THE STUDY

The limitations of this study are those inherent to retrospective studies where data have been collected in a clinical context. The study is not compared with a control group. We are aware that in our study the subset of factors taken into account is very limited. This is partly due to the small number of patients affected and events, which limit the number of variables amenable to logistic regression testing.

Conflict of interest: none declared.

REFERENCES


APPENDIX A. CONFERENCE DISCUSSION

Dr E. Bacha (New York, NY): The nice thing about your study is that you have chosen to isolate the bicuspid pulmonary valves, excluding those with left ventricular outflow tract obstructions or other anomalies. Thus, your group is really a clean cohort of patients specifically with bicuspid pulmonary valve and no other anomalies, and that makes it a very interesting group to study.

Noteworthy is the association of bicuspid pulmonary valve with complex coronaries, something that makes sense to me but that I was not really aware of before. Those are obviously excellent technical results.

Now, to my questions. A 10% reoperation rate for a left coronary artery stenosis seems high at first glance, even if you say that those patients mostly had more complicated coronaries than the typical transposition.

First question: Do you routinely cath these patients post-op or just in the case of symptoms of problems?

Dr Angeli: In our unit, we are used to performing coronary catheterization in the presence of a difficult reimplantation technique or in the case of symptomatic patients. So every time that we have data about complex coronary reimplantation, we routinely perform angiographic examination.

Dr Bacha: So when you have a doubt or routinely for everybody?

Dr Angeli: No, not routinely for everybody, but in the case of doubt.

Dr Bacha: Moving on to another subject, which is dilated aortic root and aortic regurgitation. I would have expected a higher rate of aortic root dilatation and aortic regurgitation in this patient population, akin to patients with bicuspid aortic valve and cystic medial necrosis. You only had one reoperation. I would have expected more for that indication.

Can you speculate as to why that is, that you do not have even more aortic root dilatation and more aortic regurgitation that required a reop or reimplantation technique?

Dr Angeli: All the patients had the trap door technique, even the one that was reoperated, so I cannot say. But analyzing the patient that was reoperated, this was the only one where immediately in the theater we observed a severe mismatch, which was really important, between the pulmonary artery and the aorta.

In the immediate postoperative period, we evaluated this patient with a very strict follow-up, and we saw that the root was progressively dilated. It means that at 11 years old, this patient had an aortic root, a descending aorta of 49 mm.

Dr Bacha: This patient did not have a VSD or other anomalies?

Dr Angeli: No. And I want to stress this. We had a mismatch. In the presence of the bicuspid valve, the mismatch of the vessel was not always associated with a VSD.

Dr F. Lacour-Gayet (New York, NY): I really enjoyed your paper and want to share with you our observations on the long-term results of the arterial switch in regard to aortic root dilatation.

It is clear that patients with a large native pulmonary root are at risk of ultimately developing aortic root dilatation and insufficiency. So in this regard, for the past 20 years we have used a technique that tries to correct the mismatch between the native aortic root and the ascending aorta by using the right coronary button as a patch-enlargement of the ascending aorta. So I was very interested in your group of patients who are really at risk for late aortic root dilatation.

My question is, what is your feeling and what is in your mind about the prognosis of patients who are in the long-term developing severe aortic root dilatation? There could be a risk of aortic regurgitation and also rupture. From your study, do you see a way to prevent this?

Dr Angeli: Observing our patients during this ten years of follow-up, the number of patients with root dilatation was not so great because it is a small series of patients. But certainly, the tendency of the aortic root is to dilate. So I expect an increased number of root dilatations, more so than aortic regurgitation.

Concerning the surgical strategy, we believe that, as you said, in some cases where there is a huge mismatch, it is important to use a button technique and sometimes reimplant the coronary artery above the line higher than usual.

Surprising in this series, all the patients that dilated the root had a trap door technique, and it was correlated with the anatomy and the necessity of obtaining no kinking of the coronary artery.

So it was impossible to use the button technique in this situation. We strictly analyzed this, and we posed the question to ourselves as well.