의학석사 학위논문

유아기에서
우심실-폐동맥 간 도관을 이용한
양심실 교정의 결과

Outcomes after Biventricular Repair
Using a Conduit between the Right Ventricle and
Pulmonary Artery in Infancy

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의 학 과
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지 도 교 수 박 천 수

이 논문을 의학석사학위 논문으로 제출함

2024 년 8 월

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장동희의 의학석사학위 논문을 인준함

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Abstract

Background

We investigated the outcomes of biventricular repair using a right ventricle to pulmonary artery (RV-PA) conduit placement in patients aged <1 year.

Methods

Patients aged <1 year who underwent biventricular repair using an RV-PA conduit from 2011-2020 were enrolled in this study. The outcomes of interest were death from any cause, conduit reintervention, and conduit dysfunction (peak velocity of ≥3.5 m/sec or moderate or severe regurgitation).

Results

Overall, 141 patients were enrolled. The median age at initial conduit implantation was 6 months. The median conduit diameter z-score was 1.3. The overall 5-year survival rate was 89.6%. The multivariable analysis revealed a younger age (p=0.006) and longer cardiopulmonary bypass time (p=0.001) as risk factors for overall mortality. During follow-ups, 61 patients required conduit reintervention, and conduit dysfunction occurred in 68 patients. The 5-year freedom from conduit reintervention and dysfunction rates were 52.9% and 45.9%, respectively. In the multivariable analysis, a smaller conduit z-score (p<0.001) emerged as a shared risk factor for conduit reintervention and dysfunction. Analysis of variance revealed a nonlinear relationship between the conduit z-score and conduit reintervention or dysfunction. The hazard ratio was lowest among patients with a conduit z-score of 1.3 for reintervention and 1.4 for dysfunction.

Conclusion

RV-PA conduit placement can be safely performed in infants. A significant number of patients required conduit reintervention and had conduit dysfunction. Using a slightly over-sized conduit with a z-score of 1.3 may reduce the risk of conduit reintervention or dysfunction.

Keywords: Right ventricle to pulmonary artery conduit, Infancy, Conduit reintervention, Conduit dysfunction, Conduit diameter z-score

목 차

표 차례

그림 차례

INTRODUCTION

In patients undergoing surgery for complete repair of various congenital cardiac defects, such as discontinuous right ventricular outflow tract (RVOT) or Ross operation for congenital aortic valve diseases, it is necessary to establish continuity between the right ventricle (RV) and the pulmonary artery (PA). This is achieved through the placement of an RV-PA conduit. Various conduits, such as homografts, porcine-valved Dacron conduits (Hancock; Medtronic Inc., Minneapolis, MN, USA), bovine jugular vein-valved conduits (Contegra; Medtronic Inc.), and polytetrafluoroethylene tubes (PTFE; W.L. Gore & Associates Inc., Newark, DE, USA) with or without a PTFE membrane valve, have been used to establish RV-PA continuity. However, homografts, which were traditionally the preferred option, are no longer widely available in most countries due to a decline in tissue donors [1-3]. Consequently, alternative conduits, which have been proven to be non-inferior to homografts are being increasingly employed in these operations [1,4].

Although surgery using an RV-PA conduit has excellent survival outcomes, the conduit failure and reintervention rates, which significantly impacts patient outcome are still high [3-5]. Among several factors influencing the risk of RV-PA conduit reintervention, patient age and weight play particularly significant roles. Consequently, the selection process for neonates and small infants poses a challenging task. [3,6,7].

Most previous studies on RV-PA conduits have included patients of varying ages, with little focus on neonates and infants. Moreover, many of these studies included results obtained using homografts. Here, we focused on younger patients for whom selecting a conduit type and size is difficult, as well as on patients who underwent an RV-PA conduit placement since 2011 (i.e., during a period when various conduits, such as Contegra and PTFE tubes, have begun to be used). In particular, we investigated the outcomes of RV-PA conduit placement for biventricular repair in patients aged <1 year.

METHODS

Patient selection and data collection

This study was approved by the institutional review board of Asan Medical Center (approval number: 2023 1557-0001; approval date: July 21, 2023), and the requirement for obtaining informed consent was waived given the retrospective study design.

Our institutional Pediatric and Congenital Cardiothoracic Surgery Database was searched to identify patients aged <1 year who underwent biventricular repair using an RV-PA conduit between January 2011 and September 2020. Patients who received homografts were excluded. Baseline characteristics, morphological characteristics, operative details, and postoperative outcomes were collected through a retrospective review of electronic medical records. Follow-up data were obtained from outpatient visit records and telephone contact.

Definitions

The outcomes of interest were death from any cause or transplantation, conduit reintervention or reoperation, and conduit dysfunction. The dates of death, first reintervention, and first documentation of conduit dysfunction were the study endpoints.

Early mortality was defined as any death that occurred either within 30 days after the initial operation or before hospital discharge. Conduit reintervention was defined as any catheter-based or surgical reintervention performed on the conduit during follow-up. Catheter-based interventions included balloon dilatation or stenting of the conduit. Catheter interventions aimed solely at the PAs were not included in conduit reintervention. Patients who underwent conduit replacement during reoperation for reasons unrelated to conduit dysfunction were included in the analysis of time-to-conduit-reintervention but were censored for conduit dysfunction. The decision between catheter-based or surgical reintervention was made by interventional cardiologists and surgeons.

Serial echocardiographic examinations following RV-PA conduit implantations were reviewed to evaluate conduit function. Conduit dysfunction was classified into conduit stenosis, regurgitation, stenosis and regurgitation, or endocarditis, defined based on echocardiographic findings. The first documentation date was designated as the date on which the echocardiogram with abnormal findings was performed. To evaluate size mismatch, the conduit size was converted to a z-score using a standard formula. The echocardiographic assessment was conducted based on the recommendations of the European Association of Echocardiography (EAE) and the American Society of Echocardiography (ASE) [8]. Conduit stenosis was graded by measuring the maximum velocities across the conduit using continuous Doppler, and was defined as conduit dysfunction with a velocity ≥3.5m/ sec. Conduit regurgitation was graded by measuring the dimension of the insufficiency

jet using color-flow Doppler and was expressed on a five-grade scale (0, none; 1, trivial; 2, mild; 3, moderate; and 4, severe). Conduit dysfunction was defined as moderate or severe regurgitation.

No individual re-review of echocardiogram results was conducted; instead, results were solely based on the reports of the patients' cardiologists. The clinical follow-up frequency was not predetermined; it was conducted at the discretion of the patients' cardiologist. Postoperatively, all patients received intravenous heparin (5 U/kg/h), which was switched to antiplatelet treatment (aspirin at 5mg/kg/d) upon discharge.

Surgical techniques

After a midline incision was made and median sternotomy was performed, cardiopulmonary bypass (CPB) was established by aortobicaval cannulation. Immediately thereafter, systemic-to-PA shunts or persistent arterial ducts were occluded. Under moderate hypothermic CPB and cardioplegic arrest, intracardiac procedures, such as closure of ventricular or atrial septal defects and right ventricular incision for the RV-PA connection, were performed. During rewarming after the release of the aortic cross clamp (ACC), the distal end of the RV-PA conduit was first anastomosed to the PA, after which the proximal end was beveled and connected to a longitudinal incision on the RV. The conduit was chosen at the surgeon's discretion. If necessary, narrow segments of the PA were augmented using various patch materials. Intraoperative transesophageal echocardiography was routinely performed to evaluate procedural success after the patient was weaned from CPB.

Statistical analysis

Normality of the data was assessed using the Shapiro-Wilk test. Categorical variables were described as absolute numbers with percentages, and continuous variables were described as medians with interquartile ranges.

The time of initial conduit implantation was considered as the starting point for analysis, with survival time measured from the date of the initial conduit implantation to the date of either death or the last follow-up. Similarly, the time of freedom from conduit reintervention or dysfunction was regarded as the date of initial conduit implantation to the date of conduit reoperation, dysfunction, or the last follow-up, respectively. Patients who died were treated as censored for both the freedom from conduit reoperation and dysfunction outcomes.

The probabilities of survival, freedom from conduit reintervention, and freedom from conduit dysfunction were estimated using the Kaplan-Meier method. Survival curves was compared between groups using the log-rank test. P-values<0.05 were considered statistically significant. Factors associated with death or transplantation, conduit reintervention, and conduit dysfunction were identified using a logistic regression model and Cox proportional hazard models. Analysis of variance (ANOVA) was used to examine the significance of nonlinear relationships, and restricted cubic splines were used to analyze variables with a nonlinear relationship with the outcome. These results are reported using partial effect plots. Variables with a

p-value<0.05 in the univariable analysis were further assessed in multivariable analysis. In all analyses, confidence intervals (CIs) were set at the 95% level. Statistical analyses were performed using R software ver. 4.3.0 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Patients' characteristics

A total of 141 patients between January 2011 and September 2020 were included. **Table 1** summarizes the patients' baseline characteristics. The median age and body weight at initial conduit implantation were 6 months (interquartile range, 1–8 months) and 6.5 kg (interquartile range, 3.8–7.6 kg), respectively. Of these patients, 25 (17.7%) were neonates, and 16 (11.3%) weighed <3kg. Moreover, 26 infants (18.4%) were born prematurely. Chromosomal abnormalities were found in 25 patients (17.7%). The primary diagnosis was categorized into 5 groups. Pulmonary atresia with ventricular septal defect was the most common category, accounting for 58.1% (n=82) of cases.

Table 1. Baseline characteristics of the patients

Characteristic	Value
Total no. of patients	141
Age at operation (mo)	6 (1-8)
Neonate at operation (<28 days)	25 (17.7)
Weight at operation (kg)	6.5 (3.8-7.6)
Low weight at operation (<3.0 kg)	16 (11.3)
Gender	
Male	62 (44.0)
Female	79 (56.0)
Premature	26 (18.4)
Chromosomal anomalies	25 (17.7)
DiGeorge syndrome/22q11.2 microdeletion	9 (6.3)
Down syndrome	3 (2.1)
CHARGE syndrome[a)]	2 (1.4)
VACTERL syndrome[b)]	1 (0.7)
Others	10 (7.0)
Primary cardiac diagnosis	
Pulmonary atresia with VSD	82 (58.1)
Truncus arteriosus	18 (12.7)
DORV/ToF	16 (11.3)
ToF/Absent pulmonary valve syndrome	10 (7.0)
Others	15 (10.6)

Values are presented as number, median (interquartile range), or number (%). VSD, ventricular septal defect; DORV, double outlet right ventricle; ToF, tetralogy of Fallot.
[a)] CHARGE is an abbreviation for several of the features common in the disorder: coloboma, heart defects, atresia choanae (also known as choanal atresia), growth retardation, genital abnormalities, and ear abnormalities. [b)] VACTERL syndrome is based on an acronym for the affected organs and systems: V (vertebral anomalies), A (anal atresia), C (cardiovascular abnormalities), TE (tracheoesophageal fistula), R (renal anomalies), and L (limb defects).

Operative details

Table 2 describes the operative details of the patients. Previous palliative cardiac surgery was performed in 95 patients, of which a modified Blalock-Taussig shunt (n=65, 46%) was most commonly performed. More than half of patients (n=95, 67.3%) had undergone at least one type of previous surgery; among them, 18 patients (12.7%) had undergone two or more types of surgeries. The conduit types used for RV-PA connection were Contegra in 82 patients (54.2%), a homemade membrane-valved PTFE conduit in 34 patients (24.1%), a valveless PTFE conduit in 19 patients (13.5%), and a Hancock conduit in 6 patients (4.3%). Conduits with a 12-mm diameter were the most commonly used (61 patients; 43.2%). The median z-score of the conduit diameter was 1.3 (interquartile range, 0.8–1.8). At initial conduit implantation, concomitant pulmonary arterioplasty was performed in 92 patients (65.2%).

The differences in characteristics according to conduit type are described in **Table 3**. Valveless PTFE conduits tended to be used more commonly in younger patients with lower body weight. Additionally, in these patients, the conduit diameter z-score was significantly smaller, with valveless PTFE grafts utilized in all nine cases where an 8-mm graft was used. Furthermore, the ACC and CPB times were significantly longer in this group.

Table 2. Operative details

Variable	Value
Previous palliative cardiac surgery	
Modified Blalock-Taussig shunt	65
Central shunt	14
Pulmonary artery banding	9
Pulmonary artery angioplasty	8
MAPCA unifocalization	8
Modified norwood operation	4
Closure patent ductus arteriosus	3
Valvuloplasty	3
Truncal separation	1
Others	2
No. of previous cardiac surgery	
0	46 (32.6)
1	77 (54.6)
2	14 (9.9)
≥3	4 (2.8)
Type of conduit	
Bovine jugular vein (Contegra) conduit	82 (54.2)
Valved PTFE conduit	34 (24.1)
Valveless PTFE	19 (13.5)
Porcine-valved Dacron (Hancock) conduit	6 (4.3)
Conduit diameter (mm)	12 (12-14)
8	9 (6.3)
10	13 (9.2)
12	61 (43.2)
14	55 (39)
16	3 (2.1)
Conduit/Weight ratio	1.99 (1.7-2.8)
Conduit diameter, Z-score	1.34 (0.8-1.8)
Concomitant pulmonary artery angioplasty	92 (65.2)
Cardiopulmonary bypass time (min)	151 (123-203)
Aortic cross-clamp time (min)	54 (40-88)

Values are presented as median (interquartile range) or number (%). MAPCA, major aortopulmonary collateral arteries; PTFE, polytetrafluoroethylene

Table 3. Preoperative and operative characteristics according to the type of conduits

Characteristic	All	Contegra	Valved PTFE	Valveless PTFE	Hancock	p-value
Total no. of patients	141	82	34	19	6	
Age at operation (mo)	6 (1–8)	6 (4–8)	5 (1–9)	1 (0–5)	11 (7–12)	<0.001
Weight at operation (kg)	6.5 (3.8–7.6)	6.7 (5.3–7.7)	6 (3.7–7.7)	3.2 (2.8–6.1)	7.7 (7.0–8.6)	<0.001
Male gender	62 (44.0)	36 (85.0)	13 (38.0)	8 (42.0)	5 (83.0)	0.235
Premature	26 (18.4)	17 (20.4)	5 (14.7)	3 (15.7)	1 (16.6)	0.873
Chromosomal anomalies	25 (17.7)	10 (12.1)	11 (32.3)	2 (10.5)	2 (33.3)	0.039
Primary cardiac diagnosis						0.002
Pulmonary atresia with VSD	82 (58.1)	52 (63.4)	17 (50.0)	7 (36.8)	6 (100.0)	
Truncus arteriosus	18 (12.7)	9 (10.9)	3 (8.8)	6 (31.5)	-	
DORV/ToF	16 (11.3)	11 (13.4)	4 (11.7)	-	-	
ToF/Absent pulmonary valve syndrome	10 (7.0)	4 (4.8)	6 (17.6)	1 (5.2)	-	
Others	15 (10.6)	6 (7.3)	4 (11.7)	5 (26.3)	-	
Conduit diameter (mm)	12 (12–14)	12 (12–14)	12 (12–14)	10 (8–10)	14 (14–14)	<0.001
8	9 (6.3)	-	-	9 (47.3)	-	
10	13 (9.2)	-	7 (20.5)	6 (31.5)	-	
12	61 (43.2)	43 (52.5)	16 (47.0)	2 (10.5)	-	
14	55 (39.0)	38 (46.3)	10 (29.4)	2 (10.5)	5 (83.3)	
16	3 (2.1)	1 (1.2)	1 (2.9)	-	1 (16.6)	
Conduit diameter, Z-score	1.34 (0.8–1.8)	1.47 (0.9–2.0)	1.00 (0.8–1.7)	0.08 (-0.2–0.8)	1.27 (1.0–1.6)	<0.001
Cardiopulmonary bypass time (min)	151 (123–203)	143 (119–175)	176 (147–209)	204 (149–246)	153 (141–172)	0.007
Aortic cross-clamp time (min)	54 (40–88)	48 (37–73)	61 (48–90)	95 (76–110)	45 (42–57)	0.001

Values are presented as median (interquartile range) or number (%). PTFE, polytetrafluoroethylene; VSD, ventricular septal defect; DORV, double outlet right ventricle; ToF; Tetralogy of Fallot

Survival

There were 8 early deaths (5.6%) reported: 4 due to low cardiac output syndrome, 2 due to respiratory failure, and 2 due to sepsis. The median follow-up duration from initial conduit implantation was 4.4 years (interquartile range, 2.4–6.2 years). There were 6 late deaths (4.2%) recorded: respiratory failure in 1 patient, sepsis in 1 patient, gastrointestinal disease in 1 patient, and unknown causes in 3 patients who died outside the hospital. The overall survival rates were 91.5% and 89.6% at 1 and 5 years, respectively (**Figure 1**). In the univariable analysis, younger age, lower body weight, no previous palliative surgery, and longer CPB or ACC time were associated with overall mortality. In the multivariable analysis, younger age (p=0.006) and longer CPB time (p=0.001) were identified as risk factors for overall mortality (**Table 4**).

Figure 1. Overall survival after right ventricle to pulmonary artery conduit insertion. The shaded area represents 95% confidence intervals.

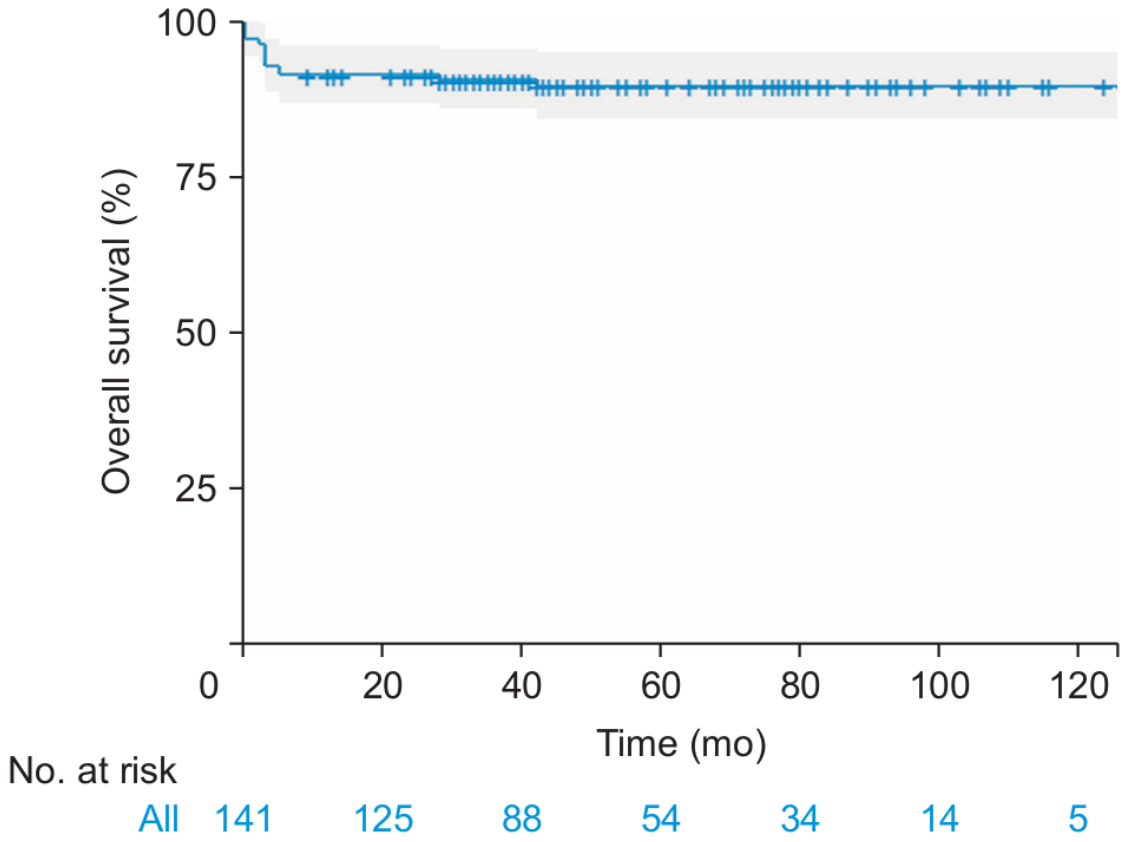


Table 4. Factors associated with overall mortality (n=14).

Variable	Univariate analysis		Multivariate analysis	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Age at operation (mo)	0.76 (0.64-0.91)	0.003	0.78 (0.65-0.93)	0.006
Weight at operation (kg)	0.63 (0.46-0.85)	0.002		
Prematurity	2.52 (0.84-7.52)	0.097		
Previous palliative cardiac surgery	0.34 (0.11-0.99)	0.048	0.95 (0.22-4.13)	0.953
Chromosomal abnormality	0.75 (0.16-3.39)	0.718		
Conduit diameter, z-score	1.53 (0.76-3.08)	0.232		
Concomitant pulmonary arterioplasty	0.36 (0.12-1.05)	0.063		
Type of conduit	1.01 (0.60-1.68)	0.968		
Primary cardiac diagnosis	1.36 (0.98-1.88)	0.063		
Cardiopulmonary bypass time	1.01 (1.01-1.01)	0.001	1.01 (1.00-1.01)	0.001
Aortic cross-clamp time	1.01 (1.00-1.03)	0.001		

HR, hazard ratio; CI, confidence interval

Conduit intervention

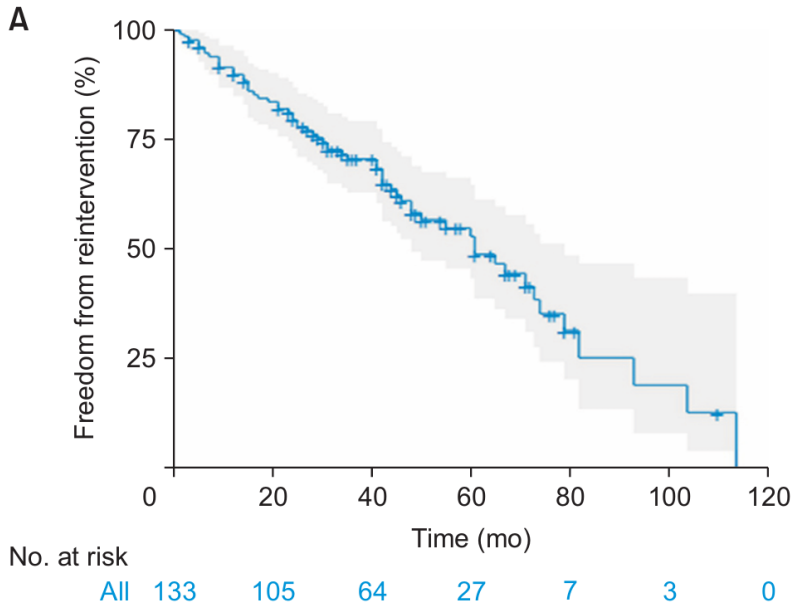
During the follow-ups, 61 patients required conduit reintervention; 44 patients underwent surgical reintervention and 17 patients underwent catheter-based reintervention at a median of 29 months after the initial conduit implantation. The indications for conduit reintervention included stenosis in 30 patients (49.1%), regurgitation in 8 patients (13.1%), combined stenosis and regurgitation in 15 patients (24.5%), infective endocarditis in 2 patients (3.2%), and other indications in 6 patients (9.8%). The freedom from conduit reintervention rates were 90% and 52.9% at 1 and 5 years, respectively (**Figure 2A**).

In the univariable analysis, younger age, lower body weight, no previous cardiac surgery, a smaller conduit diameter z-score, and the use of a valved or valveless PTFE conduit were associated with conduit reintervention. In multivariable analysis, a smaller conduit diameter z-score (p=0.003) was identified as a risk factor for conduit reintervention (**Table 5**).

Figure 3 shows the freedom-from-reintervention rate according to the type of conduit, which had been identified as a factor associated with reintervention in the univariable analysis. The freedom- from-reintervention rate was higher with the Contegra than with the valved PTFE (p=0.014) or valveless PTFE conduits (p=0.020) according to the log-rank test.

ANOVA demonstrated that the conduit diameter z-score had a significant nonlinear relationship with conduit reintervention (p=0.012). To account for this nonlinearity, restricted cubic splines were used to model the relationship, which showed that the lowest risk was attained at a conduit diameter z-score of 1.3 (**Figure 2B**).

Figure 2. Conduit reintervention following right ventricle to pulmonary artery (RV-PA) conduit insertion. (A) Kaplan-Meier curve for free dom from conduit reintervention and (B) a partial effect plot for the RV-PA conduit diameter z-score and the log-transformed related hazard ratio (HR) for conduit reintervention. The shaded area represents the 95% confidence interval. The arrow indicates the conduit diameter z-score (1.3) with the lowest risk of conduit reintervention.



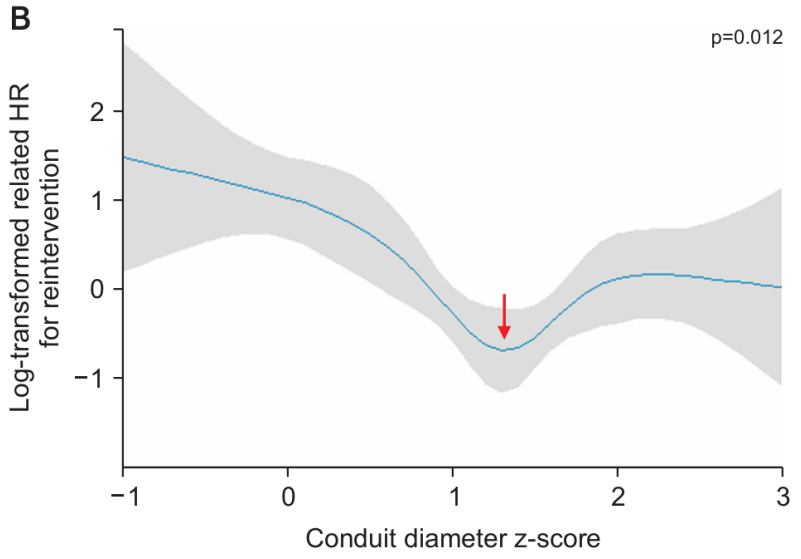


Figure 3. Conduit reintervention following right ventricle to pulmonary artery (RV-PA) conduit insertion, stratified by each type of conduit. Kaplan-Meier Curve showing significant differences between groups (Contegra vs Valved PTFE, p=0.014; Contegra vs Valveless PTFE, p=0.020).

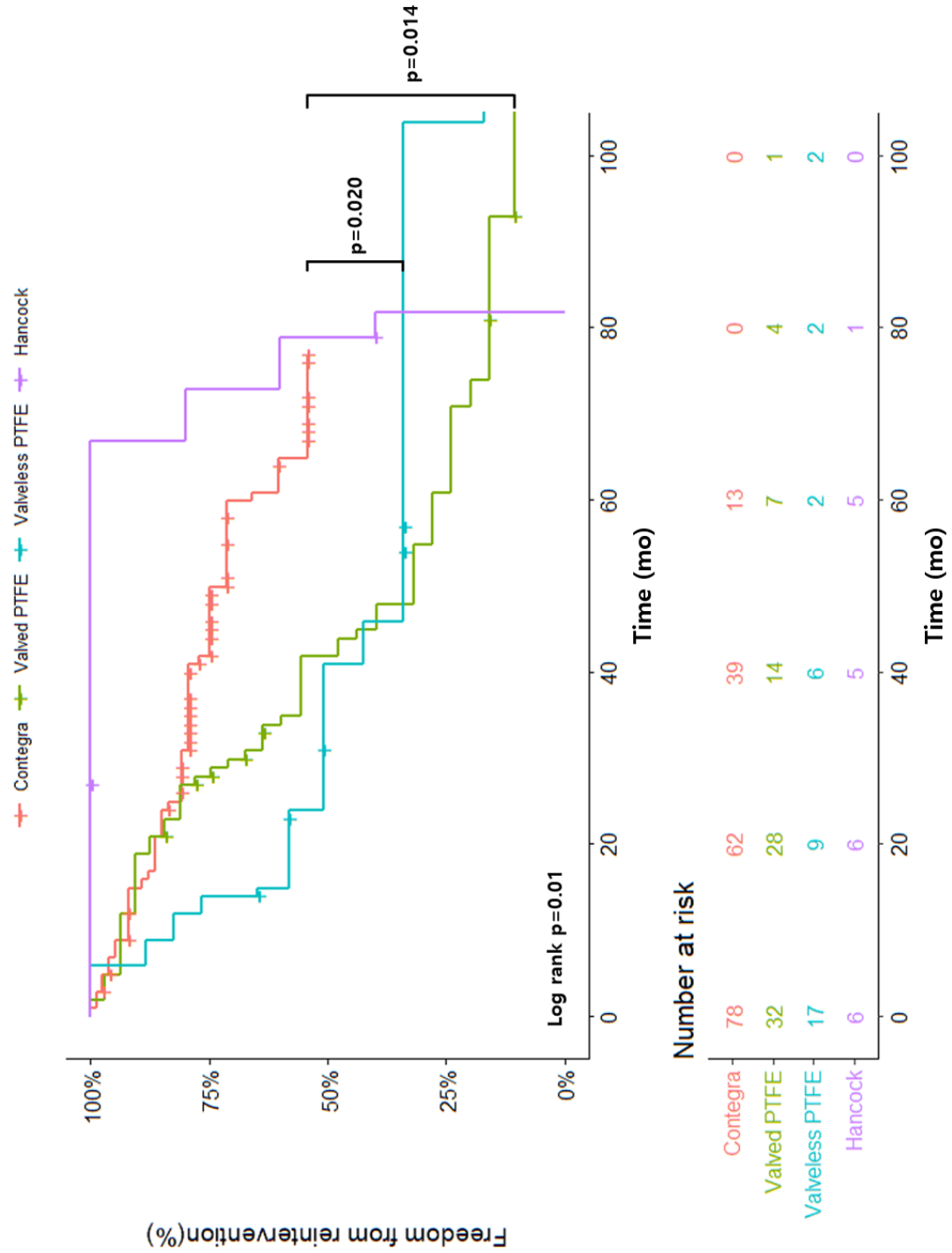


Table 5. Factors associated with conduit reintervention (n=61).

Variable	Univariable analysis		Multivariable analysis	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Age at operation (mo)	0.87 (0.81-0.93)	<0.001	0.92 (0.82-1.03)	0.175
Weight at operation (kg)	0.76 (0.67-0.87)	<0.001		
Prematurity	0.63 (0.28-1.38)	0.252		
Previous palliative cardiac surgery	0.30 (0.18-0.52)	0.001	0.44 (0.18-1.06)	0.068
Chromosomal abnormality	0.71 (0.36-1.42)	0.341		
Conduit diameter, Z-score	0.59 (0.42-0.84)	0.003	0.57 (0.40-0.83)	0.003
Concomitant pulmonary arterioplasty	0.73 (0.42-1.25)	0.253		
Type of conduit	0.78 (0.61-0.98)	0.038	1.05 (0.82-1.03)	0.742
Contegra conduit	Reference			
Valved PTFE conduit	2.33 (1.28-4.24)	0.005		
Valveless PTFE	2.43 (1.13-5.19)	0.021		
Hancock valved conduit	1.10 (0.37-3.30)	0.857		
Primary cardiac diagnosis	1.21 (0.93-1.34)	0.225		
Cardiopulmonary bypass time	1.00 (0.99-1.00)	0.330		
Aortic cross-clamp time	1.00 (0.99-1.01)	0.308		

HR, hazard ratio; CI, confidence interval; PTFE, polytetrafluoroethylene.

Conduit dysfunction

During follow-up, conduit dysfunction occurred in 68 patients, at a median interval of 21 months. The causes of conduit dysfunction included stenosis in 29 patients (42.6%), regurgitation in 22 patients (32.3%), combined stenosis and regurgitation in 15 patients (22%), and infective endocarditis in 2 patients (2.9%). The freedom-from-conduit dysfunction rates were 84% and 45.9% at 1 and 5 years, respectively (**Figure 4A**).

In the univariable analysis, younger age, lower body weight, no previous cardiac surgery, smaller conduit diameter z-score, use of a valveless conduit, and longer ACC time were associated with conduit dysfunction. In multivariable analysis, younger age, smaller conduit diameter z-score, and longer ACC time were identified as independent risk factors for conduit dysfunction (**Table 6**).

Given the small number of patients and extremely skewed age in the Hancock and valveless PTFE groups, and an inevitable insufficiency at the beginning in cases with a valveless PTFE conduit, freedom from conduit dysfunction was compared only between the Contegra and valved PTFE conduits. When conduit dysfunction was analyzed separately for the dysfunction mechanism, such as stenosis and regurgitation, valved PTFE conduits showed lower freedom-from-conduit-stenosis (p=0.02), while Contegra showed lower freedom-from-regurgitation rates (p=0.04) (**Figure 5**).

According to ANOVA, the conduit diameter z-score showed a significant nonlinear relationship with conduit dysfunction (p=0.043). To account for this nonlinearity, restricted cubic splines were used to model the relationship, which revealed that the lowest risk was attained at a conduit diameter z-score of 1.4 (**Figure 4B**). Furthermore, conduit-specific ANOVA analysis was conducted to investigate whether the conduit diameter z-score thresholds differed significantly across the conduit types. A significant nonlinear relationship was observed only for the Contegra, and restricted cubic splines demonstrated that the lowest risk was at a diameter z-score of 1.1 (**Figure 6**).

Figure 4. Conduit dysfunction following right ventricle to pulmonary artery (RV-PA) conduit insertion. (A) Kaplan-Meier curve for freedom from conduit dysfunction, and (B) a partial effect plot for RV-PA conduit diameter z-score and the log-transformed related hazard ratio (HR) for conduit dysfunction. The shaded area represents the 95% confidence interval. The arrow indicates the conduit diameter z-score (1.4) with the lowest risk of conduit dysfunction.

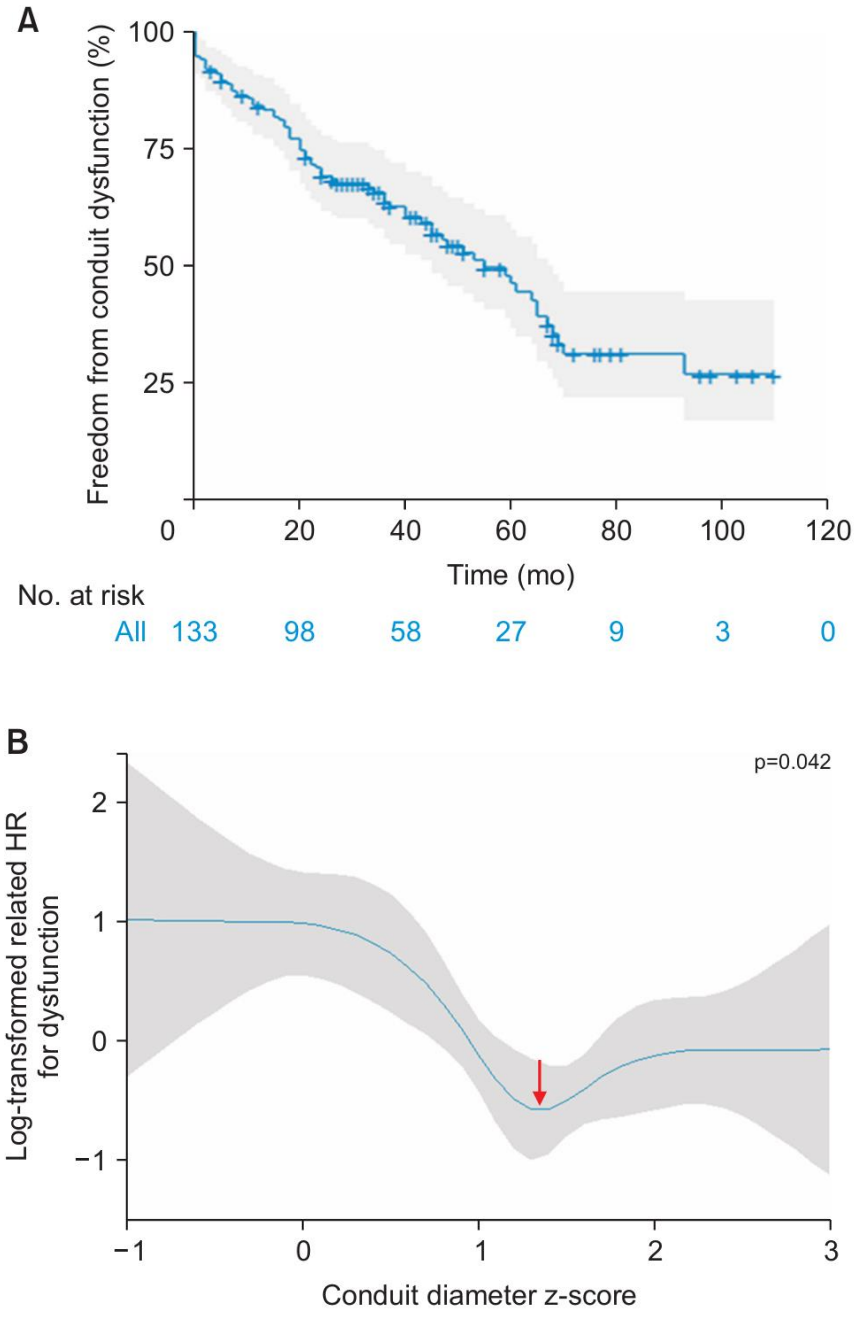
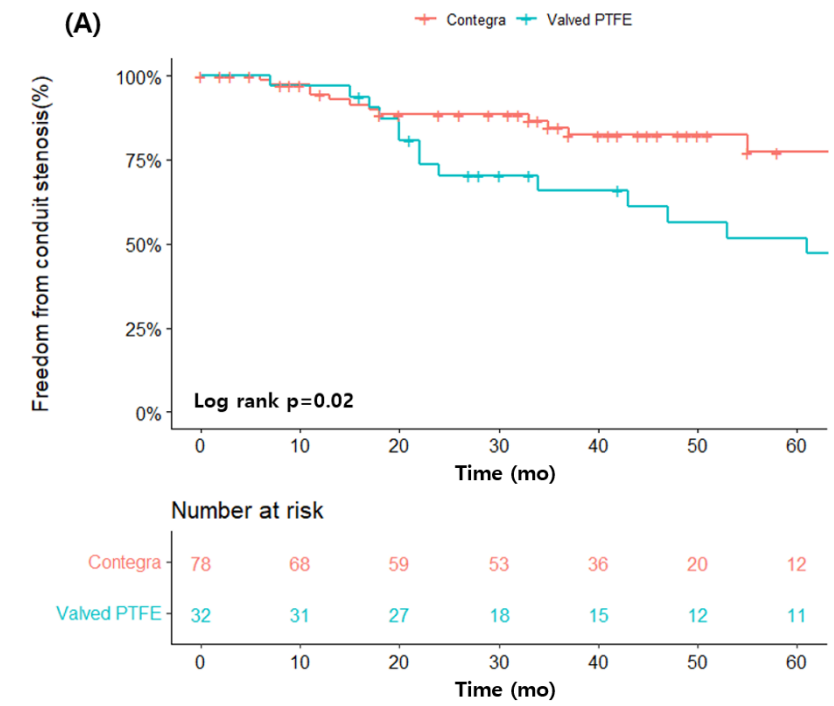


Table 6. Factors associated with conduit dysfunction (n=68).

Variable	Univariable analysis		Multivariable analysis	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Age at operation (mo)	0.89 (0.83-0.95)	0.001	0.86 (0.78-0.95)	0.003
Weight at operation (kg)	0.83 (0.73-0.93)	0.003		
Prematurity	0.49 (0.22-1.07)	0.076		
Previous palliative cardiac surgery	0.49 (0.30-0.81)	0.005	1.15 (0.56-2.36)	0.699
Chromosomal abnormality	0.74 (0.38-1.42)	0.374		
Conduit diameter, z-score	0.58 (0.42-0.81)	<0.001	0.67 (0.48-0.95)	0.024
Concomitant pulmonary arterioplasty	0.62 (0.37-1.03)	0.068		
Type of conduit	1.35 (1.07-1.70)	0.010	1.29 (0.95-1.75)	0.094
Contegra conduit	Reference			
Valved PTFE conduit	1.18 (0.65-2.14)	0.574		
Valveless PTFE	5.98 (3.22-11.10)	<0.001		
Hancock valved conduit	0.81 (0.24-2.68)	0.736		
Primary cardiac diagnosis	1.11 (0.93-1.32)	0.166		
Cardiopulmonary bypass time	1.00 (0.99-1.00)	0.709		
Aortic cross-clamp time	1.01 (1.00-1.02)	0.003	1.01 (1.00-1.02)	0.009

HR, hazard ratio; CI, confidence interval; PTFE, polytetrafluoroethylene.

Figure 5. (A). Kaplan-Meier curves for freedom from conduit stenosis with the Contegra and valved PTFE conduits. (B). Kaplan-Meier curves for freedom from conduit regurgitation with the Contegra and valved PTFE conduits.



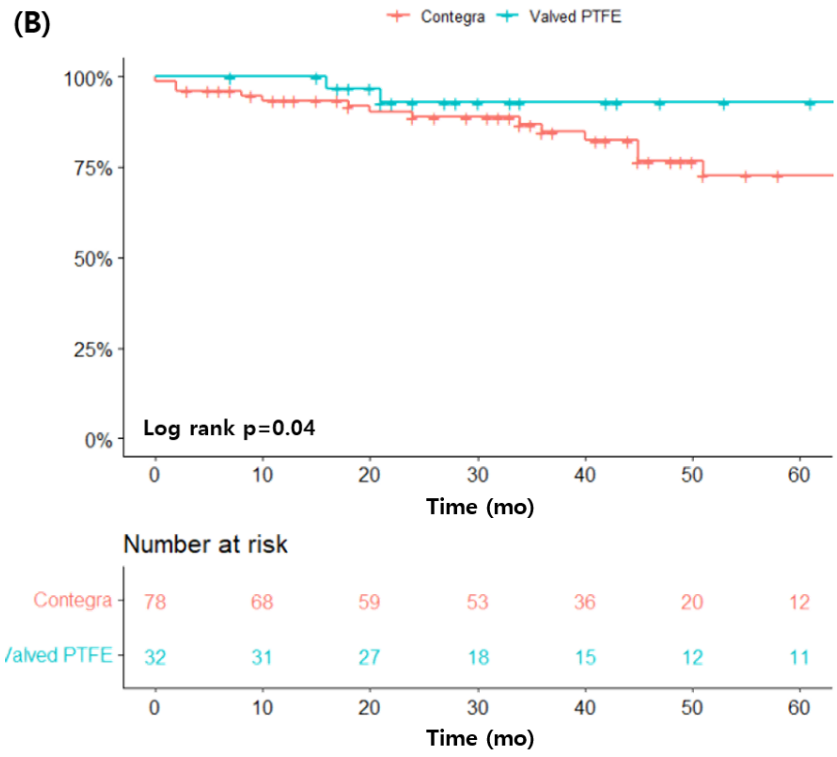
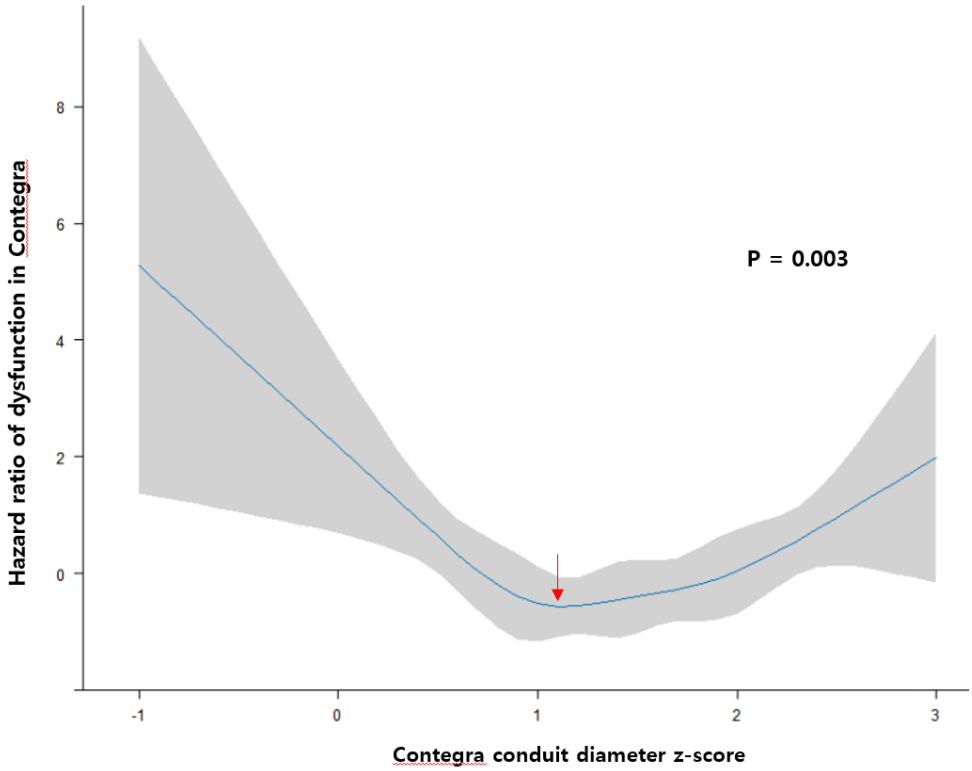


Figure 6. A partial effects plot for RV-PA conduit diameter z-score and the hazard ratio (HR) for conduit dysfunction in the Contegra. The shaded area represents the 95% confidence intervals. The arrow indicates the conduit diameter z-score (1.1) with the lowest risk of conduit dysfunction.



DISCUSSION

The use of an RV-PA conduit to establish continuity between the ventricle and pulmonary circulation is essential for achieving complete repair of various congenital cardiac defects associated with a discontinuity between the RV and the PA. Given the diversity in patient age, diagnosis, underlying conditions, and other factors, surgeons carefully consider various circumstances when choosing an RV-PA conduit. With information from numerous series, surgeons strive to select the conduit that offers the greatest durability.

Corrective surgery, including RVOT reconstruction using an RV-PA conduit, is a safe procedure with a low mortality risk. The findings of this study support this conclusion, although overall mortality was not negligible. According to our multivariable analysis of survival, younger age and longer CPB time are mortality risk factors. A possible explanation is that younger patients requiring repair had more severe disease; therefore, poor preoperative conditions might have affected their surgical outcomes. Additionally, a longer CPB time might have been associated with mortality because it indicates higher disease complexity and a worse preoperative heart condition.

Despite significant improvements in the survival of RVOT reconstruction using an RV-PA conduit, the rate of conduit reintervention remains high [2]. Caldarone et al. [7] reported a strong relationship between conduit failure and age at the time of implantation, and Willetts et al. [1] reported that weight was the most significant factor associated with conduit failure. Similarly, younger age was identified as an independent risk factor for conduit dysfunction in our study. Due to the limited conduit sizes available for small babies, regardless of the conduit type, placing an adequate-sized conduit within the limited space is difficult. Consequently, external compression, which may cause conduit failure, is more likely to occur [9,10]. Conduit failure occurs earlier in small babies due to somatic outgrowth [6]. Furthermore, age-related immune mechanisms that affect conduits are more prevalent in younger patients, and the likelihood of requiring reintervention increases over time because of rapid degeneration and calcification [4,6,11]. Saxena et al. [3] also reported that most patients required conduit replacement before 5 years of age. Thus, the selection of the conduit type or size in small patients, such as neonates and infants is challenging. Consequently, we exclusively evaluated patients aged <1year in this study.

An interesting finding in our study was that a longer ACC time was a risk factor for conduit dysfunction. Given that most patients who require longer ACC may be younger, the same explanation of the association between younger age and conduit dysfunction may be applicable to that between conduit dysfunction and longer ACC time.

Although an appropriate conduit size is critical for the longevity of the implanted RV-PA conduit in young children [12,13], earlier studies have made inconsistent recommendations regarding the conduit size. Poynter et al. [14] noted that an oversized conduit could be advantageous for durability when considering somatic

growth in patients aged <2 years. Conversely, Askovich et al. [15] demonstrated that an oversized conduit with a z-score ≥2.7 may reduce conduit durability. An oversized conduit may cause external compression due to limited space, while a size discrepancy between the conduit and the confluent pulmonary artery may result in aneurysmal conduit dilatation. This can lead to subsequent pulmonary valve and distal PA distortion, accelerating pulmonary valve insufficiency and failure [7,15,16].

We here identified the conduit diameter z-score as a shared risk factor for both conduit reintervention and conduit dysfunction, and the results indicated that a higher conduit diameter z-score was associated with lower risk. Furthermore, the lowest risk was observed at a conduit diameter z-score of 1.3 and 1.4 for conduit reintervention and conduit dysfunction, respectively, which suggests that both a too-large or too-small conduit diameter could be disadvantage patients. Karamlou et al. [12] reported that a conduit diameter z-score of 1.3 was associated with improved outcomes in patients aged <2 years at initial implantation. Recently, Kim et al. [17] suggested that an oversized conduit may have poor longevity, and even without a valve, smaller conduits may be better for small babies. We found that the conduit diameter z-score with the lowest hazard for conduit dysfunction was 1.1 in Contegra conduit, whereas it was 1.4 for conduits overall. This finding suggests that the Contegra might be better placed in a size that closely fits the patients, which may be attributable to the function of Contegra being influenced more by conduit geometry than that of other conduit types.

Allografts have been predominantly used to establish RV-PA connections for over 50 years and have long been believed to be the most durable option. However, many countries and centers, including ours, are experiencing extreme graft shortages. Therefore, since 2011, alternative conduits such as homemade membrane-valved PTFE or valveless PTFE conduits, Contegra, and Hancock conduits have been exclusively used at our center.

Since its introduction in 1999, the Contegra has been predominantly used in many countries because of its advantages, such as being easy to handle and having a wide range of sizes for selection. Furthermore, the durability of the Contegra was comparable to [6,10], and may even be better than that of homografts [16]. However, Mery et al. [13] reported that Contegra, particularly in younger patients, was associated with a higher incidence of distal conduit stenosis and early conduit insufficiency. Another concern about the Contegra is the high incidence of infective endocarditis. Previous studies on Contegra-related endocarditis have reported an infective endocarditis incidence of approximately 10%, which was higher than that of homografts [3, 13]. In our study, while only two patients developed conduit failure due to infective endocarditis, both had been implanted with a Contegra.

Homemade PTFE valved conduits began to be used in earnest by Japanese groups and are a good alternative to RV-PA conduits, with a low reoperation or reintervention risk [11,18-21]. The ePTFE was known to have low tissue affinity and less cellular or fibrous deposition, making it less prone to calcification or long-term stenosis [11,18]. Our center adopted a homemade tricuspid PTFE-valved conduit that was made using the

technique introduced by Kim et al. [22] in 2013.

Hancock conduits have long been used and show comparable outcomes to those of other RV-PA conduits [6,23]. However, as inferred from our findings, the Hancock conduit is predominantly utilized in older children who can accommodate larger conduits [1]. In Kaplan-Meier analysis, Contegra conduit seemed better in terms of reintervention than were valved or valveless PTFE conduits, although it is noticeable that the mechanism of dysfunction leading to reintervention is different between two conduits and should be considered when interpreting the results.

Additionally, conduit superiority in terms of freedom from dysfunction differed according to the mechanism of dysfunction. Valved PTFE conduits showed a higher risk of conduit stenosis, while the Contegra showed a higher risk of conduit regurgitation. From this finding, it can be inferred that Contegra might be more vulnerable to regurgitation development, while valved PTFE conduits might be better protected in regurgitation development due to their inherently fixed structure characteristics, which differ from those of the easily deformable Contegra. Future research should investigate suitable conduits for individual patient characteristics, based on the advantages and disadvantages of each conduit type.

Using conduit reintervention alone as the endpoint for conduit failure may overlook patients who underwent reoperation without conduit dysfunction and those who developed valve dysfunction but did not undergo reintervention. Therefore, we divided the endpoints and set conduit dysfunction based on echocardiogram results to achieve a more sensitive outcome. Furthermore, we censored early death for the analysis of conduit failure, as it was presumed that early death was more likely caused by factors other than conduit failure or degeneration.

LIMITATION

This study had inherent limitations due to its retrospective, single-center design. Throughout the study period, the predominantly used conduits changed based on availability and surgeons' preferences, without definitive criteria. This variation precluded a fair comparison and hindered the ability to draw meaningful conclusions. Although the number of events was sufficient to conduct a multivariable analysis, results should be interpreted cautiously given the small number of patients and events. The frequency of follow-up and criteria for reintervention were not standardized and were left to the clinician's discretion, which may impact the relevance of the results.

CONCLUSION

The results of this study reveal that RV-PA conduit placement in infants can be performed safely. However, a significant number of patients may require conduit reintervention and may have conduit dysfunction. Using a slightly oversized conduit with a z-score of 1.3 might reduce the risks of conduit reintervention or dysfunction.

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국문 요약

배경

본 연구는 1세 미만의 환아에서 우심실-폐동맥 도관 삽입을 이용한 양심실 교정의 결과를 조사하였다.

방법

본 연구에서는 2011년 1월부터 2020년 9월까지 우심실-폐동맥 도관을 이용한 양심실 교정을 받은 1세 미만의 환자들을 포함시켜 분석하였다. 본 연구에서 확인하고자 하는 결과는 모든 원인에 의한 사망, 모든 원인에 의한 도관 재수술 및 재시술 (재개입), 도관 기능장애 (최고 속도 3.5m/sec 이상의 도관 협착 또는 중등도 이상의 도관 역류) 였다.

결과

본 연구의 코호트는 총 141명의 환자가 포함되었다. 초기 도관 삽입시의 중앙 연령은 6개월 이었고, 중앙 도관 직경 z-점수는 1.3 이었다. 전체 5년 생존률은 89.7% 였다. 다변량 분석에서 어린 연령 (p=0.006)과 더 긴 심폐우회 시간 (p=0.001)이 전체 사망률의 위험 요인으로 나타났다. 추적 관찰 동안 61명의 환자에서 도관 재개입이 필요하였고, 68명의 환자에게 도관 기능장애가 발생하였다. 5년간 도관 재개입 및 기능장애로부터의 회피율은 각각 52.9%와 45.9% 였다. 다변량 분석에 따르면 작은 도관 z-점수 (p<0.001)가 도관 재개입 및 기능장애의 공통 위험요인으로 나타났다. 분산 분석에서는 도관 z-점수와 도관 재개입 또는 기능장애 사이에 비선형 관계가 있음을 보여주었다. 위험 비율은 도관 재개입의 경우 z-점수 1.3, 기능장애의 경우 1.4인 환자들에서 가장 낮았다.

결론

우심실-폐동맥 도관 삽입은 영아에서 비교적 안전하게 수행될 수 있다. 그러나 상당수의 환자들이 도관 재개입을 필요로 하였고, 도관 기능장애를 보였다. 약간 큰 도관 (z-점수 1.3)을 사용하는 것이 도관 재개입 또는 기능장애의 위험을 줄일 수 있었다.