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ARTICLE

Natural History of Kawashima Palliation in Single-Ventricle and Interrupted Inferior Vena Cava Heart Disease in China 11 Years Result

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ABSTRACT

Background: The long-term outcomes of patients treated with a Kawashima procedure and keeping the antegrade pulmonary blood flow (AnPBF) in single-ventricle (SV) and interrupted inferior vena cava (IVC) heart disease is still uncertain as yet. **Methods:** We investigated 18 patients who underwent the Kawashima procedure with SV physiology and an interrupted IVC between January 2009 and June 2018, perioperative, operative and postoperative characteristics were recorded. **Results:** A total of 18 patients underwent the Kawashima procedure at a median age of 2.7 years (range 0.5–24.7 years), of which 12 (66.7%) were male and 6 (33.3%) were female. The mean saturation was 76.2 ± 8.5% in preoperative period and 94.2 ± 2.2% in postoperative period. All patients had kept AnPBF. The median duration of mechanical ventilation was 12 h (range 2.5–22.5 h) and the median duration of pleural drainage was 5 days (range 2–27 days). The median hospital stay was 9 days (range 6–70 days). There was no operative death and no mortality was seen in early postoperative period. Follow-up was 100% completed, with an average follow-up period of 6.1 ± 2.7 years (range 1–11 years). 4 patients died during the follow-up. The overall 5 and 10 years' survival rates estimated by Kaplan-Meier method were 88% and 68%, respectively. Although there were no significant differences in the duration of postoperative follow-up between the death group and the survival group ($p > 0.05$), the major systemic ventricular end-diastolic diameter (SVEDD) ($p = 0.018$) and the degree of AVVR ($p = 0.001$) showed significant difference between the two groups. The diameters of main pulmonary artery showed significant growth in both the death group ($p = 0.015$) and the survival group ($p = 0.012$) over time. SVEDD had no significant increase in the survival group ($p = 0.665$) but was significantly larger in the death group ($p = 0.014$). Multivariable risk factors of late mortality in patients treated with Kawashima procedure were follow-up AVVR ($p = 0.044$; HR: 3.124; 95%CI: 1.030–9.473) and SVEDD ($p = 0.031$; HR: 9.766; 95%CI: 1.226–77.8). 14 patients (100%) were all in New York Heart Association (NYHA) functional class I and the mean saturation was 93 ± 2% at last follow-up. Only one patient finished Fontan completion. **Conclusions**: The Kawashima procedure with AnPBF can be safely performed with acceptable early and long outcomes. Although some previous studies have shown the risk of pulmonary arteriovenous malformations (PAVMS) after Kawashima procedure in the mid- and long-term, our findings are in contradiction with it. No PAVMs occurred in all the survivors. Kawashima procedure with open AnPBF may be a good option for unsuitable Fontan candidates.

KEYWORDS

Interrupted inferior vena cava; single ventricle; Kawashima palliation; antegrade pulmonary blood flow (AnPBF); pulmonary arteriovenous malformations (PAVMS)

1 Introduction

In 1984, Kawashima reported his initial experience in patients with functional single ventricle (SV) and interrupted inferior vena cava (IVC) treated by bidirectional cavopulmonary shunt (BCPS) [1]. Interruption of the IVC with azygous or hemiazygous continuation above the diaphragm can present with many complex congenital heart diseases along with heterotaxy syndromes, left atrial isomerism, polysplenia and SV [2]. Kawashima procedure leads the most of the systemic venous return (80%) was drained to the pulmonary circulation except for the hepatic venous return. Unfortunately, up to 57% of the patients undergoing a Kawashima procedure may gradually reducing systemic oxygen saturation due to developing pulmonary arteriovenous malformations (PAVMS) in the subsequent years Kawashima procedure [3]. Many researchers have found that the exclusion of hepatic venous blood flow from the pulmonary circulation induced the development of PAVMS [4–9]. The antegrade pulmonary blood flow (AnPBF) is the main pulmonary artery connected with right ventricle. The pulsatile AnPBF may bring about the hepatocardiac venous return, increase arterial oxygen saturation, promote pulmonary artery growth, and prevent the formation of PAVMS [10,11]. The proportion of patients who eventually complete total cavopulmonary connection (TCPC) in some Asian countries is lower than that in developed Western countries. Therefore, maintaining the AnPBF during Kawashima procedure has become a popular choice in China. The long-term outcomes of patients who treated with a Kawashima procedure with AnPBF were still uncertain as yet [12]. To explore these issues, we decided to retrospectively review our experience with patients who underwent a Kawashima procedure with AnPBF.

2 Materials and Methods

2.1 Patients

The study population included all children who underwent a Kawashima procedure with AnPBF between 2009 and 2018 at the Fuwai Hospital. Anatomical characteristics, echocardiographic and catheterization data were reviewed. Follow-up data were obtained recently, and diagnosis of PAVMS was identified by hypoxia (spo2 < 90%). The systemic arterial oxygen saturation measured by pulse oxymetry (spo2) in room air was greater than 90% diagnosed normal patients without PAVMs. Ethics approval was granted by the Fuwai Hospital Ethics and Research Committee. Written informed consent was obtained from parents.

2.2 Surgical Procedures

The Kawashima procedure involved the division of the superior vena cava (SVC) below its junction with the azygous or hemiazygous continuation of the IVC end of the SVC to the right or left pulmonary artery in an end-to-side fashion. 9 Patients with bilateral SVC had bilateral BCPS. In all patients the Kawashima procedure was performed through a median sternotomy using cardiopulmonary bypass under mild hypothermia with aortic and bicaval cannulation. Cardioplegic arrest was used in 5 patients for atrioventricular valve repair (AVR). All the patent ductus arteriosus (PDA) and the major aortopulmonary collateral arteries (MAPCAs) were ligated or occluded.

2.3 Statistical Analysis

Continuous data are presented as mean ± SD or median (range), while categorical data are presented as frequency (percentages). For the within- and between-group analyses, independent-sample t tests and x^2 analyses were used, respectively. The survival rate was calculated using Kaplan-Meier method and compared using the log-rank test. Risk factors for developing PAVMS or death were investigated by Cox regression analysis. The risk associated with each variable was expressed as a hazard ratio (HR) and 95% confidence interval (CI). Any association with p-value < 0.05 was considered as statistically significant. All statistical analyses were performed using SPSS version 25 (IBM SPSS STATISTIC).

3 Results

From 2009 to 2018, 18 patients underwent the Kawashima procedure with a median age of 2.7 years (range 0.5–24.7 years), including 12 males (66.7%) and 6 females (33.3%). Patients' characteristics are summarized in Tab. 1. The mean saturation in preoperative period was 76.2 ± 8.5%. All patients had open AnPBF. Preoperative mean PAP was 14 ± 2 mmHg, and postoperative CVP was 13.3 ± 3.3 mmHg. Cardiopulmonary bypass time (CPB) was 61 min, and aortic cross-clamp was needed in 5 patients because of atrioventricular valve repair (AVR). There was no case occurred intraoperative complications and no mortality during early perioperative period. Mean saturation in postoperative period was 94 ± 2%. Median duration of mechanical ventilation was 12 h (range 2.5–22.5 h). Median duration of pleural drainage was 5 days (2–27 days). The median hospital stay was 9 days (range 6–70 days).

Table 1: Baseline patient's characteristics

Demographics	Patients
Number of patients	18
Male	12 (67%)
Female	6 (33%)
Age distribution	
0–1 years	3
1–3 years	6
>3 years	9
Interrupted IVC	18
Bilateral Superior Caval Vein (SVC)	9
Left atrial isomerism	8
Polysplenia	6
Inversus	5
Dextrocardia	7
Dominant ventricle	
Right	14
Left	4
Atrioventricular valve	
Single atrioventricular valve	10
Common atrioventricular valve	8
AV regurgitation	
None	3
Trivial	10
Mild	3
Mod	1
Severe	1

Note: DORV: Double Outlet Right Ventricle, VSD: Ventricular Septal Defect, PS: Pulmonary Stenosis, PA: Pulmonary Atresia, SV: Single Ventricle, HLH: Hypoplastic Left Heart, TGA: Transposition of Great Arteries, AV: Atrioven-Tricular Valve, IVC: Inferior Caval Vein, BT: Blalock–Taussig, RPA: Right Pulmonary Artery, LPA: Left Pulmonary Artery, TAPVC: Total Anomalous Pulmonary Venous Connection, PAP: Pulmonary Artery Pressure.

4 Follow-Up

Follow-up was 100% completed, with an average follow-up period of 6.1 ± 2.7 years (median 6.5 years, ranged from 1 to 11 years). Patients were encouraged to return for routine outpatient visits after hospital discharge. Echocardiographic studies were performed before and shortly after discharge to assess ventricular function and atrioventricular valve regurgitation (AVVR). The degree of valve regurgitation was graded from 0 to 4 using Sellers' classification and is numerically presented as follows: 0, none; 1, trivial; 2, mild; 3, moderate; and 4, severe [13]. 4 patients died during the follow-up. The overall 5 to 10 years' survival rates estimated by Kaplan-Meier method were 88% and 68%, respectively (Fig. 1). The patient's characteristics of death group and survival group are summarized in Tabs. 2 and 3.

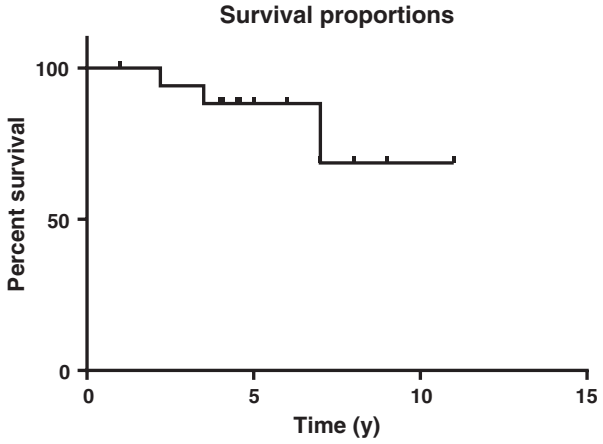

Figure 1: Survival curve

Table 2: Baseline patient's characteristics of two groups

Characteristics	Survival (n = 14)	Death (n = 4)	*p*-value
Body weight (kg)	16.9 ± 16.1	13.9 ± 8.9	0.726
Age (years)	5.0 ± 6.2	2.5 ± 2.7	0.460
Oxygen saturation (%)	74.4 ± 8.4	82.2 ± 6.1	0.107
Hemoglobin (g/l)	162.9 ± 39.1	146.7 ± 15.6	0.438
Main pulmonary arterial diameters (mm)	10.5 ± 3.4	9.0 ± 1.4	0.412
Pulmonary valve velocity (m/s)	4.2 ± 0.5	4.2 ± 0.5	0.971
Pulmonary valve pressure(mmHg)	71.5 ± 17.5	69.3 ± 16.2	0.825
Atrioventricular valve regurgitation degree (≥moderate)	1/14 (7.1%)	1/4 (25%)	0.063
Main ventricular (Right)	10/14 (71.4%)	4/4 (100%)	0.225
Diameter of main ventricular (mm)	38.9 ± 20.5	39.5 ± 17.4	0.96
Cardiopulmonary bypass time (min)	68.1 ± 32.1	83.0 ± 33.7	0.429
Ventilation (h)	12.4 ± 6.7	12.5 ± 5.7	0.977
ICU (d)	4.0 ± 5.2	2.3 ± 1.3	0.520
Hospital stay (d)	13.8 ± 12.8	23.5 ± 3.1	0.348
Pleural drainage time (d)	6.5 ± 6.2	4.7 ± 1.9	0.594
Follow-up (y)	6.3 ± 2.7	4.9 ± 2.4	0.391

Table 3: Follow-up characteristics of two groups

Characteristics	Survival (n = 14)	Death (n = 4)	*p*-value
Pulmonary valve velocity (m/s)	4.2 ± 0.7	3.3 ± 1.9	0.133
Pulmonary valve pressure (mmHg)	73.3 ± 21.0	54.3 ± 37.7	0.189
Atrioventricular valve regurgitation degree (≥moderate)	1/14(7.1%)	4/4(100%)	0.001
Diameter of main ventricular (mm)	38.1 ± 18.3	64.5 ± 15.0	0.018
Main pulmonary arterial diameters (mm)	12.3 ± 3.9	10.3 ± 0.9	0.322

The degree of AVVR of the death group was heavier than that of survival group. The cases need atrioventricular valve repair in the death group and survival group were 2 (50%) and 3 (21%) respectively. Although there were no significant differences in the duration of postoperative follow-up between the death group and the survival group, the major systemic ventricular end-diastolic diameter (SVEDD) (p = 0.018) and the degree of AVVR (p = 0.001) showed significant difference between the two groups. During follow-up we found that the diameters of main pulmonary artery showed significant growth in both the death group (p = 0.015) and the survival group (p = 0.012) compared with preoperative condition. However, SVEDD had no significant increase in the survival group (p = 0.665) but was significantly larger in the death group (p = 0.014) (Fig. 2, Tab. 4). The AVR of the survival group had no obvious change but showed a trend of turning better, while that of the death group showed a trend of turning worse (Fig. 3).

The multivariable risk factors of late mortality in patients treated with Kawashima procedure were follow-up AVVR (p = 0.044; HR: 3.124; 95%CI: 1.030–9.473) and SVEDD (p = 0.031; HR: 9.766; 95% CI: 1.226–77.8). 14 patients (100%) were all in New York Heart Association (NYHA) functional class I and the mean saturation was 93 ± 2% at last follow-up. Only one patient finished Fontan completion and valve replacement.

5 Discussion

The Kawashima procedure has become a standard intermediate step toward TCPC for SV with interrupted IVC patients. The main sources of additional pulmonary blood flow include systemic-to-pulmonary shunts and AnPBF. Systemic to pulmonary shunts may increase perioperative mortality, negatively affect left pulmonary artery growth, and potentially increase pulmonary vascular resistance. Controversy still exists about AnPBF after Kawashima procedure. Pulsatile AnPBF may improve arterial oxygen saturation, stimulate pulmonary artery growth, and prevent the PAVMS. However, it may also augment the superior vena cava (SVC) pressure, producing persistent pleural effusions and functional SV volume overload [14,15]. In our study, the median duration of pleural drainage as well as the mean length of hospital stay was similar to those reported in other studies even though all patients keep AnPBF between the single ventricle and the pulmonary [16–18]. Both low preoperative PAP and low postoperative CVP were deemed crucial. In our series, all previously existing systemic-to-pulmonary shunts, including Blalock-Taussig shunts, major aortopulmonary collateral arteries, and PDA, were excluded before Kawashima procedure. If the mean pulmonary artery pressure was more than 16 mm Hg, the main pulmonary artery was banded with a strip of polytetrafluoroethylene. This policy minimized the risk of increased pulmonary vascular resistance.

Our study found there were significant differences in the major SVEDD (p = 0.018) and the degree of AVVR (p = 0.001) between the death group and the survival group during the follow-up period. The multivariable risk factors of late mortality in patients treated with Kawashima procedure were follow-up

AVVR (p = 0.044; HR: 3.124; 95%CI: 1.030–9.473) and SVEDD (p = 0.031; HR: 9.766; 95%CI: 1.226–77.8). We thought the excessive systemic ventricular volume overload deteriorates the systemic atrioventricular valve and ventricular function [19–21]. However, compared with the death group, there was no significant increase in end-diastolic meridian in the survival group. Heavier degree of AVVR was observed in the death group so we inferred that there might be some children in the death group suffering from more serious condition where the risk factors of TAPVC, AVR and seniority were combined which already leads to the overload of functional SV and aggravation of AVVR before operation. Among the 4 patients in death group, 3 patients were complicated with Common atrioventricular valve regurgitation and 1 patient was complicated with TAPVC. A lot of researches had found that TAPVC, AVR and seniority were the risk factors for the long-term survival [22]. The survival group included 3 cases of pulmonary artery banding (PAB) surgery, while the death group had none. And we found that pulmonary valve velocity and pulmonary valve pressure are both lower in death group during the follow-up period. Thus, performing the PAB surgery for patients with these risk factors may reduce the risk of death throughout life.

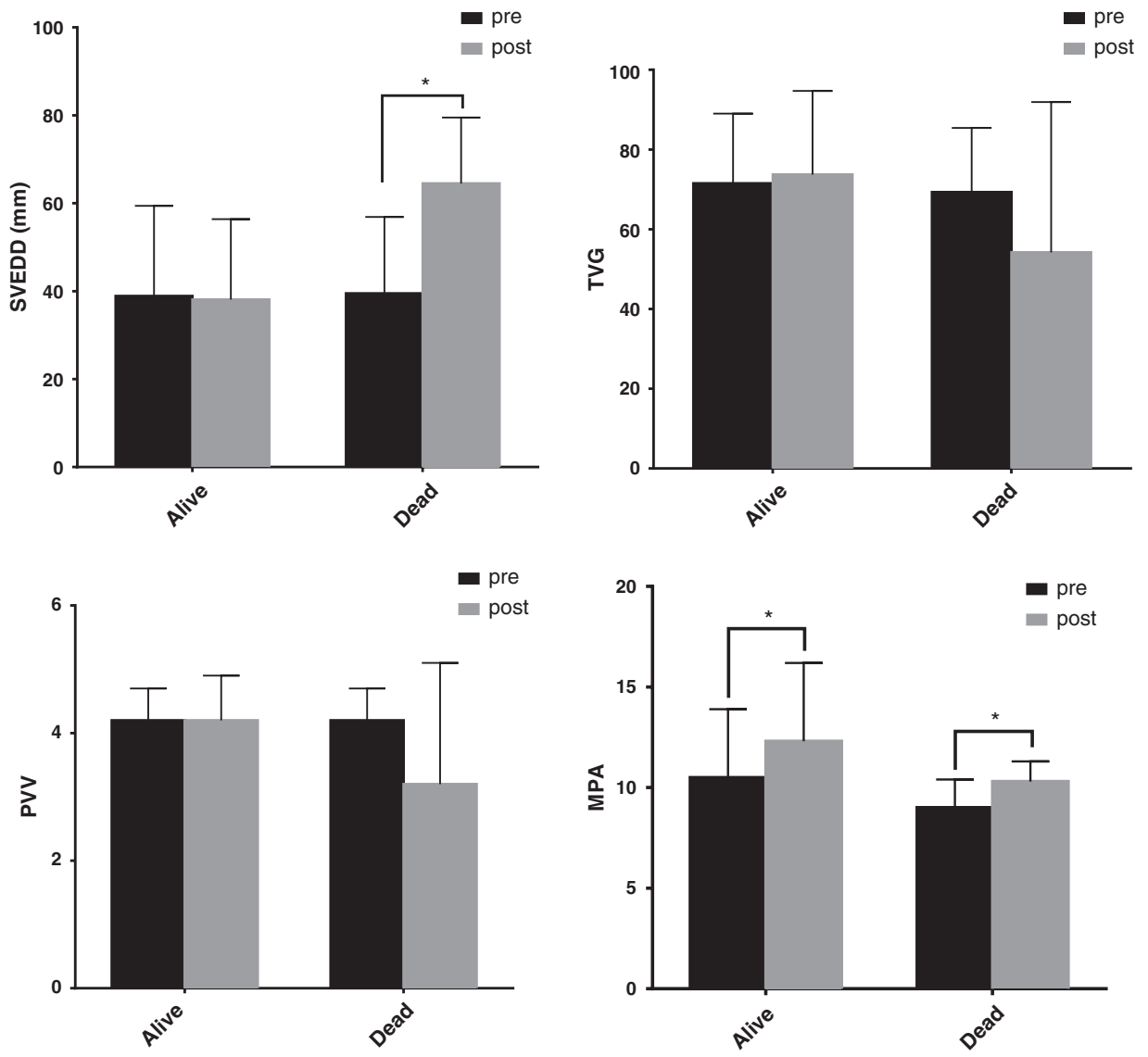

Figure 2: Follow-up characteristics of two groups

Table 4: Follow-up patient's characteristics of two groups

Variables	Alive		*p*-value	Dead		*p*-value
	Pre	Post		Pre	Post	
SVEDD (mm)	38.9 ± 20.5	38.1 ± 18.3	0.665	39.5 ± 17.4	64.5 ± 15.0	0.014
PVV (m/s)	4.2 ± 0.5	4.2 ± 0.7	0.838	4.2 ± 0.5	3.2 ± 1.9	0.301
TVG (mmHg)	71.5 ± 17.5	73.7 ± 21.0	0.719	69.3 ± 16.1	54.2 ± 37.7	0.321
MPA (mm)	10.5 ± 3.4	12.3 ± 3.9	0.012	9.0 ± 1.4	10.3 ± 1.0	0.015

Note: PVV: Pulmonary Valve Velocity, SVEDD: Systemic Ventricular End-Diasotic Diameter, TVG: Transpulmonary Valve Gradient, MPA: Main Pulmonary Artery Diameter.

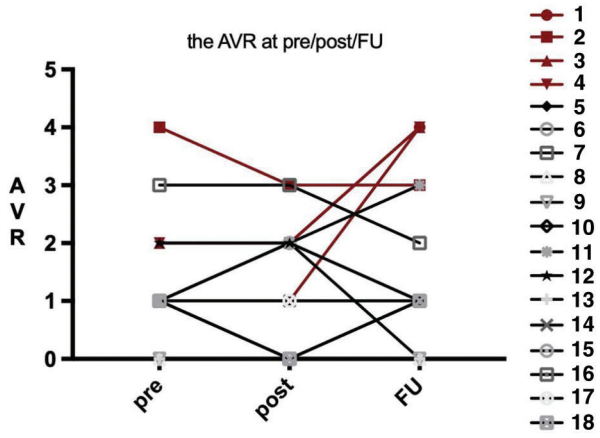

Figure 3: Atrioventricular valve regurgitation at pre/post/follow-up

PAVMS seems to be more frequent occurrence after Kawashima, with a reported incidence rate of between 17% and 58% [2,3]. The development of these malformations has been attributed to the absence of liver-derived factors in the pulmonary circulation [4–8]. Maldistribution of pulmonary blood flow due to favourable flow in lower lobe and non-pulsatile blood flow to pulmonary circulation is implicated in its pathogenesis [23]. Because of the limited follow-up time for patients undergoing a Kawashima procedure, the proportion of patients who eventually develop PAVMs is still unknown. But in our studies no one develop to PAVMS with follow-up 6.5 years (1–11 years). We believe this is due to the presence of AnPBF between the single ventricle and the pulmonary artery. This strategy can help to drain hepatic factor into the pulmonary circulation and protect against PAVMS development with the aid of pulsatile blood flow to pulmonary circulation. Therefore, we think that Kawashima procedure with AnPBF can eliminate the risks related to PAVMS. In 2017, Dr. Takashi Kido reported that a total of 17 patients underwent Kawashima surgery between 1987 and 2010, 11 of whom underwent the procedure as inter-stage palliation (planned Fontan group). The remaining 6 patients underwent the Kawashima operation initially as definitive surgery (non-scheduled group). Likewise, he suggested that the Kawashima operation with AnPBF may provide definitive palliation for unsuitable Fontan candidates. Some other articles also support this opinion [24–26]. In China, low economic status and underdeveloped insurance system lead to the dismal Fontan completion rate. Most families only have one chance to come to big cities for surgery. So the Kawashima operation will be their last operation. Moreover, Fontan physiologic course also can result in many systemic complications, such as hepatic dysfunction, protein-losing enteropathy, plastic bronchitis, hypoxia, and arrhythmias [27,28]. Especially for patients with interrupted

IVC, many studies have shown that extra-cardiac conduits only draining the hepatic venous blood flow is more prone to run a risk of thrombus formation than traditional extra-cardiac Fontan [20,29]. The progressive cyanosis caused by both systemic venous collaterals and PAVMS could still remain in Fontan patients [12,20]. Kawashima operation with AnBPF allows distribution of hepatic venous blood and pulsatile blood flow to the pulmonary arteries without any prosthetic tube grafts, minimizes arrhythmogenic atrial incisions, and does not require a future Fontan operation. Our studies showed that Kawashima operation with AnBPF could stimulate pulmonary artery growth and maintain normal saturation.

Overall survival estimated by the Kaplan-Meier method was 88% at 5 years and 68% at 10 years in our study. 14 patients' survival (100%) were all in New York Heart Association (NYHA) functional class I and the mean saturation was 93 ± 2% at last follow-up. Survival is similar to those reported in other studies [22]. In 2016, Dr. Bahaaldin Alsoufi reported a study about 67 patients with heterotaxy and a functional single ventricle and their overall 8-year survival rate was 66%. He found that mortality-related factors were accidental reoperation and repair of total anomalous pulmonary venous connection (TAPVC) in the contemporaneous matched patients with non-heterotaxy single ventricle anomalies.

6 Limits

Our studies are limited in a median of 6.5 years after Kawashima operation. It is still unclear whether some of these patients will never have complications or deformities, thus avoiding the need for Fontan completion. Only spo2 > 90% in room air was considered normal in PAVMs diagnosis. Next, we will recall all survivors for a thorough examination in our hospital to do further research. They will be divided into two groups, one taking PAB and the other having a hepatic–to–azygos connection operation. The complications, survival rate and quality of life will be compared between the two groups.

7 Conclusions

Kawashima procedure with AnPBF can be performed safely with acceptable early and long-term results. Although some previous studies have shown the risk of PAVMS after Kawashima procedure in the mid- and long-term, our findings have not confirmed that. No PAVMs occurred in all the survivors. Accordingly, we believe that giving the Kawashima procedure with AnPBF in patients with SV and an interrupted IVC is feasible, and further follow-up studies are needed to confirm it.

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Conflicts of Interest: All authors declare no conflicts of interest to report regarding the present study.

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