Anatomical Risk Factors for Reintervention after Arterial Switch Operation for Taussig–Bing Anomaly

Running Head: Reinterventional factors post TBA Repair

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Word Count: 4446/4500

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Abstract

Background: This study aimed to determine the factors related to reintervention, especially for pulmonary artery stenosis (PS), in patients with Taussig–Bing anomaly (TBA) after arterial switch operation (ASO).

Methods: This retrospective study included 34 patients with TBA who underwent ASO between 1993 and 2018. Preoperative anatomical and physiological differences and long-term outcomes were determined using a case-matched control with transposition of the great arteries (TGA) with ventricular septal defect (VSD) and TBA with an anterior and rightward aorta.

Results: The median age and body weight at ASO were 43 (16–102) days and 3.6 (2.8–3.8) kg, respectively. Aortic arch obstruction and coronary anomalies were present in 64% and 41% patients, respectively. The hospital mortality rate was 11%, including one cardiac death, and late mortality rate was 2.9%. Furthermore, 41% patients underwent 26 reinterventions for PS. Patients undergoing PS-related reintervention had a significantly larger native pulmonary artery: aortic annulus size ratio than those not receiving reintervention (1.69 vs. 1.41, $P = 0.02$). This ratio was the only predictor of PS-related reintervention; it was significantly higher in the TBA group than in the TGA/VSD group. PS-related reintervention was required more in the TBA group than in the TGA/VSD group.

Conclusions: Regardless of complex coronary anatomy and associated anomalies, early and late survival were acceptable. Postoperative PS was strongly associated with having a larger native pulmonary valve, suggesting that an optimal surgical reconstruction was required for achieving an appropriate aortopulmonary anatomical relationship during ASO. (243 words)

Introduction

Double-outlet right ventricle with subpulmonary ventricular septal defect (VSD) was first described by Taussig and Bing in 1949[1]. The unique anatomy of Taussig–Bing anomaly (TBA), particularly, subpulmonary VSD with malalignment of the infundibular septum and frequent association with aortic arch obstruction and complex coronary anomalies, makes achieving optimal surgical repair a challenge, including arterial switch operation (ASO) and aortic arch reconstruction. Recent advancements in surgical techniques and perioperative management has resulted in improved outcomes of primary repair[2,3]. However, reintervention rate in patients with TBA is significantly higher than that in those with simple transposition of great arteries (TGA), accounting for about 22% to 40%[4-7]. Previous studies have emphasized that reintervention is more frequently observed in right-sided lesions, such as right ventricular outlet tract obstruction (RVOTO) and pulmonary artery stenosis (PS); the freedom from RVOTO or PS was 19% to 45%[3,8,9].

We sought to evaluate the long-term clinical outcomes, determine the factors related to reintervention, especially for PS after ASO, and determine whether the associated anomalies in patients with TBA affect reintervention. A case-match study was performed comparing anatomical characteristics and long-term outcomes between patients with TBA and TGA/VSD.

Patients and Methods

Out of 38 patients, a retrospective study of 34 patients with TBA, who underwent ASO at Okayama University Hospital between 1993 and 2018, was performed. Four patients who underwent Kawashima (n = 1), Damus–Kaye–Stansel procedure with Rastelli (n = 1), and Fontan (n = 2) operations were excluded. This study was approved by our hospital's Institutional Review Board. The requirement for obtaining informed consent was waived due to the study's observational nature. In this study, TBA was defined using Van Praagh criteria: true double outlet right ventricle; great arteries originating predominantly from the right ventricle, following the 50% rule; bilateral coni; VSD beneath the pulmonary artery (PA), with no pulmonary stenosis; and no pulmonary-mitral continuity[10]. The PA typically arises biventricularly, with the aorta positioned rightward and slightly anterior, or alongside the PA (side by side)[11].

Surgical technique

All procedures were performed under cardiopulmonary bypass with aortic and bicaval venous cannulation. Intraventricular rerouting of the VSD to the PA was performed with an expanded polytetrafluoroethylene patch. Both outflow tracts were carefully inspected, and resection of any obstructive infundibular structures was performed. The ascending aorta was transected above the sinotubular junction, and the PA was transected just before bifurcation. The coronary artery buttons were excised from the aorta and reimplanted using the open technique. The neo-pulmonary root was augmented with a fresh autologous pericardium. Lecompte maneuver was performed in all patients with an anterior and rightward aorta and some patients with arteries that lie side by side. Our strategy for aortic arch repair was to reconstruct the aortic arch without any patch materials, such as a homograft. End-to-end anastomosis was usually conducted; only two cases underwent the swing back technique[12]. Two-stage repair was performed for the high-risk for cardiopulmonary bypass.

Case-match control

Patients with TGA with VSD (TGA/VSD) were selected as case-match control. Seventeen patients with TBA an anterior and rightward aorta were matched, excluding one patient who did not undergo Lecompte maneuver because the swing back technique was utilized. In patients with TGA/VSD, a single best fit was chosen according to the preoperative anatomy assessed by echocardiogram and the surgical technique used, namely, aorta-PA relationship, Lecompte maneuver, aortic annulus size, and body weight at ASO.

Statistical analysis

Continuous variables were reported as median (interquartile range) for skewed data or mean (standard deviation) for values with normal distribution. Categorical variables were reported as absolute frequency (percentage). Patients' characteristics were compared between those who underwent PS reintervention and those who did not. Continuous variables were compared using Student's *t*-test or Mann–Whitney U test based on data normality of. Categorical variables were compared using Fisher exact tests or chi-square test. Risk factors for time-related outcomes were tested using Cox regression analysis. Univariate analysis identified variables with P-value < 0.15 that were entered in a stepwise fashion into a multivariate Cox proportional hazards regression model to determine the independent predictors of outcomes. The hazard ratio (HR) and 95% confidence interval (CI) were reported for significant multivariate risk factors. Estimate for freedom from reintervention was made by the Kaplan–Meier method. The level of statistical significance was set at P-value < 0.05. All statistical analyses were performed with SPSS version 22 (Chicago, IL).

Results

Patients' and anatomical characteristics

Patients' characteristics are demonstrated in Table 1. Median age and weight at total repair were 43 (16–102) days, 3.6 (2.8–3.8) kg, respectively. Four infants died in the hospital. Follow-up was available in 30 survivors (88%), with a median duration of 17.1 (9.6–21.0) years. Eight patients (23%) underwent two-stage repair with initial palliation: arch repair in 4, pulmonary artery banding in 1, and both procedures in 3.

Anatomical characteristics are shown in Table 1. The position of the aortic valve in relation to the pulmonary valve was anterior and rightward in 19 patients (55%) and side by side in 15 patients (45%). A usual coronary artery arrangement, with the left anterior descending and circumflex arteries arising from sinus 1 and the right coronary artery arising from sinus 2 (classified as 1LCx-2R by the Leiden Convention) was noted in 15 patients (44%), whereas the majority had various atypical branching patterns. Fourteen patients (41%) had coronary anomalies including a single coronary artery and intramural coronary artery. Aortic coarctation (CoA) was present in 22 patients (64%). Subaortic RVOTO requiring a relief at the time of ASO was found in seven patients (20%).

Operative and postoperative data

The mean cross-clamp time was 132±34 min. Lecompte maneuver was used in all patients with an anterior and rightward aorta and 10 out of 15 patients with side by side position of the great arteries as shown in Figure 1. Two patients who underwent VSD enlargement needed a permanent pacemaker implantation for complete heart block. The aortic arch was basically reconstructed with extended end-to-end anastomosis, and the swing-back technique was utilized in two patients.

Hospital mortality, defined as death within 30 days if discharged, or no time limit if remaining in the hospital, occurred in four patients (11%) (Supplementary Table 1). Late mortality occurred in one patient (2.9%). Four months after an uncomplicated ASO and CoA repair, the patient succumbed to severe pneumonia complicated by sepsis.

Reintervention

Surgical or transcatheter reintervention was required in 12 patients with a median follow-up period of 3.0 (0.1–20.5) years (Table 2). No mortality occurred upon reinterventions. Eight patients underwent eight catheter reinterventions, including PA balloon angioplasty (n = 7) and aortic arch balloon angioplasty (n = 1). Eight patients underwent 18 reoperations, including pulmonary arterioplasty (n = 7), relief of RVOTO (n = 4), aortic arch repair (n = 3), relief of LVOTO (n = 1), residual VSD closure (n = 1), aortic valve replacement (n = 1), and tricuspid valve repair (n = 1). Four patients underwent seven pulmonary arterioplasty, as one patient underwent four repetitive pulmonary arterioplasty. PS occurred at the bifurcation level of the main PA with bilateral PA in all four patients. The typical positional relationship between the aorta and PA is demonstrated in Figure 3. Although three patients did not originally have subaortic RVOTO, they underwent a RVOTO relief as a concomitant procedure to relieve PS.

PS-related reintervention

Patients were divided into two groups: those who underwent reintervention for PS including catheter intervention (PS group, n = 10) and others (non-PS group, n = 24). Association of variables with reintervention for PS is shown in Table 3. Age, body weight at ASO, and aorta-PA relationship were comparable between the two groups. CoA was associated in 90% of the PS group and 54% of the non-PS group (P = 0.061). Two-stage repair was more frequently performed in the PS group than in the non-PS group (50% vs. 12%, P = 0.023). The native PA annulus to aortic annulus ratio was significantly higher in the PS group than in the non-PS group (PS group; 1.69 [IQR, 1.60–1.82] vs. 1.41 [1.18–1.62], P = 0.018). The native PA annulus to aortic annulus ratio of all patients, excluding two patients who underwent swing back technique, was plotted according to Lecompte maneuver utilization (Figure 1). One patient who did not have a relatively large annulus for TBA (native PA annulus to aortic annulus ratio: 1.22) suffered from PS at the bifurcation level of the main PA. She underwent main PA banding plus aortic arch repair as a palliation surgery on day 14. While waiting for ASO, banding tape for the main PA was migrated to the bifurcation with the bilateral PA causing PS. Eight months later, she underwent PA plasty at the timing of ASO; however, PS remained.

All 18 patients with an anterior and rightward aorta underwent Lecompte maneuver, six (30%) of them caused PS. Ten patients with side by side position of the arteries underwent Lecompte maneuver; four (40%) of them had PS. The other four patients who did not undergo Lecompte maneuver entirely avoided PS, as shown in Figure 1. In a univariate analysis, native PA annulus to aortic annulus ratio ≥1.6 (HR 11.0; 95% CI, 1.35–90.1, *P* = 0.020) and two-stage repair (HR 3.77; 95% CI, 1.07–13.2, *P* = 0.033) were associated with PS-related reintervention. In a multivariate analysis, the native PA annulus to aortic annulus ratio ≥1.6 (HR 9.20; 95% CI, 1.06–79.9, *P* = 0.036) was the only predictor of PS-related reintervention (Table 4).

The PS-related reintervention rate was 34.4% at 10 years (10 of 29). Freedom from PS-related reintervention was stratified by the native PA annulus to aortic annulus ratio. It was lower in the patients with annulus ratio ≥1.6 than in those with annulus ratio <1.6 (33.3% vs 94.2% at 10 years, HR 19.1; 95% CI, 5.06–72.1, *P* <0.001; Figure 2).

Case-match control: TBA with an anterior and rightward aorta versus TGA/VSD

No statistical difference was found in age and body weight at ASO between the two groups preoperatively (Table 5). CoA was associated in 76% of the TBA group and was not entirely associated in the TGA/VSD group (P <0.001). Aortic annulus size did not differ between the two groups (8.2 vs. 8.1, P = 0.713). However, the PA annulus size was significantly larger in the TBA group (11.3 [IQR, 10.8–14.0] vs. 8.9 [7.7–9.4], P <0.001) and the native PA annulus to aortic annulus ratio was significantly higher in the TBA group than in the TGA/VSD group (1.50 [IQR, 1.23–1.71] vs. 1.02 [0.9–1.1], P < 0.001). Two-stage repair was performed more often in the TBA group than in the TGA/VSD group (4 vs. 0 patients, P = 0.033). PS-related reintervention was more often required in the TBA group than in the TGA/VSD group (6 vs. 1 patients, P = 0.034). More than mild aortic insufficiency during the follow-up was more often found in the TBA group than in the TGA/VSD group (mild, 6 vs. 2, P = 0.049; moderate, 3 vs. 0, P = 0.045). Neo-aortic valve size was larger in the TBA group than in the TGA/VSD group (139%N vs. 119%N, P <0.001) (Table 6).

Comment

Primary total repair for TBA can be performed in almost all neonates with good results. Therefore, it is indicated for the treatment of complex lesions[2,3]. Despite good clinical outcome in most patients, a high proportion needed various reinterventions and reoperations during the follow-up periods[4-6].

Univariate Cox regression analysis identified TBA as a significant predictor of reoperations for RVOTO and PS[6,8,13-14]. Therefore, the present study focused on long-term functional outcomes. In our study, PS was most commonly seen, in approximately 30%, at a much higher rate than recoarctation of aortic arch or RVOTO. All patients with PS were found to have stretched PA at the bifurcation level, which was compressed by the dilated ascending neo-aorta, especially by a huge sinus Valsalva (Figure 3). Analyzing the native PA annulus to aortic annulus ratio, patients with PS had significantly larger native PA annulus which was reconstructed as neo-aortic annulus. Another important finding was that patients with TBA had a larger native PA annulus compared to the TGA/VSD patients because of associating anomalies, which appeared to be the anatomical factor resulting in higher PS-related reintervention.

Large native PA annulus to aortic annulus: effect of preoperative anatomy and physiology

Patients with PS had a tendency to have larger native PA and CoA, and more frequently underwent two-stage repair than the non-PS patients. Not all patients with CoA underwent two-stage repair. However, two-stage repair was entirely performed in patients with CoA. Existence of CoA increases blood flow toward the native PA, which grows at the annulus and sinus of Valsalva of the native PA.

Two-stage repair is divided into two patterns, arch repair only or PA banding plus arch repair. The former procedure causes growth of the annulus and sinus of Valsalva of the PA, and the latter procedure provokes dilation of the sinus of Valsalva and distortion of the PA valve[2]. A dilated Valsalva of the native PA had become more distended while waiting for total repair (Figure 4). In our study, eight patients had staged repair. Before and after surgery, the sinus geometry of Valsalva and annulus was examined using computed tomography in three patients only, proving to be the ones that expanded toward the short axis while waiting. Although subaortic RVOTO boosts pulmonary blood flow, there was no correlation with PS in this study.

Impact of Lecompte maneuver

In general, Lecompte maneuver is not recommended in patients with side by side arteries[14]. Reviewing a large study about TBA, whether patients with side by side position of the great arteries should have Lecompte maneuver is controversial[2,9,15,16]. In our study, Lecompte maneuver was performed in all patients with an anterior and rightward aorta and in all patients with side by side position of the great arteries at first. However, the PS rate was so high in patients with side by side position of the great arteries that the policy was corrected to not perform Lecompte maneuver since

1998. Subsequently, all four patients with side by side position of the great arteries including two patients with native annulus ratio ≥1.6 avoided both PS-related reintervention and compression of the left coronary artery. The anatomical fact that the retroaortic space is larger compared to that in patients with an anterior and rightward aorta may support our technique of choice. As the principle is to allow the neo-PA to lie in its most natural position without tension, we believe that Lecompte maneuver is not required in this parallel arrangement of the great arteries. Although we did not shift the anastomosis site in the PA bifurcation across the right side, this procedure may be added.

Comparison to TGA/VSD

The striking difference between TBA with an anterior and rightward aorta and TGA/VSD was overriding the PA complexity of associating anomalies. Overriding PA increases blood flow toward PA, which grows the native PA. CoA was associated more often in the TBA group. In some cases, presence of CoA led to two-stage repair. Despite having an aortic annulus size similar to that in the TGA/VSD group, the PA annulus size was significantly larger in the TBA group. Preoperative larger native PA resulted in larger neo-aorta, which resulted in further PS-related reintervention because of the large neo-aortic root pushing forward on the PA; this has been observed in another study as well[16].

Bovés et al. compared the preoperative size of the great arteries' annulus and concluded that patients with TGA/VSD had larger native PA than patients with TGA with intact ventricular septum defect due to VSD[17]. This theory could also be applied to patients with TBA. Aortic insufficiency worsened in TBA. However, no reintervention for the aortic valve was needed in both groups.

Limitation

The current report has limitations of a retrospective study. Changes in perioperative management during the study period may have affected our results. Additionally, the small cohort size due to this disease rarity and the multiple variables in this series reflected a development of different surgical approaches regarding to initial palliative versus single-stage total correction.

Conclusions

Survival after ASO for TBA can be high despite concomitant major anomalies such as aortic arch obstruction, subaortic stenosis, and unusual coronary patterns. In this study, postoperative PS occurs more frequently in patients who had larger native PA, correlating with the association of CoA and two-stage repair. Optimal surgical reconstruction to achieve an appropriate aorto-pulmonary anatomical relationship with arch reconstruction at the time of ASO and close life-long surveillance is required.

Acknowledgements and Disclosures: None

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Table 1. Demographic and anatomical characteristics (n = 34)

Characteristic	n (%) or median (IQR)
Demographic	
Male	26 (76)
Median age at surgery (d)	43 (16–102)
Median weight at surgery (kg)	3.6 (2.8–3.8)
Aorta-pulmonary artery relationship	
Aorta anterior and rightward	19 (55)
Side by side	15 (45)
Coronary configuration*	
1LCx-2R	15 (44)
1R-2LCx	5 (14)
1L-2RCx	4 (11)
1LR-2Cx	2 (5)
1LCxR	3 (8)
2RLCx	3 (8)

Intramural coronary artery	1	(3)
Aortic coarctation	22	(64)
Subaortic RVOTO	7	(20)
Subpulmonary LVOTO	7	(20)
Other cardiac anomalies		
Ebstein's anomaly	1	(3)
Primary management of Taussig–Bing anomaly		
Primary total repair	26	(76)
Two-stage repair	8	(23)

IQR, interquartile range; L, left anterior descending anterior artery; Cx, left circumflex artery; R, right coronary artery; RVOTO, right ventricular outflow tract obstruction; LVOTO, left ventricular outflow tract obstruction

*Coronary configuration according to Leiden Convention

Table 2. Surgical or transcatheter reintervention (n = 34)

Reintervention	n (%)	No. of procedures
Any reintervention	12 (35)	26
Transcatheter reintervention	8 (23)	8
Pulmonary artery balloon angioplasty		7
Aortic arch balloon angioplasty		1
Surgical reintervention	8 (23)	18
Pulmonary arterioplasty		7
Relief of RVOTO		4
Relief of LVOTO		1
Aortic arch repair		3
Residual ventricular septal defect closure		1
Aortic valve replacement		1
Tricuspid valve repair		1

RVOTO, right ventricular outflow tract obstruction; LVOTO, left ventricular outflow tract obstruction

Table 3. Association of variables with reintervention for pulmonary artery stenosis

Variable	PS (n = 10)		No PS (n = 24)		*P*-value
Preoperative variables					
Male	7	(70)	18	(75)	0.611
Median age at surgery (d)	51	(15–172)	42	(16–92)	0.803
Median weight at surgery (kg)	3.6	(3.0–3.9)	3	(2.9–3.4)	0.566
Anatomical variables					
Aorta-PA relationship					
Aorta anterior and rightward	6	(60)	13	(54)	0.678
Side by side	4	(40)	11	(46)	0.678
Native PA annulus to aortic annulus ratio	1.69	(1.60–1.82)	1.41	(1.18–1.62)	0.018
Aortic coarctation	9	(90)	13	(54)	0.061

Subaortic RVOTO	1 (11)	6 (25)	0.299
Operative variables			
Primary total repair	5 (50)	21 (88)	0.023
Two-stage repair	5 (50)	3 (12)	0.023
Cross-clamp time (min)	125 (107-171)	120 (106-150)	0.418
Lecompte maneuver			
Yes	9 (90)	19 (79)	0.586
No	1 (10)	5 (21)	0.586

Data presented as median (interquartile range) or n (%). PS, pulmonary artery stenosis; PA, pulmonary artery; RVOTO, right ventricular outflow tract obstruction

Table 4. Risk analysis associated with PS-related reintervention

Factor	*P*-value (Univariate)	HR (95% CI); *P*-value (Multivariate)
Weight at surgery <3 kg	0.160	
Native PA annulus to aortic annulus ratio ≥1.6	0.020	9.20 (1.06–79.9); *P* = 0.036*
Preoperative aortic coarctation	0.101	3.60 (0.41–32.8); *P* = 0.249
Preoperative subaortic RVOTO	0.291	
Two-stage repair	0.033	2.46 (0.65–9.33); *P* = 0.185
Cross-clamp time >120 min	0.960	

HR, hazard ratio; CI, confidence interval; PS, pulmonary artery stenosis; PA, pulmonary artery; RVOTO, right ventricular outflow tract.

Only variables having a *P*-value < 0.15 in the univariate analysis are displayed and entered into the multivariate Cox regression model.

* *P*-value < 0.05 (multivariate)

Table 5. Pre- and perioperative case-match control (TGA/VSD)

Variable	Taussig–Bing anomaly (n = 17)	TGA/VSD (n = 17)	*P* value
Preoperative variables			
Median age at surgery (d)	54 (15–110)	17 (12–24)	0.072
Median weight at surgery (kg)	3.2 (2.9–3.9)	3.3 (3.0–3.6)	0.377
Anatomical variables			
Aorta anterior and rightward	17 (100)	17 (100)	1.00
Coronary configuration			
1LCx-2R	11 (64.7)	15 (88.2)	0.106
1LR-2Cx	0 (0)	1 (5.8)	0.310

1LCxR	3	(17.6)	0	(0)	0.070
2RLCx	3	(17.6)	1	(5.8)	0.287
Intramural coronary artery	1	(5.8)	1	(5.8)	1.00
Associating anomalies					
Aortic coarctation	13	(76.4)	0	(0)	<0.001
Subaortic RVOTO	5	(29.4)	0	(0)	0.015
Subpulmonary LVOTO	5	(29.4)	0	(0)	0.015
Great arteries					
Aortic annulus size	8.2	(6.8–9.5)	8.1	(7.6–8.9)	0.713
PA annulus size	11.3	(10.8–14.0)	8.9	(7.7–9.4)	<0.001
Native PA annulus to aortic annulus ratio	1.50	(1.23–1.71)	1.02	(0.9–1.1)	<0.001

Operative variables					
Primary total repair	13	(76.4)	17	(100)	0.033
Two-stage repair	4	(23.5)	0	(0)	0.033
Cross-clamp time (min)	122	(104–166)	81	(70–101)	<0.001
Lecompte maneuver	17	(100)	17	(100)	1.00
Hospital mortality	1	(5.8)	0	(0)	0.310

Data presented as median (interquartile range) or n (%). TGA, transposition of great arteries; VSD, ventricular septal defect; L, left anterior descending anterior artery; Cx, left circumflex artery; R, right coronary artery; RVOTO, right ventricular outflow tract obstruction; LVOTO, left ventricular outflow tract obstruction; PA, pulmonary artery

Table 6. Postoperative case-match control

Variable	Taussig–Bing anomaly (n = 17)	TGA/VSD (n = 17)	*P* value
Any reintervention	8 (47.0)	1 (5.9)	0.007
PS-related reintervention	6 (35.2)	1 (5.9)	0.034
Aortic valve-related reintervention	0 (0)	0 (0)	-
Long-term follow-up echocardiogram	n = 14	n = 17	
Age at echocardiogram (m)	116 (42–198)	115 (49–156)	0.534
Interval from surgery (m)	96 (37–197)	115 (49–156)	0.653
Aortic insufficiency			
None	0 (0)	3 (17.6)	0.098
Trivial	5 (35.7)	12 (70.5)	0.052

Mild	6	(42.9)	2	(11.7)	0.049
Moderate	3	(21.4)	0	(0)	0.045
Severe	0	(0)	0	(0)	-
Aortic valve size (%N)	139	(133–173)	119	(108–126)	<0.001

Data presented as median (interquartile range) or n (%). TGA, transposition of the great arteries; VSD, ventricular septal defect; PS, pulmonary artery stenosis

Figure legend

Figure 1. Relationship between native PA annulus and aortic annulus classified with performance of Lecompte maneuver and postoperative PS

Figure 2. Freedom from PS-related reintervention stratified by native PA annulus to aortic annulus ratio

Figure 3. Stretched PA at the bifurcation level being compressed by dilated ascending neo-aorta

Figure 4. Expanding Valsalva of the native PA (red arrow head) while waiting for total repair (A: before palliation, B: before total repair)