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의학박사 학위논문

이엽성 폐동맥 판막이 대혈관 전위의 동맥 치환술 후 새로운 대동맥궁 및 대동맥 판막의 기능에 미치는 영향

The impact of bicuspid pulmonary valve in aortic position after arterial switch for transposition of the great arteries on neoaortic root and valve

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이 논문을 의학박사학위 논문으로 제출함

2021 년 2 월

울 산 대 학 교 대 학 원

의　　학　　과

전 보 배

전보배의 의학박사학위 논문을 인준함

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Abstract

Objective Neoaortic valve regurgitation which might be related to root dilatation is one of the major concerns following arterial switch operation (ASO) for transposition of the great arteries (TGA). However, the future of native bicuspid pulmonary valve (BPV) in aortic position remains unclear. This study investigated the effect of bicuspid neoaortic valve on neoaortic root morphology, function, and the long-term clinical outcomes after ASO for TGA using propensity score matching (PSM).

Methods From January 1997 to December 2018, 442 patients underwent ASO for TGA. Patients who underwent staged repair (n=15), were repaired at extremely old age (> 1 year, n=9), and died before discharge (n=46), and were lack of echocardiographic data at discharge (n=20) were excluded. Among a total of 352 eligible patients, 18 patients (5.1%) had a BPV. After PSM (1:4), 15 patients with BPV (bicuspid group) and 60 corresponding patients with tricuspid pulmonary valve (tricuspid group) were enrolled for analysis. The change in dimension of neoaortic root and neoaortic valve function, and clinical outcome were compared in both groups.

Results Age (12 days vs 12 days, p=0.827) and body weight (3.2kg vs 3.2kg, p=0.786) at repair were similar in both groups. The median duration of follow-up was 9.9 years (4 months ~ 22.3 years). There was one late death 10 months after repair in tricuspid group. Freedom from all-cause reoperation at 10 years was 93.3 ± 6.4 % in bicuspid group and 87.0 ± 4.7 % in tricuspid group (p=0.839). Reoperation for neoaortic valve or root was required in 3 patients (2 in bicuspid group and 1 in tricuspid group) during follow-up without intergroup difference. Indexed dimension (z-score) of neoaortic annulus did not change in both groups (p=0.575), although there was an increasing tendency in z-score of neoaortic sinus without intergroup difference (p=0.69). Deterioration in neoaortic valve function was more prominent in bicuspid group (common odds ratio [OR] 1.40, 95% confidence interval [CI] 1.17-1.69, p<0.001 in bicuspid group vs common OR 1.12, 95% CI 1.01-1.23, p=0.029 in tricuspid group; p=0.028).

Conclusions Reoperation for neoaortic root or valve rarely occurred regardless of the number of neoaortic cusp. Neoaortic sinus might outgrow the norm regardless of the number of neoaortic valve cusp, while neoaortic annulus remained unchanged. Deterioration of aortic valve function was more prominent in bicuspid group, which suggests that the neoaortic valve function would be deteriorated mainly by valve itself, not root pathology.

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Introduction

The arterial switch operation (ASO) has been used as a standard surgical treatment for transposition of the great artery (TGA) since its first documented success [1]. For now, the ASO could be performed with very low operative mortality in experienced centers [2, 3], although there still remain concerns regarding residual problems including neoaortic root dilatation, neoaortic valve regurgitation (neoAR), coronary insufficiency, and pulmonary artery stenosis in the long-term.

In normal position, a bicuspid aortic valve is known to be associated with aortic root dilatation with various prevalence and degree of dilatation depending upon the phenotype. Moreover, a bicuspid pulmonary valve is more likely to be degenerated than pulmonary valve with three cusps [4]. Therefore, is it a reasonable question what happen to the bicuspid pulmonary valve which had become an aortic valve during ASO in the long-term. There were some studies investigating clinical outcomes after ASO for TGA with bicuspid pulmonary valve, changes in aortic root dimension and progression of neoAR [4, 5]. However, a small number of cases, lack of comparison among patients with different cusp morphology, and the use of simple paired comparison for evaluating change in neoaortic root dimension with different time intervals are limitations of previous studies.

This study investigated the effect of bicuspid neoaortic valve on neoaortic root morphology and function, and the long-term clinical outcomes after ASO for TGA using propensity score matching (PSM).

Methods

Patient selection and data collection

From January 1997 to December 2018, 442 patients underwent ASO for TGA. Patients who underwent staged repair (n=15), were repaired at extremely old age (> 1 year, n=9), and died before discharge (n=46), and were lack of echocardiographic data at discharge (n=20) were excluded from this study. Among a total of 352 eligible patients, 18 patients (5.1%) had a BPV. Propensity score matched analysis was used to compare the morphologic and clinical outcomes between bicuspid and tricuspid pulmonary valve in aortic position. Variables used to generate the propensity score included sex, age at operation, ventricular septal defect (VSD), Taussig-Bing anomaly and arch obstruction. After one-to-four matching with propensity scores, 15 patients with BPV (bicuspid group) and 60 corresponding patients with tricuspid pulmonary valve (tricuspid group) were enrolled for analysis (Figure 1). We reviewed the electronic medical records of the study cohort to collect and collate data regarding patients' characteristics, anatomical details, operative details, perioperative and follow-up data. All serial echocardiographic images for individual patients were reviewed to obtain the information about the neoaortic root dimension, neoaortic valve function and other morphological or functional measurements. Sections that are difficult to accurately identify with echocardiography in neonatal patients, such as commissural orientation and the phenotype of the bicuspid valve, may be assisted by computed tomography or magnetic resonance imaging. Preoperative computed tomography has been used at our institution in all patients who underwent the surgery for complex congenital heart disease since 2015.

The study was approved by the institutional review board (IRB approval no. S2020-2228-0001), and the requirement for informed consent was waived because of the retrospective nature of the study design.

Definition

Serial measurements of the neoaortic annulus and sinus were taken in the parasternal long axis view and adjusted for body surface to calculate z-scores by referring the data from Cincinnati Children's Hospital [6]. The severity of neoAR was assessed on the basis of Doppler echocardiographic findings following the American Society of Echocardiography (ASE) guidelines [7]; none to trivial, 0; mild, 1; mild to moderate, 2; moderate to severe, 3; severe, 4. Significant neoAR was defined as the degree of regurgitation equal to or greater than grade 2.

The outcome of interest was the composite of all-cause death, major complications within 30 days after surgery, development of significant (neoAR) and neoaortic root dilatation. Major complications included unplanned reoperation, cardiac arrest, arrhythmia requiring permanent pacemaker implantation, circulatory instability requiring mechanical support, acute renal failure requiring hemodialysis or hemofiltration, neurologic deficit persisting at discharge, and deep wound infection or mediastinitis.

Surgical techniques

During the study period, ASO for TGA was performed by four surgeons. With standard aortic and bicaval venous cannulation, moderate hypothermic cardiopulmonary bypass was used for repair. Multiple dosage of antegrade cold crystalloid or blood cardioplegia was administrated indirectly and directly. After the main pulmonary artery transection, pulmonary valve was inspected to evaluate the morphological characteristic of the pulmonary valve. All the pulmonary valves, which were supposed to be a future aortic valve, were never touched in this study cohort. Decision on coronary reimplantation using trapdoor incision and before or after neoaortic reconstruction was at the individual surgeons' discretion. Deficient neopulmonary artery was augmented with autologous pericardial patch with or without treatment. Lecompte maneuver was used in all patients. All intracardiac procedures were accomplished before arterial switch procedures.

Statistical analysis

Categorical variables were presented as frequencies and percentages, and continuous variables were presented as mean with standard deviation or median with interquartile range (IQR) according to the distribution of the data. In order to minimize the effect of selection bias in this observational study, one-to-four matching based on the propensity scores estimated with morphology of pulmonary valve cusp as a dependent variable by logistic regression analysis was used. Age at operation, sex, ventricular septal defect (VSD), Taussig-Bing anomaly and arch obstruction were included as confounders. The absolute standardized mean difference was used to evaluate the balance after weighting. A standard mean difference value $\geq$0.1 was considered an indicator of meaningful imbalance. The effect of pulmonary valve cusp morphology (bicuspid vs tricuspid) on outcomes of interest, such as any death or transplant, all-cause reoperation, and reoperation related to neoaortic root or neoaortic valve was estimated using Cox's portional hazard model. We used mixed linear regression model to evaluate the difference in serial change of neoaortic root dimension between groups. The effect of neoaortic valve cusp morphology on progression of neoAR was assumed by obtaining common odd ratio derived from ordinal logistic regression model where the expected probability of each individual was expressed as probability curve. Statistical analysis was performed using SPSS Statistics version 22 (IBM, Armonk, NY, USA), R software version 3.4.4 (www.r-project.org), and GraphPad statistical software package version 5 (GraphPad, San Diego, CA, USA). A *p*-value less than 0.05 was considered statistically significant.

Results

Patients characteristics

Table 1 shows baseline and morphologic characteristics which were used as variables for calculating propensity scores. There was no residual imbalance after PSM. Table 2 shows the other baseline and morphologic characteristics. There were 36 females and 39 males. Median age and body weight at initial surgical treatment, incidence of low birth weight and prematurity were comparable between the two groups. Thirty-six patients (36/75, 48%) were prenatally diagnosed. The relationship of the great vessels was anterior posterior of in 42 patients (56.0%), rightward in 28 patients (37.3%) and side-by-side orientation in 5 (6.7%) without intergroup difference (p=0.096). Coronary artery anatomy was usual in 47 patients (47/75, 62.7%) without intergroup difference (p=0.695). Forty-five patients (45/75, 60.0%) had a VSD and 13 patients (13/75, 17.3%) were diagnosed as having Taussig-Bing anomaly. All the patients with arch obstruction were excluded through the matching process.

Operative outcomes

Closed technique which represents coronary reimplantation after neoaortic reconstruction was more frequently used in bicuspid group (9/15 [60%] in bicuspid group vs 20/60 [33.3%] in tricuspid group), but the difference did not reach statistical significance (p=0.077) (Table 3). When coronary reimplantation, trapdoor incision was used in most patients (15/15 [100%] in bicuspid group vs 58/60[96.7%] in tricuspid group, p=1.000) (Table 3). Cardiopulmonary bypass time (197 minutes [IQR, 167-230 minutes] in bicuspid group vs 161 minutes [IQR, 137-196 minutes] in tricuspid group, p=0.063) and aortic cross clamp time (121 minutes [IQR, 91-157 minutes] in bicuspid group vs 95 minutes [IQR, 81-115] in tricuspid group, p=0.009) were longer in bicuspid group. (Table 3)

Major complications included residual VSD in three patients, mediastinal bleeding in two patients, residual pulmonary artery stenosis in one patient, and pericardial effusion requiring pericardiostomy in one patient. The median hospital stay was not different between groups (13 days [IQR, 9-19 days] in bicuspid group vs 10 days [IQR, 9-15 days] in tricuspid group, p=0.240) (Table 3).

NeoAR was absent on Doppler echocardiographic exam at discharge in most patients (13 [86.7%] in bicuspid group vs 54 [90%] in tricuspid group) (Table 4).

Long-term clinical outcomes

There was one late death (1.3%) in tricuspid group. A full-term male baby with a birth weight of 3.5kg who underwent ASO, VSD closure at 2 weeks after birth, died of respiratory arrest at 10.9 months postoperatively. Follow-up was complete in all patients, and the median follow-up duration was 9.9 years (range, 4 months-22.3 years). There was no difference in overall transplant free survival between groups (Figure 2).

All-cause reoperation was required in 11 patients (11/75, 14.7%) (Table 5). Freedom from all-cause reoperation at 10 years was 93.3 ± 6.4 % in bicuspid group and 87.0 ± 4.7 % in tricuspid group without statistical significance ($p=0.839$). Reoperation for aortic valve or aortic root was rarely required during follow-up (3/75, 4.0%). One patient with tricuspid PV underwent aortic root reduction plasty at 11.9 years after repair. Another two patients with BPV needed aortic valve repair at 10 months and aortic root reduction plasty at 19.4 years after ASO, respectively (Table 5).

Neoaortic root morphology and function

Baseline neoaortic root dimension measured before discharge after ASO was similar in both groups (Table 6). Neoaortic annulus diameter absolute value increased in both groups, ($\beta=0.764$, $p<0.001$ in bicuspid group vs $\beta=0.881$, $p<0.001$ in tricuspid group), but more prominently increased in tricuspid group ($p=0.044$) (Figure 4A). Indexed neoaortic annulus diameter (z-score) remained unchanged in both groups ($\beta=0.018$, $p=0.563$ in bicuspid group vs $\beta=0.002$, $p=0.911$ in tricuspid group) without intergroup difference ($p=0.575$) (Figure 4B). Neoaortic sinus dimension in absolute value increased in both groups, ($\beta=1.104$, $p<0.001$ in bicuspid group vs $\beta=1.271$, $p<0.001$ in tricuspid group), but more prominently increased in tricuspid group ($p=0.022$) (Figure 5A). Indexed neoaortic sinus diameter (z-score) increased in both groups, but the change was statistically significant only in tricuspid group ($\beta=0.026$, $p=0.285$ in bicuspid group vs $\beta=0.037$, $p=0.005$ in tricuspid group). There is no intergroup difference ($p=0.691$) (Figure 5B)

During follow-up, the grade of neoaortic regurgitation are getting worse in both groups (common OR 1.40, 95% CI 1.17-1.69, $p<0.001$ in bicuspid group vs common OR 1.12, 95% CI 1.01-1.23, $p=0.029$). The worsening of neoaortic regurgitation was more prominent in bicuspid group ($p=0.028$) (Figure 6).

Discussion

The ASO is one of the greatest success story in the field of pediatric cardiac surgery. Since its first documented success in 1975[1], it became a standard surgical treatment for TGA with amassing knowledge and technique by leading groups in late 1980s [8, 9]. Recent reports covering ASO for TGA consistently noted low operative mortality [2, 3, 10], although long-term concerns are still lacking. NeoAR which might be related to neoaortic root dilatation is one of the major concerns following ASO [11-16]. Schwartz and colleagues from Boston demonstrated that post-ASO patients were at risk of neoaortic root dilatation and neoAR in the long-term [11]. The authors identified previous pulmonary artery band as a risk factor for development of neoaortic root dilatation, and previous pulmonary artery band, older age at repair, and presence of VSD as risk factors for development of significant neoAR. It is interesting that neoaortic root dilatation seemed not progressive and surgery for neoAR was rarely required in their report [11]. In contrast, van der Palen et al. noted that neoaortic root dilatation was progressive and associated with the progression of neoAR [14]. McMahon and colleagues [13] indicated that neoaortic root dilatation was a risk factor for development of significant neoAR. They also identified the factors associated with neoaortic root enlargement, including previous pulmonary artery banding, the presence of VSD, and Taussig-Bing anatomy.

In our study, neoaortic sinus dimension seemed to be increased over time, although only the tricuspid group showed statistical significance. Given that the bicuspid aortic valve is frequently associated with aortic dilatation partially attributable to the effect secondary to flow dynamics [17], our finding is telling other story in case of switched neoaortic bicuspid valve compared to the bicuspid aortic valve in normal position; bicuspid neoaortic valve might not affect the aorta through flow dynamics. The presence of bicuspid pulmonary valve might render coronary artery reimplantation and aortic root reconstruction difficult, and consequently neoaortic root could become more pathologic; however, we could not observe any negative findings related to technical difficulties in coronary implantation or neoaortic root manipulation on aortic root morphology or function. Our study also demonstrated that the growth of neoaortic valve annulus was proportional to the somatic growth regardless of pulmonary valve morphology. Since Leiden group noted that the growth of neoaortic valve annulus was stabilized from 2 years to 18 years of age but started to increase again at 15 years [14], longer follow-up might be mandatory to obtain solid conclusion.

Bicuspid pulmonary valve in TGA has not been considered a definite contraindication for ASO, unless unrelievable left ventricular outflow tract obstruction exists [18-21]. In our series, the prevalence of bicuspid pulmonary valve in repaired TGA was 5.1 %, which is compatible with previous reports where the prevalence was 4~7 % [4, 5, 14]. Previous studies reported that the bicuspid pulmonary valve might not have additional risk for the development of significant neoAR after ASO for TGA [4, 5]. However, most studies analyzed the data from small number of patients using simple methods, which precluded fair comparative analysis with patients having normal tricuspid pulmonary valve. Contrasting the previous reports, we directly compare the outcomes relevant to repaired-TGA among groups divided by the pulmonary valve cusp morphology. In addition, matching with propensity scores could further strengthen the power of comparison between groups with different pulmonary valve morphology in our study.

Even though surgery for neoAR in repaired-TGA patients was consistently uncommon in previous studies [11, 13] and our study as well, the occurrence of neoAR might increase as long as the follow-up period would be extended. As previously mentioned, the growth of neoaortic sinus seemed more prominent in tricuspid group, although an increasing tendency was also observed in bicuspid group. Unlike the findings from previous studies[14, 16], however, the progression of neoAR was more prominent in bicuspid group where the outgrowth of neoaortic sinus was less prominent. This finding suggests that the neoaortic valve function might be affected by neoaortic valve itself rather than neoaortic root pathology. Technically speaking, aortic manipulation such as trapdoor incision or aortic reconstruction before coronary implantation were known to be possible factors related to neoAR attributing to more prominent distortion of the sinotubular junction geometry. In our study, the trapdoor incision was used in most patients (74/75, 98.7%), and aortic reconstruction was performed before coronary implantation with similar incidence in both groups; therefore, surgical factors might not have or have a little impact on the development of neoaortic root dilatation or neoAR.

For now, the reoperation related to neoaortic valve was not frequently required. However, given that the worsening of neoAR was more prominent in bicuspid group, which was demonstrated in our study, longer and close follow-up is mandatory especially for repaired-TGA patients with bicuspid pulmonary valve.

This study was limited by the inherent disadvantages of a retrospective research. Furthermore, the impact of unmeasured factors on outcomes could not be excluded, although propensity adjustment might account for the measured confounders. Surgical technique and perioperative or follow-up management has been changed during the study period. Throughout the study period, there were four individual surgeons who had different surgical skills and strategies in coronary reimplantation and neoaortic root manipulation which might affect aortic root morphology and function. Due to the small number of patients, detailed analysis regarding the morphologic difference of bicuspid pulmonary valve could not be performed.

Conclusion

Reoperation for neoaortic root or valve rarely occurred regardless of the number of neoaortic cusp. Neoaortic sinus might outgrow the norm regardless of the number of neoaortic valve cusp, while neoaortic annulus remained unchanged. Deterioration of aortic valve function was more prominent in bicuspid group, which suggests that the neoaortic valve function would be deteriorated mainly by valve itself, not root pathology.

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None.

Compliance with Ethical Standards

Conflict of Interest

The authors declare that they have no conflicts of interest.

Ethical Approval

This study was approved by the review board at the participating institution.

Informed Consent

For this type of study formal consent is not required.

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Table 1. Covariates used for calculating propensity scores

	Before PSM			After PSM			
	Tricuspid	Bicuspid	*ASD	Tricuspid	Bicuspid	*ASD	*p*
Number	**334**	**18**		**60**	**15**		
Sex			0.284			0.033	1.000
male	248 (74.3)	11 (61.1)		31 (51.7)	8 (53.3)		
female	86 (25.7)	7 (38.9)		29 (48.3)	7 (46.7)		
Age (days)	8 (6-13)	15 (8-23)	0.753	12 (8-17)	12 (7-20)	0.061	0.827
VSD			0.605			0.000	1.000
No	208 (62.3)	6 (33.3)		24 (40.0)	6 (40.0)		
Yes	126 (37.7)	12 (66.7)		36 (60.0)	9 (60.0)		
T-B anomaly			0.242			0.086	0.716
No	305 (91.3)	15 (83.3)		50 (83.3)	12 (80.0)		
Yes	29 (8.7)	3 (16.7)		10 (16.7)	3 (20.0)		
Arch obstruction			0.499			0.000	-
No	297 (88.9)	18 (100.0)		60 (100.0)	15 (100.0)		
Yes	37 (11.1)	0 (0.0)		0 (0.0)	0 (0.0)		

Abbreviations ASD, absolute standardized difference; PSM, propensity score matching; VSD, ventricular septal defect;

*ASD of >0.1 is considered meaningful imbalances

Table 2. Baseline and morphological characteristics

Number (%) or median (IQR)		Tricuspid (n=60)	Bicuspid (n=15)	*p*
Body weight (kg)		3.2 (2.9-3.6)	3.2 (2.8-3.5)	0.786
Low birth weight (2.5kg)		7 (11.7)	1 (6.7)	1.000
Prematurity(37wk)		7 (11.7)	0 (0.0)	0.333
Era of surgery	1997~2003	22 (36.7)	3 (20.0)	0.096
	2004~2010	20 (33.3)	3 (20.0)	
	2011~2018	18 (30.0)	9 (60.0)	
Coronary Patterns	Usual	37 (61.7)	10 (66.7)	0.695
	Single	9 (15.0)	1 (6.7)	
	Others	14 (23.3)	4 (26.7)	
GA relationship	A-P	30 (50.0)	12 (80.0)	0.096
	Oblique	25 (41.7)	3 (20.0)	
	Side-by-side	5 (8.3)	0 (0.0)	

Abbreviations A-P, anterior-posterior; IQR, interquartile range

Table 3. Operative outcomes

number (%) or median (IQR)		Tricuspid (n=60)	Bicuspid (n=15)	*p*
Order of coronary transfer	Closed	20 (33.3)	9 (60.0)	0.077
	Open	40 (66.7)	6 (40.0)	
Way of coronary transfer	Trapdoor	58 (96.7)	15 (100.0)	1.000
	Button hole	2 (3.3)	0 (0.0)	
CPB time (minutes)		161 (137-196)	197 (167-230)	0.063
ACC time(minutes)		95 (81-115)	121 (91-157)	0.009
Hospital stay (days)		10 (9-15)	13 (9-19)	0.240

Abbreviations ACC, aortic cross clamping; CPB, cardiopulmonary bypass; IQR, interquartile range; PV, pulmonary valve annulus; VSD, ventricular septal defect

Table 4. NeoAR grade after ASO (at discharge and last follow-up)

NeoAR grade	Bicuspid (n=15)	Tricuspid (n=60)
0	13 (86.7%)	54 (90.0%)
1	2 (13.3%)	5 (8.3%)
2	0	1 (1.7%)
3	0	0
4	0	0

Abbreviations AR, aortic regurgitation; BPV, bicuspid pulmonary valve; TPV, tricuspid pulmonary valve;

Table 5. Reintervention or reoperation after arterial switch operation

	Group	Age (Day)	Cause	Operation	Interval (Year)	Status
1	BPV	23	LAD compression, aortic root aneurysm	LAD ostial relocation, Aortic root reduction plasty	19.4	Alive
2	BPV	21	Valvar AS	1. Balloon AVP 2. AVP	0.6 0.8	Alive
3	TPV	19	VSD, subaortic ridge	VSD direct closure, Subaortic membrane excision	1.0	Alive
4	TPV	19	LPA stenosis	Ballooning	1.3	Alive
5	TPV	14	Left main bronchus compression	Aortopexy	0.1	Dead
6	TPV	12	Chylothorax	Thoracic duct mass ligation	0.2	Alive
7	TPV	5	RVOTO	PV commissurotomy, pulmonary sinus augmentation	15.5	Alive
8	TPV	6	LVOTO	VSD extension, subaortic fibromuscular membrane excision	1.6	Alive
9	TPV	17	1. Supravalvar PS 2. Aortic root aneurysm, RVOTO	1. Balloon PVP 2. Aortic root reduction plasty, RVOTR	0.7 11.9	Alive
10	TPV	17	RVOTO	MPA widening	6.4	Alive
11	TPV	16	LVOTO	Intraventricular rebaffling, subaortic membrane resection	0.4	Alive

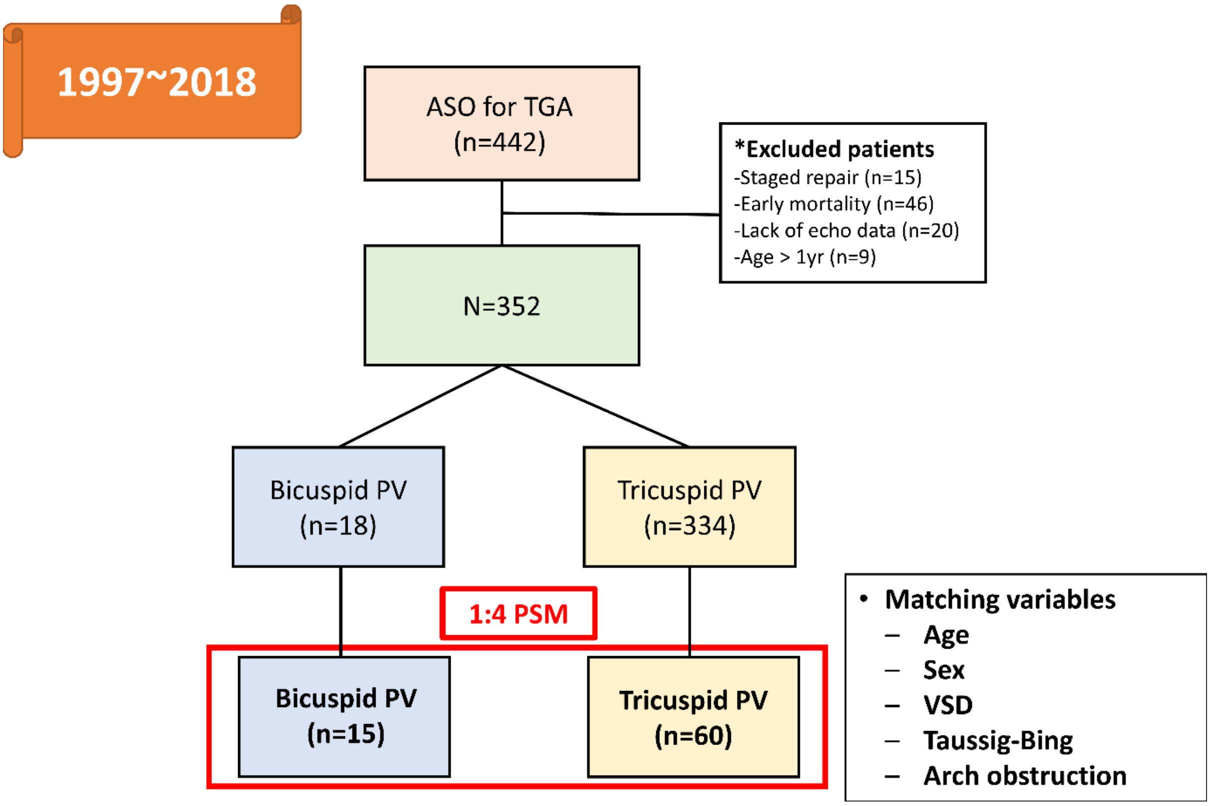
Abbreviations AS, aortic stenosis; AVP, aortic valve plasty; BPV, bicuspid pulmonary valve; LAD, left anterior descending branch; LPA, left pulmonary artery; LVOT, left ventricular outflow tract; LVOTR, left ventricular outflow tract reconstruction; MPA, main pulmonary artery; PS, pulmonary stenosis; RVOTO, right ventricular outflow tract obstruction; RVOTR, right ventricular outflow tract reconstruction; TPV; tricuspid pulmonary valve; VSD; ventricular septal defect

Table 6. Baseline neoaortic root dimension which was measured at discharge after ASO

	bicuspid PV=0	bicuspid PV=1	P-value
N	60	15	
Annulus			0.385
Mean±SD	8.33 ± 1.63	7.94 ± 1.44	
Median (IQR)	7.98 (7.25-9.05)	7.80 (6.72-9.20)	
Range (min-max)	(5.60-14.50)	(5.90-11.00)	
Annulus(z)			0.422
Mean±SD	1.48 ± 1.74	1.07 ± 2.12	
Median (IQR)	1.36 (0.46-2.51)	0.71 (-0.89-2.58)	
Range (min-max)	(-2.42-5.87)	(-2.10-5.18)	
Sinus			0.193
Mean±SD	12.42 ± 2.34	11.56 ± 2.25	
Median (IQR)	12.15 (10.50-14.10)	11.70 (9.80-12.70)	
Range (min-max)	(8.30-19.00)	(8.00-16.80)	
Sinus(z)			0.182
Mean±SD	1.93 ± 1.80	1.23 ± 1.95	
Median (IQR)	1.72 (0.71-3.23)	1.56 (-0.30-2.46)	
Range (min-max)	(-1.85-5.66)	(-2.54-5.32)	

Abbreviations IQR, interquartile range; PV, pulmonary valve; SD, standard deviation

Figure 1. Diagram for patient selection



Abbreviations ASO, arterial switch operation; TGA, transposition of the great arteries; PV, pulmonary valve; VSD, ventricular septal defect

Figure 2. Overall conditional survival after arterial switch operation

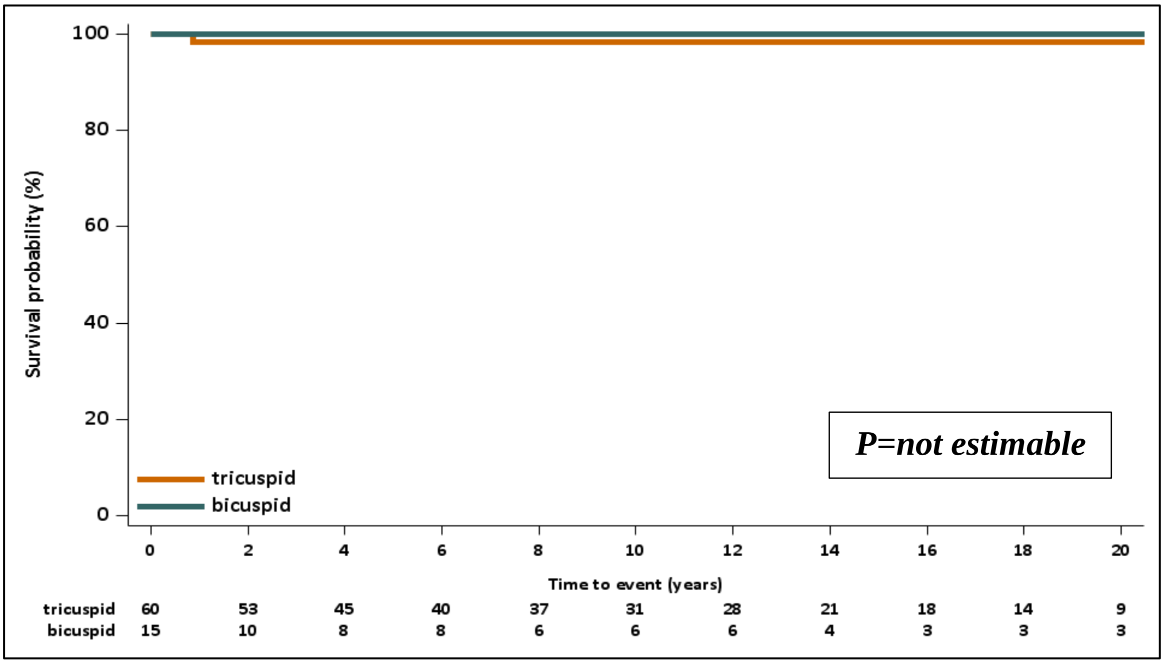
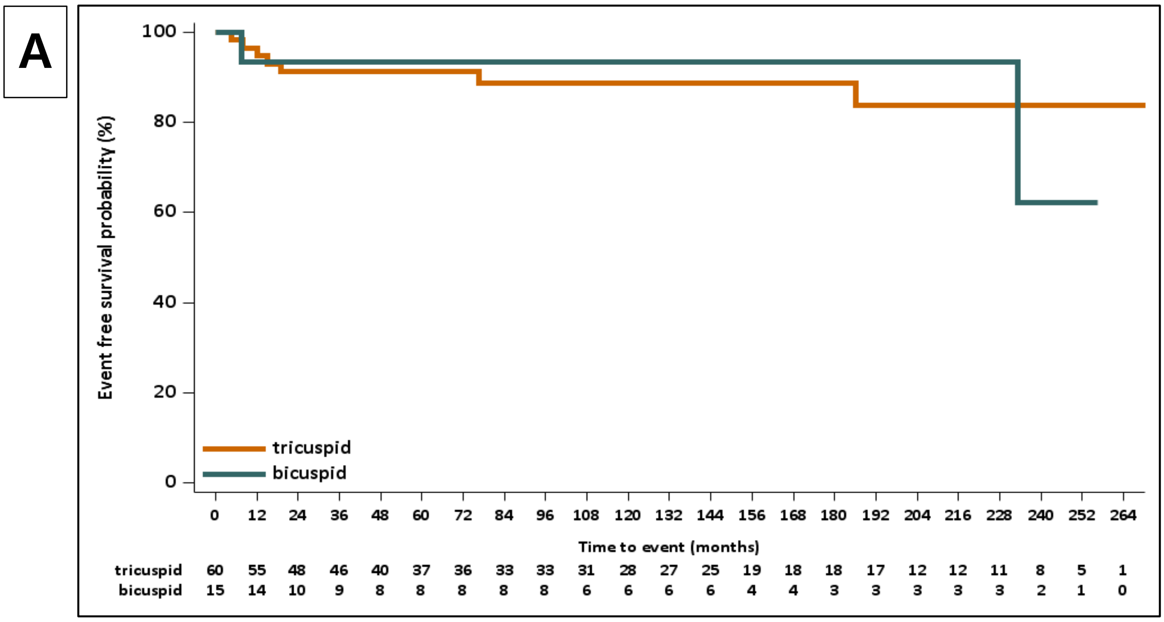


Figure 3. Reoperation free survival. (A) For all-cause reoperations (B) For reoperation related to neoaortic root or neoaortic valve



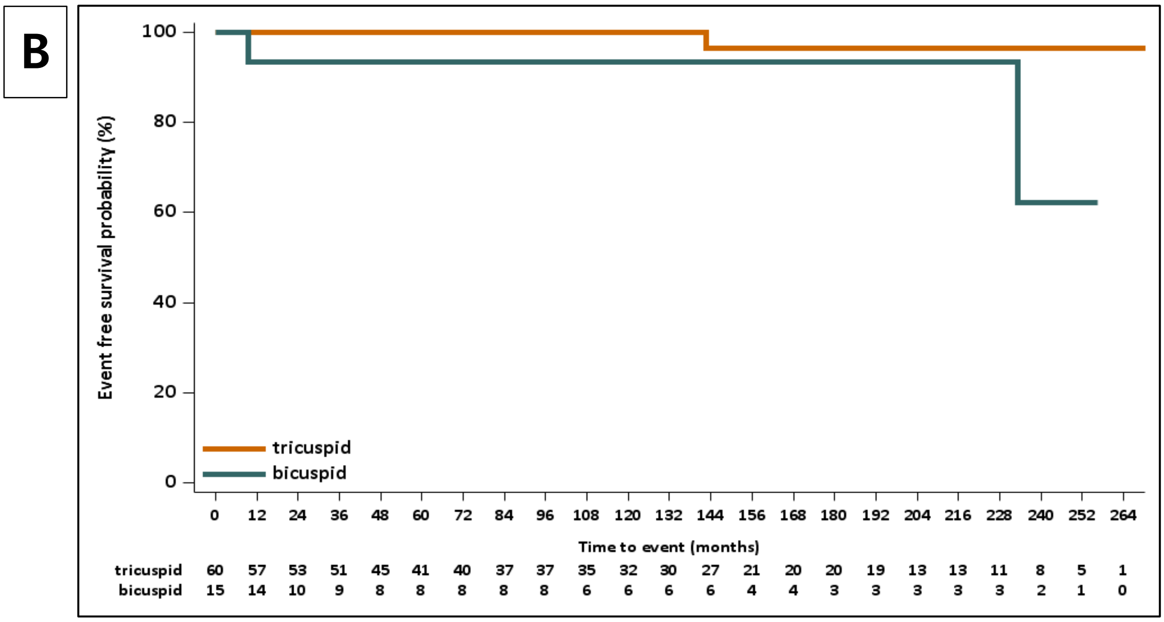


Figure 4. Serial change of neoaortic annulus dimension (A) The absolute value increased in both groups, (β=0.764, p<0.001 in bicuspid group vs β=0.881, p<0.001 in tricuspid group), but more prominently increased in tricuspid group (p=0.044), (B)The indexed value (z-score) remained unchanged in both groups (β=0.018, p=0.563 in bicuspid group vs β=0.002, p=0.911 in tricuspid group) without intergroup difference (p=0.575)

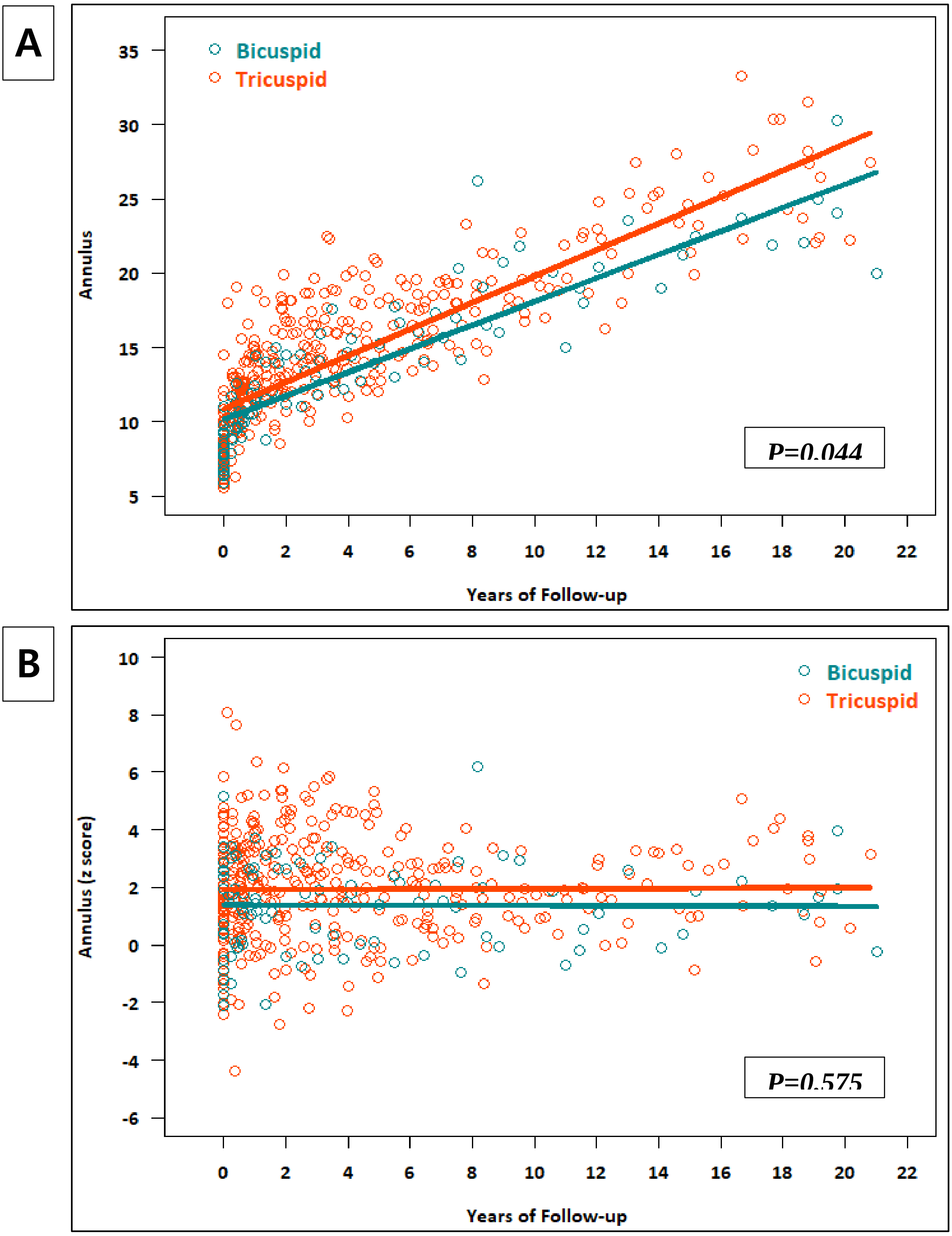


Figure 5. Serial change of neoaortic sinus dimension (A) The absolute value increased in both groups, (β=1.104, p<0.001 in bicuspid group vs β=1.271, p<0.001 in tricuspid group), but more prominently increased in tricuspid group (p=0.022), (B)The indexed value (z-score)increased in both groups but the change was significant only in tricuspid group (β=0.026, p=0.285 in bicuspid group vs β=0.037, p=0.005 in tricuspid group). There is no intergroup difference (p=0.691)

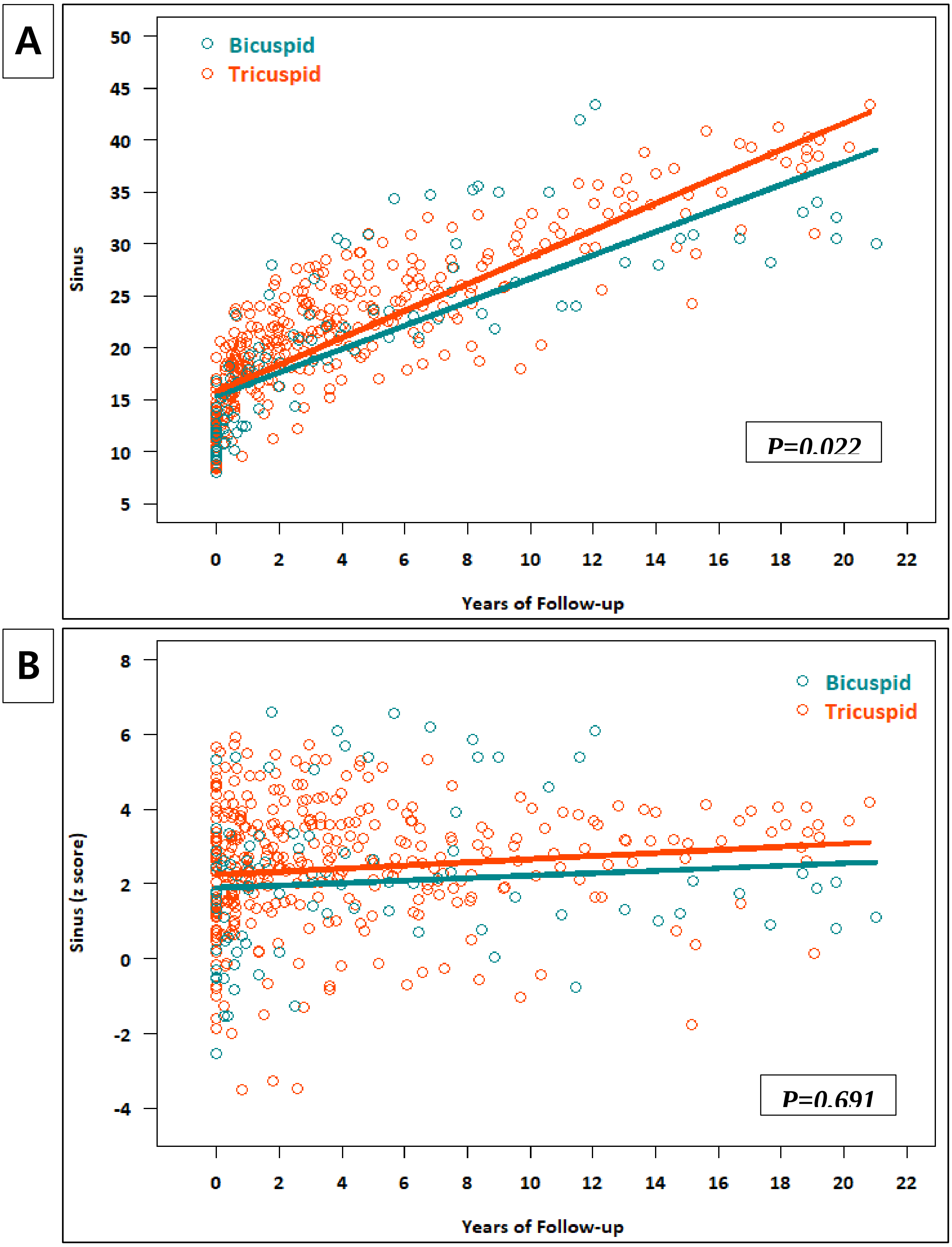
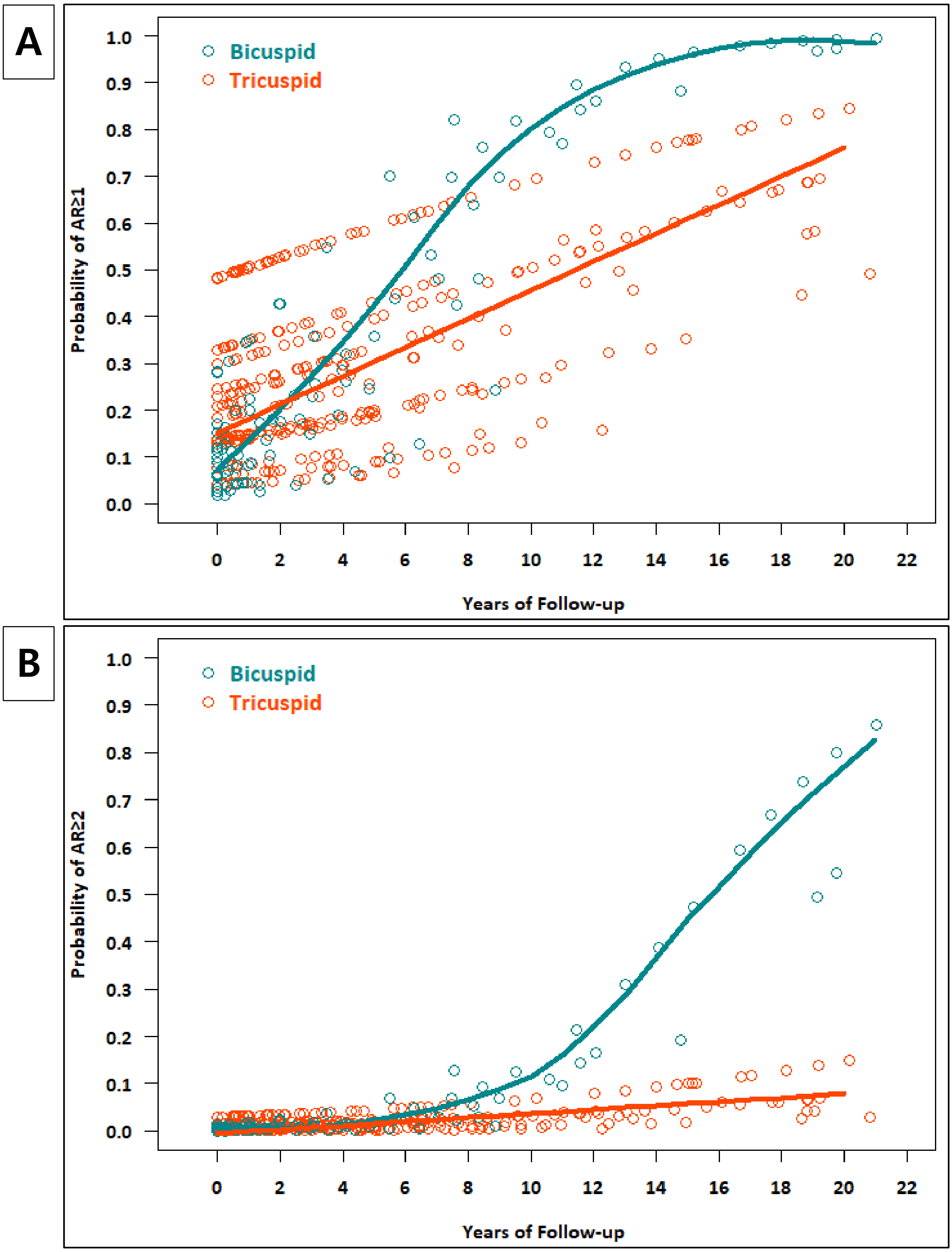


Figure 6. Probability of neo-aortic regurgitation during follow-up (A) Any regurgitation (B) Significant regurgitation (>grade 2). The grade of neoaortic regurgitation worsen in both groups (common OR 1.40, 95% CI 1.17-1.69, p<0.001 in bicuspid group vs common OR 1.12, 95% CI 1.01-1.23, p=0.029). The worsening of neoaortic regurgitation was more prominent in bicuspid group (p=0.028)



Korean abstracts (국문요약)

서론: 대동맥궁 확장과 관련하여 발생하는 새로운 대동맥판막 역류는 대혈관전위의 동맥치환술 이후의 주요 관심사 중 하나이지만 대동맥 위치에서의 이엽성 폐동맥 판막의 경과는 명확하게 밝혀져 있지 않다. 본 연구에서는 성향 점수 매칭을 이용하여 동맥치환술 이후의 대동맥판막 및 대동맥궁의 형태학, 기능 및 장기적인 임상 경과를 평가하였다.

연구 방법: 단일 기관 후향적 연구로 1997 년부터 2018 년까지 대혈관전위로 동맥치환술을 시행받은 442 명의 환아를 대상으로 하였다. 이 중 단계적 수술 (n=15), 수술 연령 1 세 이상 (n=9), 수술 후 조기 사망 (n=15) 및 심장초음파 검사 결과 누락 (n=46)의 경우는 연구에서 제외하였으며, 해당하는 352 명의 환아 중 18 명 (5.1%)의 환아가 이엽성 폐동맥 판막을 가지고 있었다. 1:4 성향 점수 매칭을 통해 15 명의 연구 대상군 (이엽성 폐동맥 판막)과 60 명의 대조군 (삼엽성 폐동맥 판막)을 설정하였으며, 연속적인 심장초음파 검사를 통해 새로운 대동맥 판막과 대동맥궁의 형태와 기능을 평가하였다.

결과: 수술 시 연령 (12 일 vs 12 일, p=0.827)과 체중 (3.2kg vs 3.2kg, p=0.786)은 두 그룹 간 유의한 차이를 보이지 않았다. 평균 경과 관찰 기간은 9.9 년 (4 개월~22.3 년) 이었으며, 사망 환자는 1 명 (수술 후 10 개월, 삼엽성 판막 그룹)이었다. 10 년 경과관찰 중 이엽성 판막의 경우 93.3 ± 6.4 %, 삼엽성 판막의 경우 87.0 ± 4.7 %의 환아가 재수술 없이 생존하였다 (p=0.84). 3 명 (이엽성 판막 그룹=2, 삼엽성 판막 그룹=1)의 환자가 대동맥궁 혹은 대동맥 판막과 관련한 재수술을 시행 받았으며, 그룹 간 차이는 없었다. 대동맥판막류는 양 군 모두 시간에 따른 큰 변화를 보이지 않았으나 (p=0.57), 대동맥궁은 시간에 따라 다소 증가되는 경향을 보였고 (p=0.69), 대동맥판막의 기능 악화는 이엽성 폐동맥 군에서 더 현저하였다 (p=0.03).

결론: 새로운 대동맥 판막의 형태와 관계 없이 대동맥궁 및 대동맥 판막에 대한 재수술은 거의 필요하지 않았다. 판막의 형태와 관계 없이 대동맥궁은 정상치보다 커졌으나, 대동맥륜은 거의 변하지 않았다. 이엽성 폐동맥 판막을 가지는 환아에서 판막 기능의 저하가 더 두드러진 것으로 보아 수술 이후 판막의 기능은 대동맥궁과 보다는 주로 판막 자체에 의해서 악화됨을 시사한다.