Article

Prognosis Analysis of Children with Interrupted Aortic Arch Complicated with Ventricular Septal Defect and Other Associated Intracardiac Defects after One-Stage Radical Surgery

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Abstract

Background: High rates of mortality and aortic arch stenosis have been reported for one-stage radical surgery of interruption of aortic arch (IAA) with ventricular septal defect (VSD) and other associated intracardiac defects, but the sample size of the study is relatively small, and the credibility of the study is not high. The risk factors of death and aortic arch stenosis will be analyzed in a large sample size of infants with IAA, VSD and other associated intracardiac defects after one-stage radical resection. **Methods**: A retrospective analysis was performed on 152 children with IAA, VSD and other associated intracardiac defects from January 2006 to January 2017 who had undergone one-stage radical resection, including 95 cases of type A and 57 cases of type B. January 2006–December 2011 as the early period, and January 2012–January 2017 as the late period. Cox proportional hazards regression model was used to analyze the risk factors for mortality and aortic arch stenosis after surgery, the overall survival rate was analyzed by the Kaplan-Meier method, and the survival curve was drawn by GraphPad Prism 8 software. **Results**: 22 cases (14.47%) died, 27 cases (17.76%) developed aortic arch stenosis. The 1-month, 3-month, 6-month, 1-year, 3-year, and 5-year survival rates were 85.53%, 85.53%, 85.53%, 84.21%, 78.95% and 75.66%, respectively. Low age (Hazard Ratio (HR) = 0.551, 95% Confidence Interval (CI): 0.320–0.984, p = 0.004), low body weight (HR = 0.632, 95% CI: 0.313–0.966, p = 0.003), large ratio of VSD diameter/aortic diameter (VSD/AO) (HR = 2.547, 95% CI: 1.095–7.517, p = 0.044), long duration of cardiopulmonary bypass (HR = 1.374, 95% CI: 1.000–3.227, p = 0.038), and left ventricular outflow tract obstruction (LVOTO) (HR = 3.959, 95% CI: 1.123–9.268, p = 0.015) were independent risk factors for postoperative death. The surgical period (January 2006–December 2011) (HR = 0.439, 95% CI: 0.109–0.964, p = 0.046) and the addition of pericardial anastomosis to the anterior aortic wall (HR = 0.398, 95% CI: 0.182–0.870, p = 0.021) were independent risk factors for postoperative aortic arch stenosis. **Conclusions**: Children with low age, low body weight, large ratio of VSD/AO, long duration of cardiopulmonary bypass, LVOTO, the surgical period (January 2006–December 2011) and pericardial anastomosis with anterior aortic wall have poor prognosis.

Keywords

interruption of aortic arch; ventricular septal defect; aortic arch stenosis; risk factors

Introduction

Interruption of aortic arch (IAA) with ventricular septal defect (VSD) and other associated intracardiac defects is a complex congenital heart disease (CHD), early one-stage radical resection is the preferred surgical treatment in most heart centers [1], especially in the neonatal period, in which one-stage radical treatment can reduce the formation of collateral vessels and post-stenosis dilatation to a great extent [2].

The challenges of IAA repair, which showed an overall 5-year survival of 60–80% and a 5-year freedom from reintervention for arch obstruction of 60–80%, were well documented by the Congenital Heart Surgeons' Society and other reports [3]. Multiple centers reported that the operative mortality rate and postoperative aortic arch stenosis rate of this disease were higher [4–7]. However, the sample size of this study are relatively small, and the credibility of the study is not high.

In this study, we considered of low age, large ratio of ventricular septal defect diameter/aortic diameter (VSD/AO), low body weight, LVOTO, long cerebral perfusion time, long intensive care unit (ICU) time, long duration of cardiopulmonary bypass, pericardial anastomosis with anterior aortic wall, type and early surgical period as the risk factors for death and aortic arch stenosis after one-stage radical resection. Meanwhile, we retrospectively studied the prognosis of a large sample size of children with IAA, VSD and other associated intracardiac defects who had un-
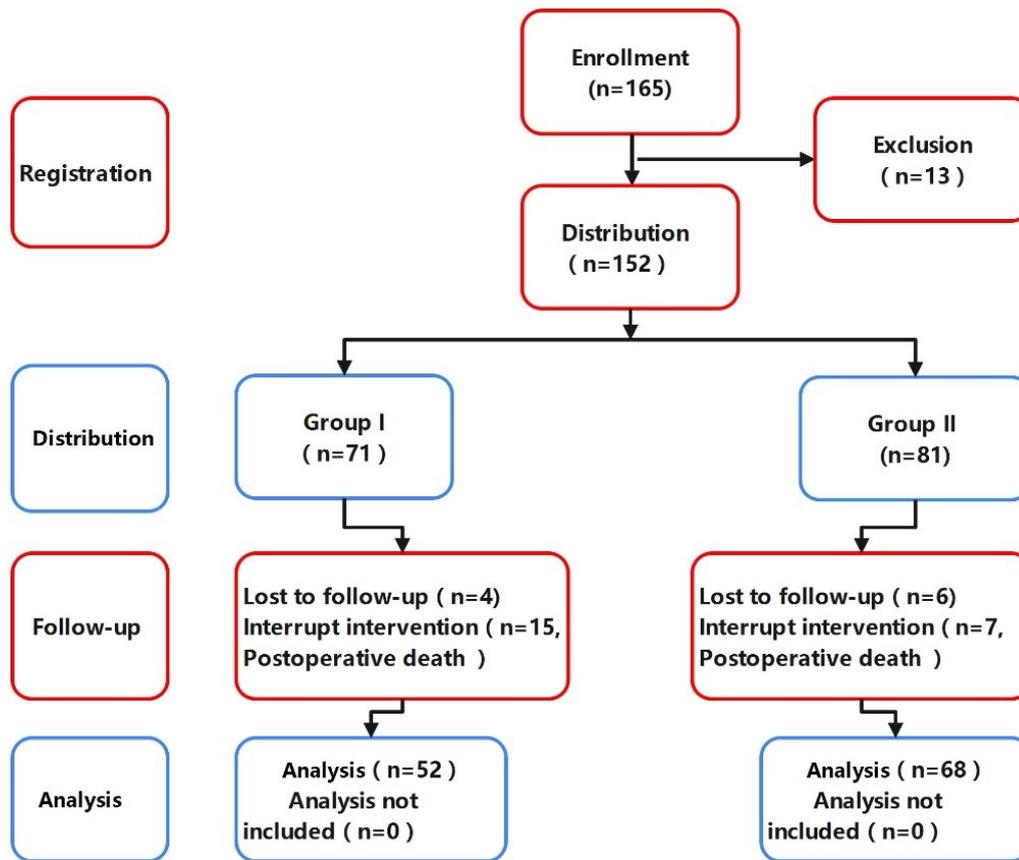
Fig. 1. Children screening flow chart. Early period: patients who had undergone surgery from January 2006 to December 2011; Late period: patients who had undergone surgery from January 2012 to January 2017.

dergone one-stage radical surgery, statistical analysis was conducted based on the above possible factors to identify the real risk factors for postoperative mortality and aortic arch stenosis, and provided reliable data for clinical reference.

Materials and Methods

The clinical data of children with IAA, VSD and other associated intracardiac defects who were admitted to our hospital from January 2006 to January 2017 and had undergone one-stage radical resection were retrospectively studied. Inclusion criteria included patients diagnosed with IAA, VSD and other associated intracardiac defects by echocardiography and/or cardiac CT, and those who had received one-stage radical surgery (Fig. 1). Exclusion criteria contained children who had been performed staged surgery and those with single ventricular structure who were unable to undergo radical surgery.

The clinical data of all children were retrospectively analyzed, including age, body weight, disease type, ratio of VSD/AO, duration of cardiopulmonary bypass, duration of cerebral perfusion, duration of ICU stay, the number and percentage of direct anastomosis of aortic arch, the number and percentage of early postoperative death, the number and percentage of postoperative follow-up death, the number and percentage of postoperative loss to follow-up, the number and percentage of postoperative aortic arch stenosis and the number and percentage of other cardiac malformations.

Ultimately, 152 children were included in this study, including 70 males and 82 females, aged 24–88 days, with a median age of 51 days, body mass of 2.43–3.33 kg, and median body mass of 2.92 kg; according to the anatomical classification, there were 95 cases of type A and 57 cases of type B (Table 1). All cases were complicated with patent ductus arteriosus (PDA), including 20 cases with LVOTO, 3 cases with type I aortopulmonary window (AP window), 2 cases with double outlet of right ventricle (DORV), 3 cases with aortic arch stenosis (AS), 3 cases with moderate to severe mitral reflux (MR), 30 cases with atrial septal defect (ASD) and 4 cases with aortic bicuspid malformation (Table 1). The study was approved by the Ethics Committee of the First Hospital of Hebei Medical University (Approval No. 20220721) and conformed to the principles of the Helsinki declaration. The requirement for informed consent was waived because of the retrospective nature of the study.

Table 1. Data of children in perioperative period.

Category	Early Period (71)		p	Late Period (81)		p
	Type A (46)	Type B (25)		Type A (49)	Type B (32)	
Age (day)	48.60 ± 17.12	46.00 ± 11.64	0.051	50.09 ± 15.61	56.54 ± 17.82	0.128
Sex (M/F)	21/25	11/14	0.894	20/29	18/14	0.174
Weight (Kg)	2.87 ± 0.19	2.89 ± 0.24	0.484	2.94 ± 0.22	2.96 ± 0.23	0.208
VSD/AO	1.54 ± 0.25	1.45 ± 0.27	0.703	1.46 ± 0.24	1.48 ± 0.27	0.451
CPBT (min)	145.50 ± 23.69	141.71 ± 25.98	0.845	141.17 ± 21.57	140.76 ± 24.38	0.102
CPT (min)	38.44 ± 10.59	39.94 ± 11.73	0.401	39.46 ± 12.26	38.94 ± 11.66	0.403
ICU Time (day)	6.98 ± 1.05	6.50 ± 1.14	0.968	6.87 ± 0.78	6.39 ± 0.89	0.286
Direct Anastomosis (n, %)	22 (47.83%)	6 (24%)	0.050	12 (24.49%)	16 (50%)	0.018
Postoperative Death (n, %)	8 (17.39%)	7 (28%)	0.296	3 (6.12%)	4 (12.50%)	0.552
Follow-up Death (n, %)	1 (2.17%)	2 (8.00%)	0.584	2 (4.08%)	0 (0.00%)	0.671
Postoperative Lost Follow-up (n, %)	3 (6.52%)	1 (4.00%)	1.000	3 (6.12%)	3 (9.38%)	0.910
Postoperative Aortic Arch Stenosis (n, %)	11 (23.91%)	3 (12%)	0.372	5 (10.20%)	5 (15.63%)	0.704
LVOTO (n)	6	7	0.217	3	4	0.552
APW (n)	2	0	0.537	0	1	0.395
DORV (n)	1	0	1.000	0	1	0.395
AS (n)	1	0	1.000	1	1	1.000
MR (n)	0	2	0.121	1	0	1.000
ASD (n)	10	1	0.103	7	12	0.016
Bicuspid aortic valve (n)	2	1	1.000	1	0	1.000

M/F, male/female; VSD/AO, ratio of VSD diameter/diameter of aortic root; CPBT, cardiopulmonary bypass time; CPT, cerebral perfusion time; ICU Time, intensive care unit time; LVOTO, left ventricular outflow tract obstruction; APW, aortopulmonary window; DORV, double outlet of right ventricle; AS, aortic arch stenosis; MR, mitral reflux; ASD, atrial septal defect.

According to the period of operation, children who had received surgery from January 2006 to December 2011 were defined as early period, and those who had undergone surgery from January 2012 to January 2017 were classified as late period. All of the children were followed up for 1 month, 3 months, 6 months and 1 year after surgery. Subsequently, they were followed up regularly every year, and received examination of echocardiography and/or cardiac CT. The diagnostic criteria of aortic arch stenosis and reoperation were as follows: (1) the peak systolic flow rate in descending aortic arch was ≥ 2.5 m/s, and the pressure gradient was ≥ 25 mmHg. (2) Cardiac CT showed that the aortic arch was clearly angulated, showing 'Gothic' changes, and was partly accompanied by left bronchial compression. Relevant materials were collected, the risk factors of postoperative mortality and aortic arch stenosis were analyzed, and the survival curve was plotted.

Surgical Technique

All of the selected children had been treated with one-stage radical surgery. During anesthesia, continuous arterial blood pressure monitoring had been performed on the right radial artery and femoral artery, nasopharyngeal temperature and anal temperature had been monitored. The ascending aorta, transverse aortic arch, brachiocephalic trunk artery, left common carotid artery, left subclavian artery and descending aorta should be fully freed to avoid injury of recurrent laryngeal nerve. The ascending aorta was cannulated, and the descending aorta was inserted through ductus arteriosus. Immediately, the two aortic cannulae above were connected by a Y-shaped connector. Meanwhile, the superior and inferior vena cava were cannulated to establish extracorporeal circulation. When rectal temperature dropped to 18–20 °C, the aorta was blocked and HTK cardioplegia was perfused into the aortic root. After cardiac arrest, the ascending aortic cannula was inserted into the brachiocephalic trunk artery for selective cerebral perfusion, and the descending aortic cannula was pulled out and clamped with blocking forceps, then the arterioductal tissue was removed and the pulmonary artery was sutured continuously. Subsequently, the descending aorta was fully dissociated and lifted up so as to avoid angulated 'Gothic' aortic arch and bronchial stenosis on one side caused by the compression of the descending part of the aortic arch. The proximal end of the descending aorta might be directly anastomosed with the distal end of the aortic arch if the distance between them was short. Otherwise, it was feasible to perform a direct anastomosis between posterior wall of aortic arch and the one of descending aorta, next the anterior wall of the anastomosis was widened from the body pericardium (Fig. 2). Diverticulum resection and subclavian artery and common carotid artery transplantation were performed in children with aberrant subclavian artery and Kommerell diverticulum. After the completion of the correction of IAA, the cardiopulmonary bypass was restored to normal. Dur-

ing the rewarming process, the correction of intracardiac malformations was performed, such as ASD or VSD repair, mitral valvuloplasty, double switch surgery, repair of the AP window and LVOTO dredging. Firstly, the aortic root needed be incised obliquely to the non-coronary sinus and the hypertrophic muscle bundle of the left ventricular outflow tract was cut off after the aortic valve was pulled open. Occasionally the atrial septum needed be split and some muscle bundles were relatively easy to remove through the mitral valve if the exposure above was insufficient. Mitral valve injury should be avoided, and mitral valvuloplasty was performed if necessary. If the VSD was located below the pulmonary valve, the subaortic tissue could be cut through the pulmonary valve approach, and then the VSD was filled to the left ventricle with a large piece of bovine pericardium patch.
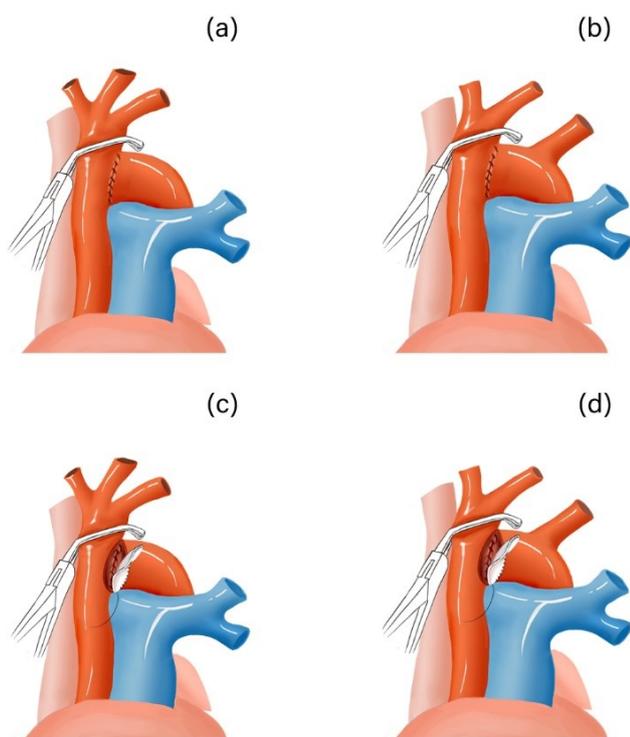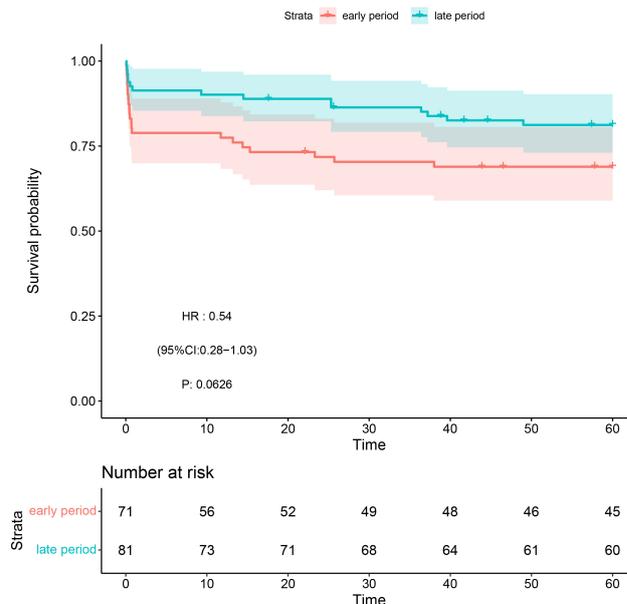

Fig. 3. Survival curve of children in different operation period. Early period: patients who had undergone surgery from January 2006 to December 2011; late period: patients who had undergone surgery from January 2012 to January 2017. HR, Hazard Ratio; CI, Confidence Interval.

Fig. 2. Correction method of Interruption of Aortic Arch (IAA). (a) Direct anastomosis for IAA of Type A. (b) Direct anastomosis for IAA of Type B. (c) Patch widening correction of IAA of Type A. (d) Patch widening correction of IAA of Type B.

Routine administration of dopamine, dobutamine, milrinone, adrenaline and other vasoactive drugs cardiotonic treatment were given postoperatively, and ventilator-assisted breathing was provided. In the meantime, the changes of blood gas and urine volume were closely monitored, and peritoneal dialysis or hemodialysis were given if necessary.

Statistical Analysis

SPSS 22.0 Statistics statistical software (IBM Corp., Armonk, NY, USA) was used for statistical analysis. Measurement data are expressed as mean ± standard deviation, and categorical variables were expressed as number (percentage). Categorical variables were compared using chi-square test, Fisher's exact test, and Pearson's chi-square test. The overall survival rate was analyzed by Kaplan-Meier method, the survival curve was drawn by R4.1.0 software (R Foundation for Statistical Computing, Vienna, Austria), and the flow chart was drawn by Visio software 2021(Microsoft Corp., Redmond, DC, USA). Cox proportional hazards model analysis was used to identify the risk factors for postoperative mortality and aortic arch stenosis, and visualize these risk factors with GraphPad Prism 8 software (GraphPad Software, Inc., San Diego, CA, USA). $p < 0.05$ indicated that the difference was statistically significant.

Results

One-stage radical surgery was performed in 152 children, with the median duration of cardiopulmonary bypass of 126.70 min (range, 108–179 min), the median duration of cerebral perfusion of 35.81 min (range, 21–46 min), and the median length of ICU stay of 6.72 days (range, 4.70–8.87 days) (Table 1). Due to myocardial edema and hemodynamic instability, 58 children were given delayed chest
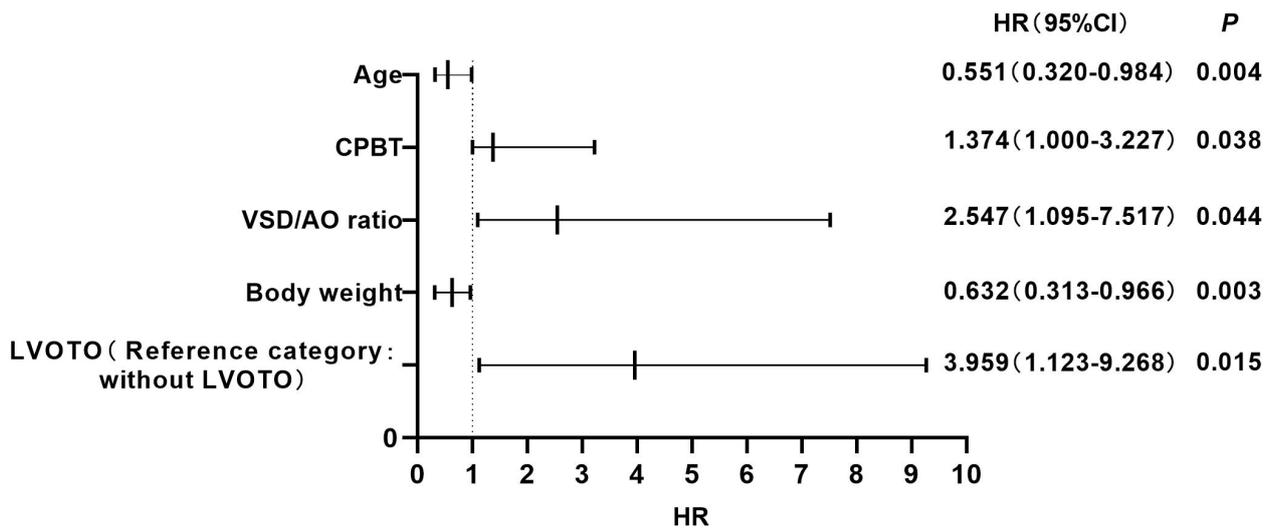
Fig. 4. Independent risk factors for death after one-stage repair of IAA with VSD and other associated intracardiac defects. HR, Hazard Ratio; *p*, *p* value; 95% CI, 95% confidence interval; VSD/AO, ratio of VSD diameter/aortic diameter; CPBT, cardiopulmonary bypass time; LVOTO, left ventricular outflow tract obstruction.
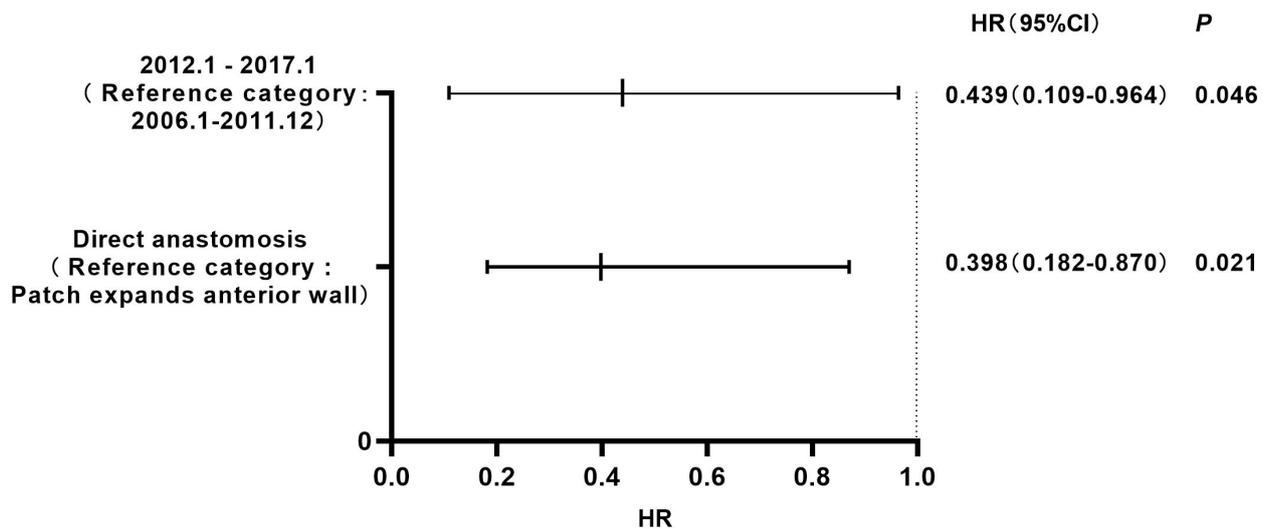

Fig. 5. Independent risk factors for aortic obstruction after one-stage radical resection of IAA combined with VSD and other associated intracardiac defects. IAA, Interruption of Aortic Arch; HR, Hazard Ratio; *p*, *p* value; 95% CI, 95% confidence interval.

closure; 13 cases received thoracotomy to stop bleeding; 15 cases were performed bedside thoracotomy due to low blood pressure and high central venous pressure; 16 cases experienced bedside peritoneal dialysis treatment owing to oliguria or anuria. In addition, 22 cases died after surgery: 15 cases died in early peroid, including 8 cases of type A, and 7 cases of type B; there were 7 deaths in late peroid, including 3 cases of type A, and 4 cases of type B. In early peroid, causes of death included low cardiac output (n = 3), pulmonary hypertension crisis (n = 3), severe pneumonia (n = 2), postoperative massive hemorrhage (n = 1), severe pneumonia complicated with multiple organ failure (n = 2), heart failure complicated with renal failure (n = 2), and acute left heart failure complicated with respiratory failure (n = 2). In late period, mortality causes involved postoperative massive hemorrhage (n = 1), difficulty in weaning off mechanical ventilator due to aortic arch compression of the left bronchus and severe pulmonary infection (n = 2), severe pneumonia with multiple organ failure (n = 1), heart failure with renal failure (n = 1), and malignant arrhythmia (n = 2). Postoperative follow-up was performed, and the survival curves of early period and late

period were drawn (Fig. 3). The median length of postoperative follow-up was 61 months (range, 16–101 months), and 4 cases in early period and 6 cases in late period were lost to follow-up. During the period, 1 case in early period died of left heart failure after LOVTO recanalization; 1 case died of multiple organ failure due to massive hemorrhage during re-operation for aortic arch stenosis; 1 case died of heart failure and renal failure and 2 cases in late period died of severe pneumonia with multiple organ failure. The 1-month, 3-month, 6-month, 1-year, 3-year and 5-year survival rates were 85.53%, 85.53%, 85.53%, 84.21%, 78.95% and 75.66%, respectively. Cox proportional hazards model analysis indicated that low age (HR = 0.551, 95% CI: 0.320–0.984, p = 0.004), low body weight (HR = 0.632, 95% CI: 0.313–0.966, p = 0.003), large ratio of VSD/AO (HR = 2.547, 95% CI: 1.095–7.517, p = 0.044), long duration of cardiopulmonary bypass (HR = 1.374, 95% CI: 1.000–3.227, p = 0.038), and combined LVOTO (HR = 3.959, 95% CI: 1.123–9.268, p = 0.015) were associated risk factors for postoperative mortality (Table 2, Fig. 4).

Table 2. Analysis of Cox proportional risk model of death in children with IAA/VSD and other associated intracardiac defects after one-stage radical surgery.

Variables	HR	95% CI	p
Age (month)	0.551	0.320–0.984	0.004
VSD/AO	2.547	1.095–7.517	0.044
Weight (Kg)	0.632	0.313–0.966	0.003
LVOTO	3.959	1.123–9.268	0.015
CPT (h)	1.481	0.768–2.855	0.241
ICU time (h)	2.172	0.560–7.650	0.441
CPBT (h)	1.374	1.000–3.227	0.038

VSD/AO, ratio of VSD diameter/aortic diameter; LVOTO, left ventricular outflow tract obstruction (Reference category, without LVOTO); CPT, cerebral perfusion time; CPBT, cardiopulmonary bypass time; HR, Hazard Ratio; p, p value; 95% CI, 95% confidence interval.

Postoperative aortic arch stenosis occurred in 27 cases, including 17 cases in early period (12 cases of type A, 5 cases of type B), and 10 cases in late period (5 cases of type A, 5 cases of type B) (Table 1). During the postoperative follow-up, 22 cases received reoperation due to aortic arch stenosis, and the brachiocephalic trunk artery, left common carotid artery, left subclavian artery, aortic arch and descending part of aortic arch were fully separated. During this process, 15 cases were treated with the method of widening the anterior wall of the descending part of the aortic arch; the limited coarctation segments in 6 cases were removed directly, then the posterior wall of the aortic arch was directly anastomosed with the posterior wall of the descending aorta, finally the autologous pericardium was used to widen the anterior wall of anastomo-

sis. There were 5 cases with obvious compression of the left main bronchus, and all of the compressions were relieved ultimately, including 3 cases by widening descending aorta with a patch, 2 cases by descending aorta transplantation, in which the left subclavian artery was cut off, the aortic arch and descending aorta were completely released, and the left subclavian artery was anastomosed with the left common carotid artery. Finally, 4 cases died after reoperation, including multiple organ failure due to intraoperative massive hemorrhage (1 case), severe pneumonia with multiple organ failure after operation (2 cases), and heart failure with renal failure (1 case).

Unfortunately, 7 cases experienced aortic arch stenosis again after reoperation, among whom 2 cases had undergone reoperation and 5 cases had received balloon dilatation of the aorta, and all of the operations were successful.

LVOTO reoccurred in 5 cases after one-stage LOVTO recanalization, including 2 cases of aortic valve tissue hypertrophy, 2 cases with long range of left ventricular outflow tract muscular hypertrophy obstruction, and 1 case with limited range. All of the patients had undergone LOVTO recanalization, in which 3 cases had surgeries through the aortic annulus path, 2 cases combined with mitral valve path; 1 case had been given mitral valvuloplasty due to severe mitral regurgitation caused by excessive mitral valve traction.1 case died of left heart failure after operation, and the remaining patients survived.

Cox proportional hazards model analysis showed that the period of surgery (from January 2006 to December 2011) (HR = 0.439, 95% CI: 0.109–0.964, p = 0.046) and anastomosis with autologous pericardium to the anterior aortic wall (HR = 0.398, 95% CI: 0.182–0.870, p = 0.021) were independent risk factors for postoperative aortic arch stenosis (Table 3, Fig. 5).

Discussion

IAA combined with VSD is a rare cardiac malformation in clinical practice, accounting for approximately 1%–1.5% of all congenital heart disease (CHD) [4,8], and conventional screening is easily missed [9]. Such diseases are in critical condition and have poor natural prognosis, and it has been reported that the neonatal mortality rate is as high as 90% without surgical correction [8]. In addition, the incidence of reoperation is still high, especially postoperative aortic arch restenosis, which is one of the common complications and also an urgent problem to be solved [10].

In this study, analysis of Cox proportional hazards model showed that low age and low body weight were independent risk factors for postoperative mortality, which was consistent with the conclusion reported in the literature in the last decade [11]. The possible reason that the surgical tolerance of immature myocardium in infants and young children is comparatively poor probably causes the

Table 3. Analysis of Cox proportional risk model of aortic arch stenosis in children with IAA/VSD and other associated intracardiac defects after one-stage radical surgery.

Variables	Group	HR	95% CI	p
Period of Surgery	2006.1–2011.12*	-	-	-
	2012.1–2017.1	0.439	0.109–0.964	0.046
Anastomosis Mode	Indirect Anastomosis*	-	-	-
	Direct Anastomosis	0.398	0.182–0.870	0.021
Type	A*	-	-	-
	B	1.582	0.632–3.960	0.327
LVOTO	Without LVOTO*	-	-	-
	With LVOTO	3.592	1.445–8.926	0.264

*, Control group; Indirect Anastomosis, perform a direct anastomosis between posterior wall of aortic arch and the one of descending aorta, next the anterior wall of the anastomosis was widened from the body pericardium; Direct Anastomosis, The proximal end of the descending aorta was directly anastomosed with the distal end of the aortic arch; LVOTO, left ventricular outflow tract obstruction; HR, Hazard Ratio; p, p value; 95% CI, 95% confidence interval.

relatively high incidence of severe low cardiac output syndrome [12]. A total of 22 children died after surgery, with an average weight of 2.70 kg, lower than that (3.02 kg) of surviving children after operation. Horbar JD [13,14] and other studies have reported that even without CHD, low-weight infants and young children have a higher mortality rate. Such children with limited renal tubular and medullary function, and immature immune system are prone to bronchopulmonary dysplasia, respiratory failure, intestinal ischemia, necrotizing enterocolitis [15], all of which increase the risk of postoperative death in children.

Meanwhile, the mean time of cardiopulmonary bypass (169.12 min) and cerebral perfusion (67.21 min) in the children who died after surgery were respectively higher than the corresponding data (132.57 min, 32.39 min) in those who survived after surgery. Moreover, Cox proportional hazards model analysis showed that long duration of cardiopulmonary bypass, which was rarely reported in most centers, was an independent risk factor for postoperative mortality. From the specific data analysis, the proportion of newborns in postoperative deaths was 68.40%, in which premature infants accounted for 17.14%, and the proportion of neonates in survived children was 37.72%, which may be the reason for the increase in postoperative mortality. On the one hand, newborns have underdeveloped lungs, especially in premature infants, some of whom have bronchopulmonary dysplasia [16]. On the other, neonatal blood will release a large number of inflammatory factors during cardiopulmonary bypass, and the accompanying ischemia-reperfusion injury will have a serious impact on children, resulting in postoperative pulmonary infection, atelectasis, acute respiratory failure and other serious complications [17]. In summary, the above two factors are likely to result in a significant increase in postoperative mortality in neonates with such diseases.

In addition, the VSD/AO ratio was also an independent risk factor for postoperative mortality which was also rarely reported. Among the children who died after surgery, the mean VSD/AO ratio was 2.01, which was higher than that (1.13) in children who survived after surgery. All cases of postoperative death were complicated with unrestricted VSD, and were prone to severe pulmonary hypertension and left ventricular congestive heart failure [18]. Subsequently, larger VSD causes more myocardial loss, affecting the cardiac systolic function of the children seriously. Although VSD was repaired with a patch, which itself has no systolic function, the compensatory recovery of cardiac function needed time, and the larger VSD, the longer recovery time. Besides, suture avulsion is easy to occur because of the week development of myocardial tissue, resulting in residual shunt, and the greater size of VSD, the higher probability of the above complications. Moreover, there were 4 cases of postoperative death with residual shunt of VSD greater than 3 mm, easily inducing postoperative hemodynamic instability. Furthermore, postoperative ultrasound examination in 2 children who died eventually after surgery showed that larger patch protruding into the left ventricular outflow tract caused obstruction was probably the cause of postoperative death.

This study spanned from January 2006 to January 2017. After 2012, the mortality and aortic arch restenosis rates decreased significantly, which were related to our department's more effective diagnosis and treatment procedures for these diseases, targeted and improved intraoperative procedures, use of improved ultrafiltration technology, emphasis on postoperative sedation, analgesia and reduction of pulmonary hypertension, use of extracorporeal membrane oxygenation (ECMO) and continuous renal replacement therapy (CRRT).

In view of the high postoperative mortality and aortic arch restenosis rates, our department began to sum up the experience and lessons and actively learn the advanced technology at home and abroad. Since 2012, our department has opened a more active and effective channel of diagnosis, treatment and surgery, which is equipped with a professional team. For such children, bedside ultrasound examination is performed in the intensive care unit at the first time, and if necessary, CT examination of the great vessels of the heart would be given as soon as possible under the close supervision of the professional team. After a definite diagnosis, oxygen should be strictly prohibited, and prostaglandin E1 would be given in time to maintain the perfusion of the descending aorta, actively stabilize circulation, improve the internal environment, and shorten the waiting time for early surgery [5]. Secondly, we paid more attention to avoiding the compression of one main bronchus due to excessive tension or insufficient dissociation at the anastomosis site during the reconstruction of the aortic arch, which greatly reduced the incidence of postoperative pneumonia, the time of tracheal intubation and the incidence of reintubation. At the same time, since 2012, we have replaced all the cardiac protective fluid with Histidine-Tryptophan-Ketoglutarate (HTK) cardiac protective fluid, and no longer use the blood-containing crystal protective fluid in the operation of such diseases. It has been reported that HTK myocardial protective solution is more effective than blood-containing crystal protective solution in protecting myocardium, and it is more suitable for immature myocardium, the myocardial protection time is longer, and there is no need to reperfuse into the coronary artery during the surgery [19,20]. In addition, we are paying more attention to the improved ultrafiltration during surgery. Since 2012, all children were given modified ultrafiltration with stable hemodynamics. According to the blood volume, colloid osmotic pressure and hematocrit, ultrafiltration speed and the amount of filtration were selected precisely. Compared with conventional ultrafiltration, improved ultrafiltration could efficiently ultrafilter water, reduce body edema, filter out inflammatory mediators, reduce inflammatory response, and effectively improve the postoperative cardiopulmonary function of children [21]. Since 2012, our ICU team began to focus on postoperative sedation, analgesia and treatment to reduce pulmonary hypertension in children. Especially on the day of surgery, adequate sedation, analgesia and treatment to reduce pulmonary hypertension are conducive to maintaining the stable circulation of the children and effectively avoiding the occurrence of pulmonary hypertension crisis. Therefore, doctors in the intensive care unit would give propofol according to the sedative and analgesic effects of the children on the basis of routine use of fentanyl, rocuronium bromide, midazolam and other drugs. Meantime, inhalation of nitric oxide was given on the day of surgery to reduce pulmonary hypertension and right ventricular afterload. The inhalation time is gradually adjusted according to the changes in the condition of the children, and if necessary, it is combined with other drugs to reduce pulmonary hypertension, such as prostaglandin E1. Since 2012, our department began to carry out ECMO and CRRT. After surgery, 5 children were treated with ECMO due to non-maintenance of blood pressure, oliguria or anuria, and 2 children were treated with ECMO combined with CRRT. Finally, 5 cases survived. Therefore, timely ECMO or ECMO combined with CRRT maybe beneficial to improve the survival rate of children with poor cardiopulmonary function, oliguria or anuria, and long-term dependence on extracorporeal circulation.

Furthermore, Cox proportional hazards regression model analysis showed that LVOTO was an independent risk factor for postoperative death. Children with IAA are often accompanied by posterior displacement of the conical ventricular septum, resulting in subaortic stenosis and LVOTO [22], which is necessary to remove the muscle of the septum, but the surgery would increase the time of myocardial traction and cardiopulmonary bypass, and has a more serious damage to the myocardium of the left ventricle. Secondly, due to the narrow operating space and great surgical complexity, it is more likely to damage the peripheral valve and conduction system, and thus lead to serious complications and even death. Among the dead children with LVOTO, 2 cases had severe mitral regurgitation for the cause of the damage of papillary muscle or chordae tendineae and 1 case had ventricular septal perforation after operation. Postoperative III atrioventricular block occurred in 2 cases.

Currently, direct aortic anastomosis without artificial materials is widely used in most heart centers to correct the IAA [6,23], which is also an important approach to avoid long-term obstruction as much as possible. Other groups have performed aortic arch repair by direct anastomosis with patch augmentation [7,24–28]. However, patch aortoplasty using artificial materials including Dacron, and polytetrafluoroethylene, has concern of late restenosis [24,25]. There are two reasons for postoperative restenosis with artificial materials. Firstly, the preoperative aortic arch was obviously hypoplastic, which had a poor development after surgery. Secondly, there is a risk of restenosis caused by calcification and shrinkage of artificial materials. This study showed that autologous pericardial anastomosis of the anterior wall of the aorta ($p = 0.021$) was an independent risk factor for postoperative aortic arch stenosis. The proportion with autologous pericardial widening anterior wall among all the children with postoperative aortic arch stenosis was 37.04%, in which early period accounted for 25.93% and late period accounted for 11.11%. Analysis of the causes: In early period, there were 5 cases with obvious aortic arch dysplasia, which was so difficult to be directly anastomosed that autologous pericardium was used to widen the anterior wall of the aorta, and the aortic arch was not further developed after operation; 2 cases had aor-

tic arch stenosis due to postoperative autologous pericardial calcification contracture. In late period, 3 cases had undergone autologous pericardial widening of the anterior wall of the aorta due to aortic arch dysplasia, and the postoperative aortic arch stenosis was caused by both poor aortic arch development after surgery and autologous pericardial calcification contracture.

However, this study has several limitations. First, it is a retrospective study, lacking confirmation of prospective studies, and there is a lack of randomness in data selection, which may have introduced data bias. Second, this single-center study with a limited number of cases is influenced by a number of factors, including the comprehension of the disease, and the selection of surgical plan. Lastly, due to economic burdens on the family members of the children and the limited cognition of several doctors, several children with postoperative aortic obstruction failed to receive timely diagnosis and treatment.

Conclusions

In conclusion, children with low age, low body weight, large ratio of VSD/AO, long duration of cardiopulmonary bypass, LVOTO, surgical period (from January 2006 to December 2011) and anastomosis with autologous pericardium to the anterior aortic wall have poor prognosis.

Abbreviations

IAA, interruption of aortic arch; VSD, ventricular septal defect; VSD/AO, ratio of VSD diameter/aortic diameter; LVOTO, left ventricular outflow tract obstruction; CHD, congenital heart disease; PDA, patent ductus arteriosus; AP window, aortopulmonary window; DORV, double outlet of right ventricle; MR, mitral reflux; ASD, atrial septal defect; CPBT, cardiopulmonary bypass time; CPT, cerebral perfusion time.

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

HZ designed the research study. HS and LC analyzed the data. HS and LC 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 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 First Hospital of Hebei Medical University (Approval No. 20220721), which also granted exemption from obtaining informed consent.

Conflict of Interest

The authors declare no conflict of interest.

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