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Article

Comparative Analysis of Treatment Strategies for Postoperative Pulmonary Hypertensive Crisis in Congenital Heart Disease

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Abstract

Background: Pulmonary hypertensive crisis (PHC) is a serious life-threatening complication in children with congenital heart disease (CHD) after surgery, with acute onset and high mortality. However, there is still no effective means to deal with this complication. Therefore, our department developed the left atrium and right ventricle duct bridging technique to treat children with PHC, and compare its effects with conventional methods of treatment to determine the best solution for dealing with this complication. **Methods**: A retrospective analysis of 41 children with CHD surgery and postoperative PHC in our hospital from January 2015 to December 2022 was performed. According to the rescue method, the group with conventional therapy combined with left atrium to right ventricle duct bridging treatment *vs*. simple conventional therapy were defined as group A and group B respectively, with 13 cases and 28 cases in each group. The success rate of rescue, the complication rate, the length of intensive care unit stay, the delayed chest closure duration, the duration of PHC, the ratio of pulmonary circulation/systemic circulation pressure, the oxygenation index and the cardiac index at 30 min, 1 h, 2 h, 4 h and 6 h after rescue were compared between the two groups. **Results**: There was a higher success rate of rescue (84.62% *vs*. 68.86%; $p > 0.05$), lower complication rate (15.38% *vs*. 21.43%; $p > 0.05$), shorter duration of PHC (6.77 ± 2.13 min *vs*. 13.07 ± 4.05 min; $p = 0.000$), shorter duration of delayed sternal closure (32.23 ± 5.46 h *vs*. 38.14 ± 8.61 h; $p = 0.029$) and shorter length of ICU stay (81.69 ± 8.31 h *vs*. 93.57 ± 16.84 h; $p = 0.021$) in group A; After the rescue, the pulmonary artery pressure and cardiopulmonary function recovery rate in group A were faster than those in group B. **Conclusions**: In conclusion, left atrial to right ventricular duct bridging therapy is more effective in the treatment of PHC after surgery for CHD.

Keywords

pulmonary hypertensive crisis; congenital heart disease; pulmonary artery pressure; oxygenation index; cardiac index

Introduction

Following surgery for congenital heart disease (CHD) [1–6], pulmonary hypertensive crisis (PHC) is a clinical state of severe low cardiac output, hypoxemia, hypotension and acidosis caused by the rapid increase of pulmonary vascular resistance and pulmonary artery pressure induced by pulmonary hypertension, which is close to or exceeds the systemic pressure in a short time. Rapid deterioration or even death are likely to happen if PHC is not treated timely and effectively. However, at present, there is no immediate treatment for PHC. The current treatment for PHC includes sedation, adequate oxygen, inhalation of nitric oxide/iloprost, or intravenous troprostol/alprostadil to reduce pulmonary vascular resistance and pulmonary artery pressure. Unfortunately, these effects are still unsatisfactory. In our center, the bridge technique using a left atrium to right ventricle tube with heparin coating technology, which has been used for the treatment of PHC after surgery for CHD, and good results have been achieved (Fig. 1). This study compares the therapeutic effect between conventional therapy and left atrium to right ventricle duct bridging therapy to treat PHC.

Materials and Methods

Clinical Data and Grouping

A retrospective study was conducted on 41 children who had undergone surgery for CHD complicated with postoperative PHC in our hospital from January 2015 to December 2022. Inclusion criteria: (1) Children with severe pulmonary hypertension before surgery due to cardiac anatomic abnormality. (2) Children who underwent surgery for CHD. (3) Children in whom the ratio of pulmonary artery pressure to aortic pressure was ≥0.75, and the pulmonary artery pressure did not decrease significantly after inhalation of nitric oxide after the correction of the cardiac malformation. (4) The heart rate and blood pressure of the children were unstable after the correction of the heart malformation. (5) Delayed chest closure on the day of surgery due to cardiac edema, heart failure and other reasons. (6) Children who developed PHC on the day after returning to

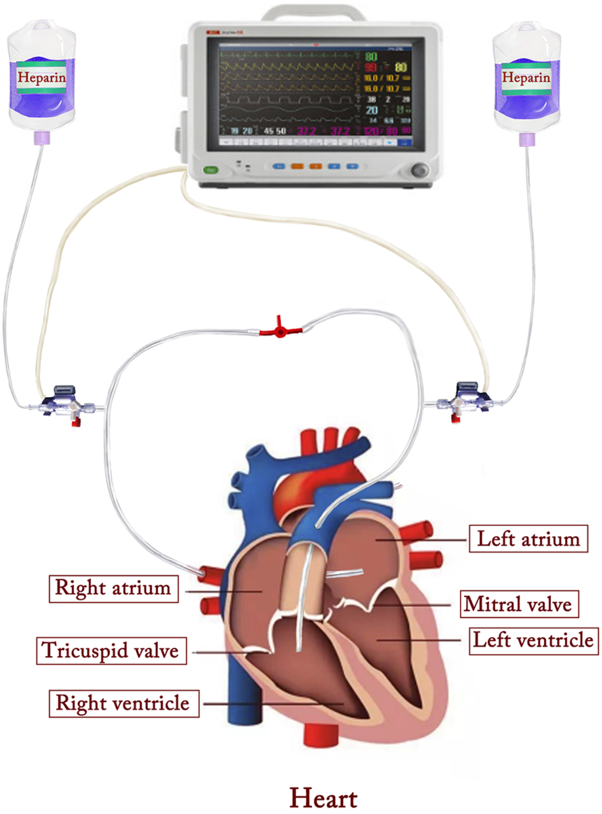

Fig. 1. Operation flow chart. The bridge technique of left atrium to right ventricle tube with heparin coating technology.

the intensive care unit (ICU). Diagnostic criteria of PHC: pressure monitoring shows that pulmonary artery pressure was instantaneously close to, at or above the aortic pressure, accompanied by alterations in blood pressure and oxygen saturation. (7) Children for whom postoperative bedside echocardiography revealed satisfactory correction of intracardiac malformation and no residual obstruction. Exclusion criteria: (1) Children with pneumonia before surgery. (2) Children who had other inherited metabolic diseases. (3) Children for whom post-operative bedside echocardiography showed unsatisfactory correction of intracardiac malformations and residual obstruction. (4) Children with stable vital signs after cardiac surgery and chest closure. Children in whom the right pulmonary vein could be successfully inserted into a 4–mm–diameter pressure–measuring tube were assigned to group A. In these children, the right pulmonary vein and pulmonary artery were inserted into a pressure measuring tube after surgery, and the two tubes were connected by a y connector. Children whose right pulmonary vein could not be inserted into the 4–mm–diameter pressure–measuring tube were assigned to group B; for these children, no tubes were inserted into the right pulmonary vein or pulmonary artery.

There were 20 males and 21 females, aged 10–87 (46.27 ± 20.70) days, with a body mass of 2.6–5.5 (4.34 ± 0.77) kg. Disease categories included 6 cases of total anomalous pulmonary venous drainage with pulmonary hypertension (TAPVD/PH), 6 cases of complete transposition of great arteries (CTGA), 9 cases of interrupted aortic arch and ventricular septal defect (IAA/VSD), 4 cases of double outlet right ventricle with pulmonary hypertension (DORV/PH), 4 cases of aortic coarctation with ventricular septal defect (COA/VSD), 4 cases of Taussig-Bing malformation (Taussig-Bing) and 7 cases of total endocardial cushion defect with pulmonary hypertension (TECD/PH), all of which had undergone corrective surgical procedures. The selected children had developed PHC after returning to the ICU, and had been given conventional therapy combined with left atrium to right ventricle duct bridging treatment with heparin coating technology and single conventional therapy respectively, which were defined as group A and group B, including 13 cases in group A and 28 cases in group B. There were no significant differences in age, sex, body weight, disease category, ratio of pulmonary circulation/systemic circulation pressure, duration of extracorporeal circulation and duration of aortic occlusion between the two groups (Table 1). The study was approved by the Ethics Committee of Hebei Children's Hospital (NO. 202136) and conformed to the principles of the Helsinki declaration. The subjects obtained the consent of the guardians and signed the informed consent.

Vasoactive Inotropic Score (VIS)

Vasoactive inotropic score (VIS) = dopamine [μg/(kg·min)] × 1 + dobutamine [μg/(kg·min)] × 1 + milrinone [μg/(kg·min)] × 10 + epinephrine [μg/(kg·min)] × 100 + vasopressin [U/(kg·min)] × 1000 + norepinephrine [μg/(kg·min)] × 100.

Treatment Methods

All of the children had undergone surgical treatment for CHD under general anesthesia and hypothermic cardiopulmonary bypass. Due to their young age, low weight and complicated medical condition, there was significant myocardial edema after surgery, and delayed sternal closure was performed. During the cardiac surgery, we employed a 5/0 prolene suture to sew a fusiform pouch on the right upper pulmonary vein and pulmonary artery, and then cut the vascular wall within the pouch with a sharp knife for group A. One pressure measurement tube with heparin coating technology was placed from the right pulmonary vein to the left atrium, and the other one was placed from the pulmonary artery to the right ventricle. The two tubes were then connected by a triplet when they got filled with blood, and the triplet wasclosed (Fig. 1). After returning to the ICU, all group A and group B children were ventilated and were connected to a non-invasive cardiac output monitoring system (Most-CareSystem; Project Engineering sirl Via Colle Ramole; Padova, Italia) to monitor their vital signs. The side holes of the left atrial and right ventricular pressure measuring tubes in group A were separately connected to a monitor through the pressure measuring equipment so

Table 1. Basic information.

Group	Age (day)	Sex (m/f)	Weight (Kg)	TAPVD (n, %)	CTGA (n, %)	IAA/VSD (n, %)	DORV/PH (n, %)	COA/VSD (n, %)	Taussig-Bing (n, %)	TECD/PH (n, %)
A (13)	47.69 ± 26.07	5/8	4.20 ± 0.81	2 (15.38%)	1 (7.69%)	3 (23.07%)	1 (7.69%)	2 (15.38%)	2 (15.38%)	2 (15.38%)
B (28)	45.61 ± 18.21	15/13	4.40 ± 0.76	4 (14.29%)	5 (17.86%)	6 (21.43%)	3 (10.71%)	2 (7.14%)	3 (10.71%)	5 (17.86%)
t/χ^2	0.297	0.811	–0.799	0.000	0.146	0.000	0.000	0.069	0.000	0.000
p	0.768	0.368	0.429	1.000	0.702	1.000	1.000	0.793	1.000	1.000

TAPVD, total anomalous pulmonary venous drainage; CTGA, complete transposition of great arteries; IAA/VSD, interrupted aortic arch and ventricular septal defect; DORV/PH, double outlet right ventricle with pulmonary hypertension; COA/VSD, aortic coarctation with ventricular septal defect; Taussig-Bing, taussig-bing malformation; TECD/PH, total endocardial cushion defect with pulmonary hypertension.

Table 2. Intraoperative and postoperative data.

Group	Pressure ratio	Extracorporeal circulation time (min)	Aortic occlusion time (min)	SpO_2 (%)	Mean arterial pressure (mmHg)
A	0.79 ± 0.07	97.08 ± 29.19	76.92 ± 22.05	78.92 ± 4.57	50.92 ± 7.49
B	0.82 ± 0.09	88.07 ± 24.02	72.50 ± 16.26	79.36 ± 3.91	33.96 ± 8.60
t	–1.174	1.043	0.723	–0.314	6.109
p	0.247	0.303	0.474	0.755	0.000

Pressure ratio, ratio of pulmonary artery systolic pressure/aortic systolic pressure; SpO_2, oxygen saturation during the rescue time; Mean arterial pressure, mean arterial pressure during the rescue time.

Table 3. Postoperative data 1.

Group	Vasoactive inotropic score	Success rate of rescue (n, %)	Incidence of complications (n, %)	Duration of PHC (min)	Duration of delayed sternal closure (h)	Length of ICU stay (h)
A (13)	12.77 ± 4.36	11 (84.62%)	2 (15.38%)	6.77 ± 2.13	32.23 ± 5.46	81.69 ± 8.31
B (28)	12.50 ± 3.39	19 (67.86%)	6 (21.43%)	13.07 ± 4.05	38.14 ± 8.61	93.57 ± 16.84
t/χ^2	0.216	0.560	0.057	–5.254	–2.265	–2.400
p	0.830	0.454	0.811	0.000	0.029	0.021

PHC, pulmonary hypertensive crisis; ICU, intensive care unit.

as to dynamically monitor the pressure of the left atrium and the right ventricle. Vasoactive drugs such as dopamine, dobutamine, milrinone, and epinephrine were used for both groups to improve cardiac function, and maintain normal arterial systolic blood pressure [7,8].

In case of pulmonary hypertensive crisis (PHC), an emergency bedside thoracotomy was administered in both groups, and the group B children received fentanyl, midazolam and other drugs to enhance sedation. Pure oxygen and nitric oxide/isoprostaglandin were administered via a breathing bag, troprostil/alprostil were pumped intravenously, and other conventional methods were performed for the rescue operation. Following this conventional treatment, the triplet in group A was immediately turned on to connect the left atrial and right ventricular pressure monitoring tubes. The blood from the right ventricule under higher pressure flowed into the left atrium under a lower pressure through the tube, which then immediately reduced the pressure on the right ventricle and simultaneously increased the aortic pressure during the PHC. When the blood pressure and oxygen saturation were stabilized, the triplet was turned off, and the pressure oxygen delivery via the breathing bag was replaced with ventilator-assisted breathing. The ventilator parameters and the corresponding drug dosage were gradually adjusted, and the conditions of children were closely monitored. After the rescue, blood pressure, oxygen saturation, the success rate of rescue, the incidence of complications, the length of ICU stay, the duration of delayed chest closure, the duration of PHC, ratio of pulmonary circulation/systemic circulation pressure, oxygenation index and cardiac index in the two groups during the rescue were compared at 30 min, 1 h, 2 h, 4 h and 6 h at the end of the rescue. The survival curves of the two groups within 60 h after surgery and the ones within 1 year after discharge were plotted. Chest X-ray, echocardiography and electrocardiogram were examined at 1, 3, and 6 months and then at 1 year after discharge to measure the postoperative cardiac function, the status of the intracardiac malformations and the changes in the pulmonary artery pressure. The body mass index (BMI) of the children was regularly monitored to evaluate the physical health and development of the children after the surgery.

Statistical Analysis

The clinical data were analyzed by SPSS 22.0 statistical software (IBM Corp., Armonk, NY, USA). The measurement data were expressed as mean ± standard deviation ($\bar{x}$ ± s), and the count data were tested by the chi-square test. The independent sample T test was used to compare

Table 4. Postoperative data 2.

Time	A			B		
	Pressure ratio	Oxygenation index	Cardiac index	Pressure ratio	Oxygenation index	Cardiac index
30 min	0.65 ± 0.07	283.55 ± 10.60	2.36 ± 0.38	0.72 ± 0.05	260.79 ± 14.66	1.69 ± 0.34
1 h	0.57 ± 0.06	300.36 ± 12.89	2.56 ± 0.33	0.68 ± 0.09	282.21 ± 17.95	2.14 ± 0.30
2 h	0.56 ± 0.05	320.55 ± 14.05	2.79 ± 0.25	0.65 ± 0.07	305.00 ± 18.51	2.60 ± 0.21
4 h	0.50 ± 0.06	359.64 ± 15.09	2.93 ± 0.22	0.58 ± 0.10	341.84 ± 20.15	2.85 ± 0.25
6 h	0.35 ± 0.06	381.73 ± 10.74	3.18 ± 0.29	0.38 ± 0.05	372.89 ± 15.37	3.02 ± 0.26
F	40.454	112.076	12.466	61.370	127.242	74.469
p	0.000	0.000	0.000	0.000	0.000	0.000
P30,1	0.043	0.033	1.000	0.666	0.003	0.000
P30,2	0.015	0.000	0.015	0.032	0.000	0.000
P30,4	0.000	0.000	0.001	0.000	0.000	0.000
P30,6	0.000	0.000	0.000	0.000	0.000	0.000
P1,2	1.000	0.005	0.797	0.993	0.001	0.000
P1,4	0.077	0.000	0.061	0.039	0.000	0.000
P1,6	0.000	0.000	0.000	0.000	0.000	0.000
P2,4	0.193	0.000	1.000	0.144	0.000	0.059
P2,6	0.000	0.000	0.034	0.000	0.000	0.000
P4,6	0.000	0.000	0.505	0.000	0.000	0.554

Pressure ratio, ratio of pulmonary circulation/systemic circulation pressure; P30,1, *p* value between 30 min and 1 h; P30,2, *p* value between 30 min and 2 h; P30,4, *p* value between 30 min and 4 h; P30,6, *p* value between 30 min and 6 h; P1,2, *p* value between 1 h and 2 h; P1,4, *p* value between 1 h and 4 h; P1,6, *p* value between 1 h and 6 h; P2,4, *p* value between 2 h and 4 h; P2,6, *p* value between 2 h and 6 h; P4,6, *p* value between 4 h and 6 h.

Table 5. Postoperative data 3.

Time	Group	Pressure ratio	Oxygenation index	Cardiac index
10 min	A	0.44 ± 0.09	326.23 ± 14.65	2.88 ± 0.33
	B	0.41 ± 0.11	329.46 ± 16.44	2.94 ± 0.26
	t	0.888	–0.605	–0.579
	p	0.380	0.548	0.566
30 min	A	0.65 ± 0.07	283.55 ± 10.60	2.36 ± 0.38
	B	0.72 ± 0.05	260.79 ± 14.66	1.69 ± 0.34
	t	–3.218	4.498	5.002
	p	0.003	0.000	0.000
1 h	A	0.57 ± 0.06	300.36 ± 12.89	2.56 ± 0.33
	B	0.68 ± 0.09	282.21 ± 17.95	2.14 ± 0.30
	t	–3.384	2.935	3.621
	p	0.002	0.007	0.001
2 h	A	0.56 ± 0.05	320.55 ± 14.05	2.79 ± 0.25
	B	0.65 ± 0.07	305.00 ± 18.51	2.60 ± 0.21
	t	–3.610	2.406	2.246
	p	0.001	0.023	0.033
4 h	A	0.50 ± 0.06	359.64 ± 15.09	2.93 ± 0.22
	B	0.58 ± 0.10	341.84 ± 20.15	2.85 ± 0.25
	t	–2.368	2.538	0.827
	p	0.025	0.017	0.415
6 h	A	0.35 ± 0.06	381.73 ± 10.74	3.18 ± 0.29
	B	0.38 ± 0.05	372.89 ± 15.37	3.02 ± 0.26
	t	–1.347	1.677	1.523
	p	0.189	0.105	0.139

10 min, 10 minutes after returning to intensive care unit; 30 min, 30 minutes after rescue; 1 h, 1 hour after rescue; 2 h, 2 hours after rescue; 4 h, 4 hours after rescue; 6 h, 6 hours after rescue; Pressure ratio, ratio of pulmonary circulation/systemic circulation pressure.

Table 6. Postoperative data 4.

Time	Group	LVEF	Pulmonary artery systolic pressure (mmHg)	BMI (kg/m^2)
1 month	A	58.36 ± 2.98	56.64 ± 9.19	16.25 ± 0.66
	B	60.00 ± 3.20	52.79 ± 7.43	16.30 ± 0.64
	t	–1.384	1.253	–0.223
	p	0.177	0.220	0.825
3 months	A	60.00 ± 2.28	52.46 ± 9.20	17.11 ± 0.98
	B	60.63 ± 3.21	48.63 ± 4.39	16.91 ± 0.71
	t	–0.574	1.546	0.658
	p	0.571	0.133	0.516
6 months	A	61.45 ± 3.23	50.27 ± 7.72	18.07 ± 1.17
	B	62.16 ± 2.87	47.16 ± 3.53	17.80 ± 1.00
	t	–0.617	1.519	0.675
	p	0.542	0.140	0.505
1 year	A	60.82 ± 3.19	49.81 ± 5.78	18.31 ± 2.15
	B	61.11 ± 3.18	47.79 ± 4.69	18.59 ± 1.64
	t	–0.238	1.050	–0.403
	p	0.813	0.303	0.690

LVEF, left ventricular ejection fraction; BMI, body mass index; 1 month, 1 month after discharge; 3 months, 3 months after discharge; 6 months, 6 months of discharge; 1 year, 1 year after discharge.

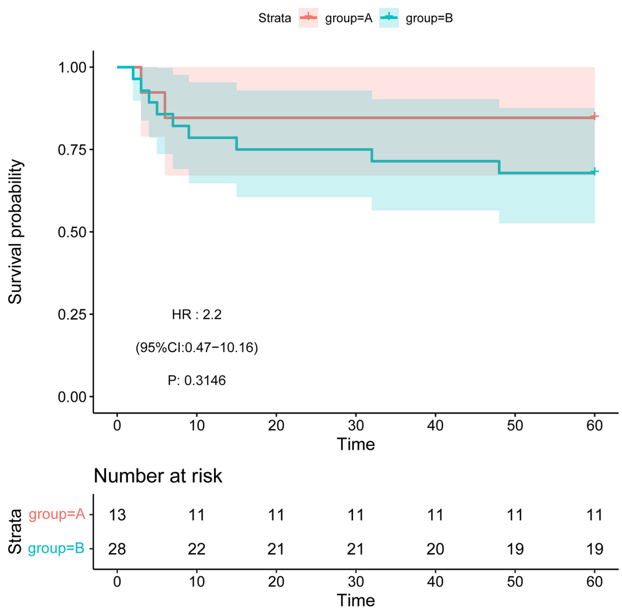

Fig. 2. Kaplan-Meier 60-hour survival curve. Cumulative survival rate at 60 hours after surgery in groups A and B.

the related indexes of the two groups at the same time. One-way repeated measures analysis of variance was used to compare the differences within a group at different periods and the variation trend of each index in the two groups. Using vegan version 2.6.2 (University of Helsinki, Helsinki, Finland) and R version 4.2.1 (The University of Auckland, Auckland, New Zealand), principal co-ordinates analysis was applied to study the similarity and divergence of sample communities; by R version 4.2.1 Cox regression models (The University of Auckland, Auckland, New Zealand) were built by survival and survminer packages (version 3.5-5) (Montpelier, Languedoc Roussillon, France), survival analysis curves and other corresponding figures were drawn by ggplot 2 (Version 3.4.0) (Rice University, Houston, TX, USA). $p < 0.05$ indicated that the difference was statistically significant, and $p < 0.01$ indicated that the difference was highly significant.

Results

There were a total of 6 cases with TAPVD, all of whom had pulmonary veins that had been surgically isolated to the left atrium. The pulmonary arteries of 6 cases with CTGA and 5 cases with Taussig-Bing showed anastomoses to the anatomical right ventricle, with the aorta anastomosed to the anatomical left ventricle. In addition, 9 cases with IAA/VSD and 4 cases with COA/VSD had undergone VSD repair, and their ascending aorta had been anastomosed to the descending aorta during cardiopulmonary bypass to restore the normal morphology of the aorta. Through the ventricular septal reconstruction, the aorta of 4 cases with DORV/PH had been separated into the left ventricle so as to restore the normal anatomy of the left and right ventricle. Moreover, 7 cases of TECD/PH had been surgically corrected with a heart malformation, which included restoration of the normal four-chamber cardiac structure and the normal anatomic structure of the mitral valve and tricuspid valve. In all these cases there were no intraoperative complications.

10 minutes after returning to ICU, there were no significant differences in pulmonary circulation/systemic circulation pressure ratio, oxygenation index, cardiac index and VIS between the two groups (all $p > 0.05$) (Tables 2,3). After the occurrence of PHC, there was no significant dif-

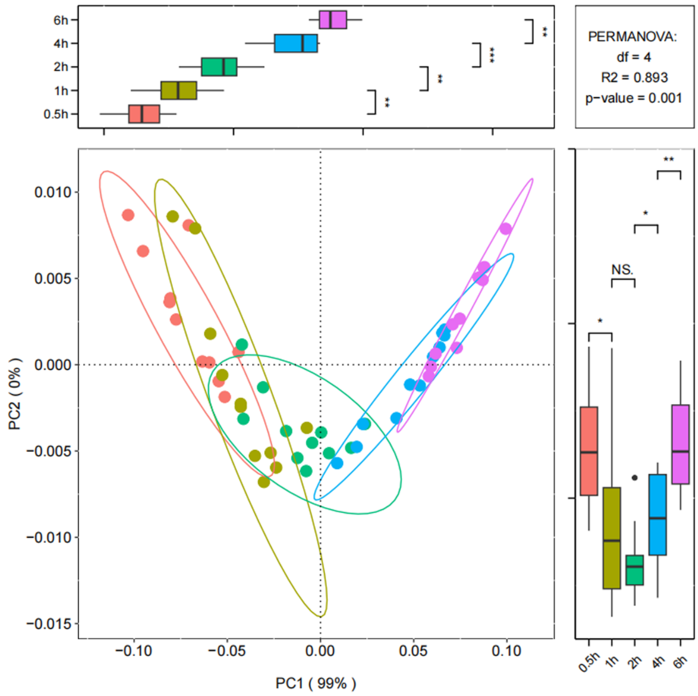

Fig. 3. PCoA analysis in group A. Principal co-ordinates analysis was used to analyze the similarity and divergence of comprehensive data of group A at five time points. PC1, the first dimension; PC2, the second dimension; Red dot, comprehensive data at 0.5 h; Grass green dot, comprehensive data at 1 h; Lake green dot, comprehensive data at 2 h; Blue dot, comprehensive data at 4 h; Purple dot, comprehensive data at 6 h; Elliptical circle, 95% confidence interval. NS.: $p > 0.05$, *: $0.01 < p < 0.05$, **: $0.001 < p < 0.01$, ***: $p < 0.001$.

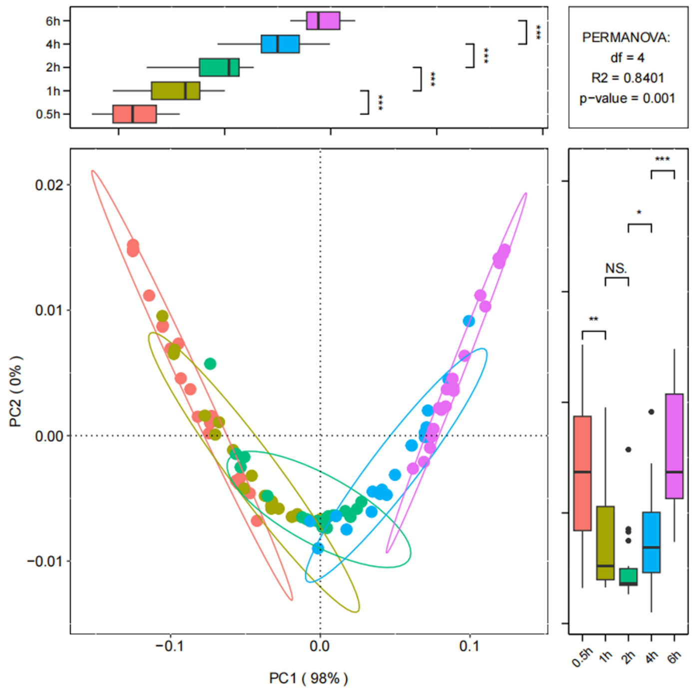

Fig. 4. PCoA analysis in group B. Principal co-ordinates analysis was used to analyze the similarity and divergence of comprehensive data of group B at five time points. PC1, the first dimension; PC2, the second dimension; Red dot, comprehensive data at 0.5 h; Grass green dot, comprehensive data at 1 h; Lake green dot, comprehensive data at 2 h; Blue dot, comprehensive data at 4 h; Purple dot, comprehensive data at 6 h; Elliptical circle, 95% confidence interval. NS.: $p > 0.05$, *: $0.01 < p < 0.05$, **: $0.001 < p < 0.01$, ***: $p < 0.001$.

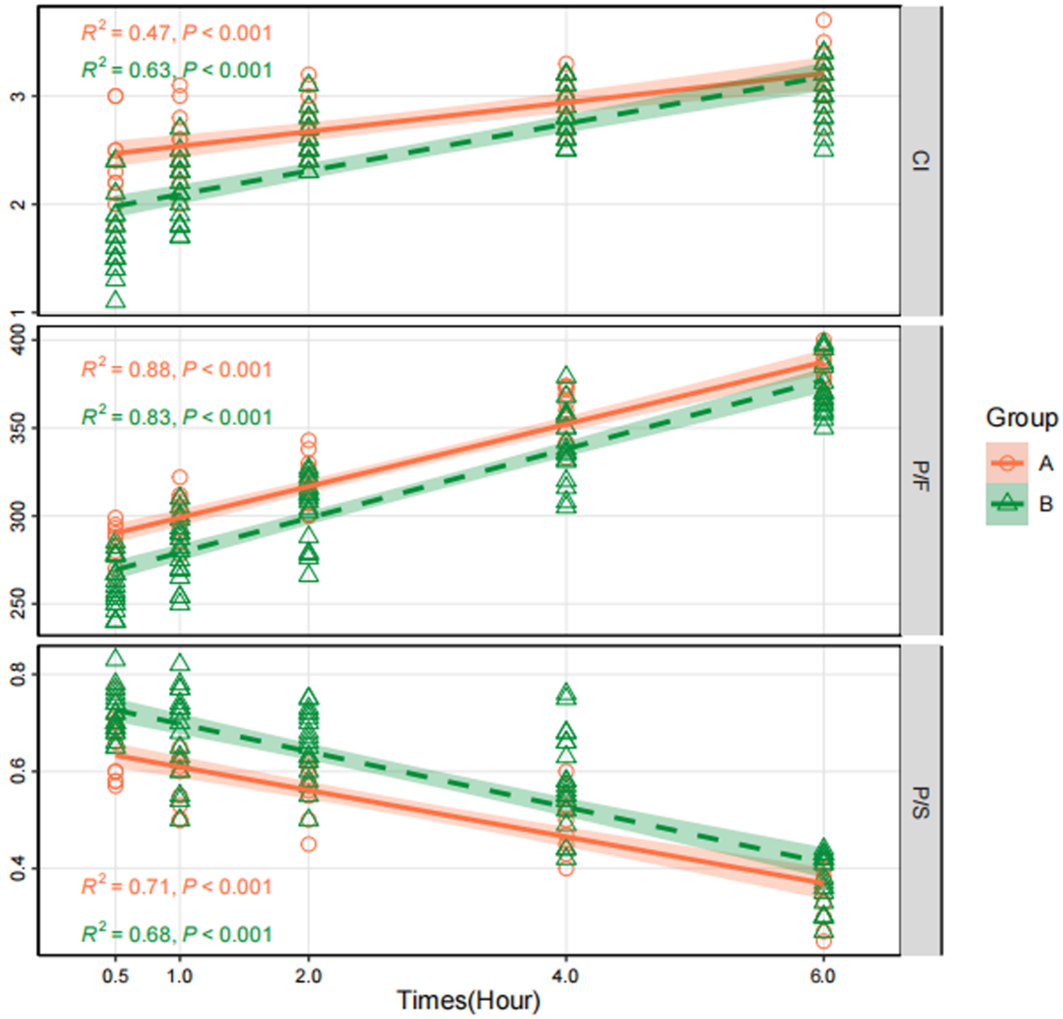

Fig. 5. Time fitting curve. Changes of CI, P/F and P/S over time in group A and B. CI, cardiac index; P/F, oxygenation index (PaO_2/FiO_2); P/S, ratio of pulmonary circulation/systemic circulation pressure; Δ, data in group A; ◯, data in group B.

ference in oxygen saturation between the two groups ($p > 0.05$), but the mean arterial pressures in group A were higher than those in group B, and the difference was statistically significant ($p < 0.01$) (Table 2). 11 cases in group A survived, 2 cases died, and the rescue success rate was 84.62%. Complications occurred in 2 cases (15.38%), in which 1 case had a large amount of bleeding and hematoma at the connection between the pressure measurement tube and the myocardial tissue, and 1 case had a large amount of tricuspid regurgitation (Table 3). In group B, 19 cases survived, and the rescue success rate was 68.86%; complications occurred in 6 cases, including 2 cases with bronchial hemorrhage, 1 case with atrioventricular valve suture avulsion, 1 case with pulmonary artery anastomotic bleeding, 1 case with cerebral hypoxia-related complications, and 1 case with right coronary artery compression due to anastomotic hematoma (Table 3). The incidence of complications was 21.43%, and there were no significant differences in the success rate of rescue and the incidence of complications between the two groups respectively (all $p > 0.05$) (Table 3). There was no statistically significant difference in the survival rate between group A and group B ($p > 0.05$) (Fig. 2).

After the rescue, the corresponding monitoring indexes of the two groups changed significantly ($R^2 = 0.893$, $p = 0.001$ *vs.* $R^2 = 0.8401$, $p = 0.001$) (Figs. 3,4); the ratio of pulmonary circulation/systemic circulation pressure in the two groups decreased ($R^2 = 0.71$, $p < 0.001$ *vs.* $R^2 = 0.68$, $p < 0.001$), the oxygenation index ($R^2 = 0.88$, $p < 0.001$ *vs.* $R^2 = 0.83$, $p < 0.001$) and cardiac index ($R^2 = 0.47$, $p < 0.001$ *vs.* $R^2 = 0.63$, $p < 0.001$) increased (Fig. 5); compared with group B, the ratio of pulmonary circulation/systemic circulation pressure in group A decreased significantly during 30 min~1 h after rescue ($p = 0.043$ *vs.* $p = 0.666$),and no significant changes occurred in the two groups at 1 h~2 h and 2 h~4 h after surgery ($p = 1.000$ *vs.* $p = 0.993$; $p = 0.193$ *vs.* $p = 0.144$) (Table 4); from 4 h to 6 h, the changes of the ratio of pulmonary circulation/systemic circulation pressure in the two groups were significant ($p = 0.000$ *vs.* $p = 0.000$) (Table 4). At 30 min~1 h, 1 h~2 h, 2

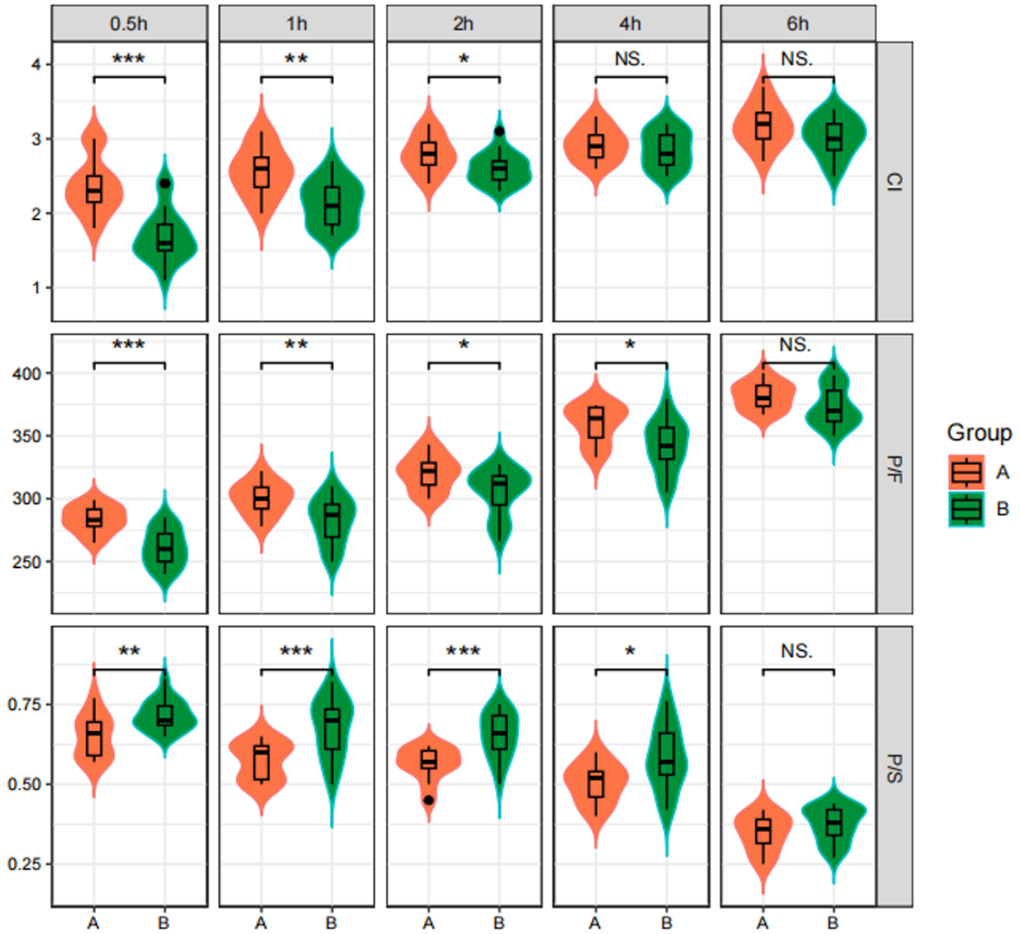

Fig. 6. Data comparison chart. Comparison chart of different monitoring indicators at different time points in group A and B. NS.: $p > 0.05$, *: $0.01 < p < 0.05$, **: $0.001 < p < 0.01$, ***: $p < 0.001$.

h~4 h, 4 h~6 h after the end of the rescue, the oxygenation index of the two groups increased significantly ($p = 0.033$ *vs.* $p = 0.003$; $p = 0.005$ *vs.* $p = 0.001$; $p = 0.000$ *vs.* $p = 0.000$; $p = 0.000$ *vs.* $p = 0.000$) (Table 4); Compared with group A, the increase of cardiac index in group B was significant at 30 min~1 h and 1 h~2 h ($p = 1.000$ *vs.* $p = 0.000$; $p = 0.797$ *vs.* $p = 0.000$) (Table 4).

The success rate of rescue in group A was higher than that in group B, and the incidence of complications was lower than that in group B, but the differences were not statistically significant (all $p > 0.05$) (Table 3). Compared with group B, there was a shorter duration of delayed chest closure ($p < 0.05$), shorter length of ICU stay ($p < 0.05$) and shorter duration of PHC ($p < 0.01$) in group A (Table 3). At 30 min, 1 h, 2 h and 4 h after the end of rescue, the ratio of pulmonary circulation/systemic circulation pressure in group A was significantly lower than that in group B ($p < 0.01$) (Fig. 6); the oxygenation index and cardiac index in group A were significantly higher than those in group B at 30 min and 1h after rescue ($p < 0.01$) (Table 5, Fig. 6). 2 hours after the rescue, the oxygenation index and cardiac index in group A were higher than those in group B, and the differences were statistically significant ($p < 0.05$) (Table 5, Fig. 6); there were no significant differences in pulmonary circulation/systemic circulation pressure ratio, oxygenation index and cardiac index between the two groups at 4 hours and 6 hours after the rescue ($p > 0.05$) (Table 5, Fig. 6). Comprehensive analysis showed that the therapeutic effect of group A was better than that of group B ($R^2 = 0.0386$, $p = 0.015$) (Fig. 7).

After discharge, 1 case in group A died of severe pneumonia, and 1 case underwent repeat surgery for aortic arch stenosis. In group B, 1 case died of malignant ventricular arrhythmia, 1 case underwent left ventricular outflow tract reconstruction due to left ventricular outflow tract obstruction, and 1 case underwent mitral valvuloplasty due to massive mitral regurgitation. No statistically significant difference was noted in the survival rate between the groups (Fig. 8). There were no significant differences in the left ventricle ejection fraction, pulmonary artery systolic pressure and BMI between the two groups during follow-up for 1 year (all $p > 0.05$) (Table 6).

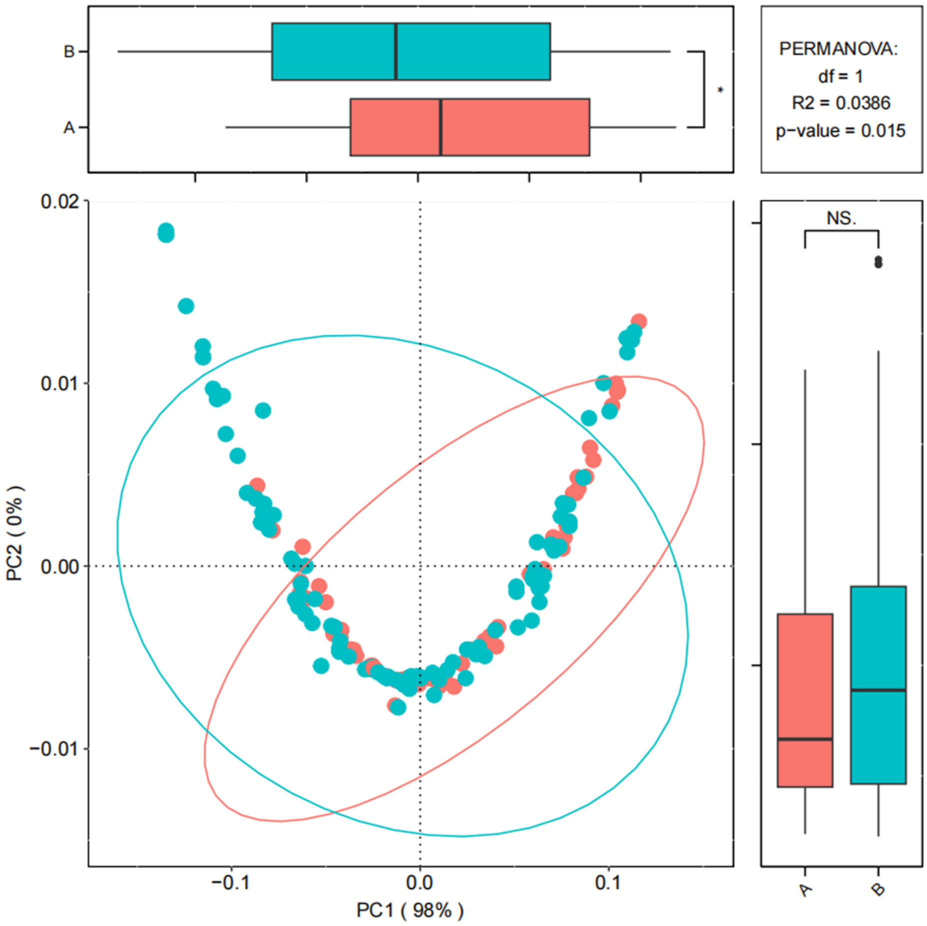

Fig. 7. PCoA analysis between group A and B. Principal co-ordinates analysis was used to analyze the similarity and divergence of comprehensive data between group A and B. PC1, the first dimension; PC2, the second dimension; Red dot, comprehensive data of group A; Blue dot, comprehensive data group B; Elliptical circle, 95% confidence interval. NS., $p > 0.05$; *, $0.01 < p < 0.05$.

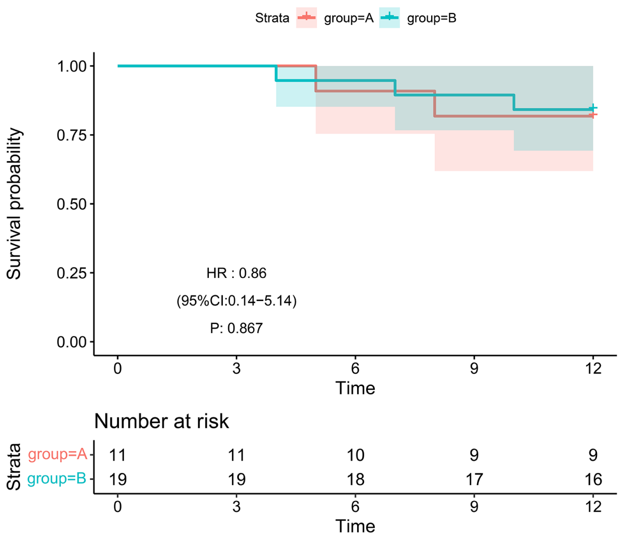

Fig. 8. Kaplan-Meier 1-year survival curve. Cumulative survival rate within 1 year after discharge in groups A and B.

Discussion

PHC is a life-threatening emergency that requires immediate intervention. It has been reported that the mortality rate caused by PHC after surgery for CHD is as high as 22%–55% [9,10]. PHC results in a sharp increase in pulmonary artery pressure induced by a variety of factors, resulting in acute right heart failure and low cardiac output syndrome [11,12]. Endogenous sympathetic neurotransmitters such as epinephrine and norepinephrine, endothelial nitric oxide synthase gene defects or dysfunction, systemic inflammatory response syndrome, hypoxia, acidosis, endothelial cell damage and pulmonary vascular intimal thickening also play roles in the pathogenesis of PHC [13–17]. At present, the treatment of PHC in most heart centers include: (1) Correct the underlying abnormalites; (2) keep the airway unobstructed and provide adequate oxygen; (3) sedation; (4) correct right heart failure and hypotension with inotropes, such as epinephrine and norepinephrine; and vasopressin to improve hemodynamics [18]; (5) the use of drugs to reduce pulmonary hypertension: including nitric oxide for inhalation; prostacycline analogues, such as iloprostaglandin; endothelin receptor antagonists, such as Bosentan; phosphodiesterase-5 inhibitors, such as sildenafil.

These treatments work toward reducing or eliminating the causes of increased right ventricular afterload. However, they almost never have an immediate effect, and there are few reports on therapies that can instantaneously relieve right heart distress and increase the systemic blood flow. Atrial septostomy or extracorporeal membrane oxygenation support (ECMO) has been used in the treatment of PHC [19,20]. Although atrial septostomy relieves right heart distress by establishing a right-to-left shunt, which needs to be carried out during the CHD surgery, it still needs to be closed in the future, thereby increasing the number of operations in children and the corresponding risks. An atrial septostomy cannot be performed in advance as we cannot predict those children who will develop PHC after surgery for CHD. Moreover, with the high cost of ECMO treatment, the best rescue time is often lost when it is performed after the occurrence of PHC.

In addition to the conventional therapy, we adopted the left atrial to right ventricular pressure tube bridging technology. When PHC occurs, the left atrial pressure tube with heparin coating connects with the heparin-coated right ventricular pressure tube, and the blood from the right ventricular under a high pressure flows smoothly into the low-pressure left atrium through the tube, which immediately relieves the right ventricular pressure and simultaneously increases the systemic blood volume to maintain the higher systemic blood pressure during the PHC.

The data from this study showed that the bridge method of left atrial to right ventricular pressure tube has obvious advantages in rescuing PHC after surgery for CHD. There was a higher rescue success rate, lower incidence of complications, shorter duration of pulmonary hypertension crisis ($p = 0.000$), shorter delayed chest closure duration ($p = 0.029$) and shorter length of ICU stay ($p = 0.021$) in group A (Table 3). After the rescue, the pulmonary artery pressure decreased faster and the cardiopulmonary function recovered faster in group A (Tables 4,5 and Figs. 5,6). However, following 1-year after discharge, we have found that this technique has no obvious advantages in promoting the recovery of cardiac function, reducing pulmonary artery pressure, and promoting the growth and development of children in the long-term.

Due to the bridge between the left atrium and the right ventricle, the venous blood with low oxygen saturation flows into the systemic circulation, resulting in a certain degree of decrease in blood oxygen saturation. However, there was no significant difference in blood oxygen saturation between the two groups during the rescue period ($p > 0.05$) (Table 2). The mean arterial pressure of the former was higher than that of the conventional treatment group during the rescue period, and the difference was statistically significant ($p < 0.05$) (Table 2). Therefore, the left atrial to right ventricular conduit bridging method has obvious advantages in the treatment of PHC after surgery for CHD.

However, this method has some shortcomings and limitations. First, it is only suitable for children with delayed chest closure after CHD surgery. Due to the bleeding caused by pulling out the manometry tube, this method cannot be used in children with closed chests following surgery. Second, the matching tube type of children with different weights needs to be discussed. In this study, the age of the children was $\leq$3 months, body weight was 4.34 $\pm$ 0.77 kg, and the diameter of the pressure–measuring tube was 4 mm. Based on the existing data analysis, the resultant effect is ideal. However, the selection of the pressure tube model suitable for older children is unknown. Furthermore, owing to the relatively small sample size, the data may not adequately reflect the true differences between the two groups. In the future, a larger sample size is needed to verify these results.

Conclusions

The effect of conventional therapy combined with a left atrium to right ventricle duct bridging treatment was superior to that of the simple conventional therapy for the rescue of PHC after CHD surgery. The advantages of this treatment will need to be further defined in a larger group of patients with PHC after CHD surgery.

Availability of Data and Materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions

XW and HZ designed the research study. HS and LC analyzed the data and wrote the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

This study was performed in accordance with the Declaration of Helsinki and was approved by Ethics Committee of the Hebei Children's Hospital (Approval No. 202136). The subjects obtained the consent of the guardians and signed the informed consent.

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Conflict of Interest

The authors declare no conflict of interest.

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