Original Article

Middle to long-term outcomes of surgical repair for atrioventricular septal defect: a single-center study

Yixuan Cai[1#^], Renwei Chen[2#], Gang Chen[1], Qiqi Shi[1], Yaping Mi[1], Huifeng Zhang[1], Bing Jia[1]

[1]Department of Cardiothoracic Surgery, Children's Hospital of Fudan University, Shanghai, China; [2]Department of Cardiothoracic Surgery, Hainan Women and Children's Medical Center, Haikou, China

Contributions: (I) Conception and design: Y Cai, R Chen, H Zhang; (II) Administrative support: H Zhang, B Jia; (III) Provision of study materials or patients: Y Cai, R Chen, Q Shi, Y Mi, H Zhang, B Jia; (IV) Collection and assembly of data: Y Cai, H Zhang; (V) Data analysis and interpretation: YX Cai, RW Chen; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Huifeng Zhang, MD, PhD; Bing Jia, MD, PhD. Department of Cardiothoracic Surgery, Children's Hospital of Fudan University, No.399, Wanyuan Rd., Minhang District, Shanghai, China. Email: zhanghuifeng@fudan.edu.cn; jia_bing@fudan.edu.cn.

Background: The exact incidence and predictors of mortality and left atrioventricular valve (LAVV) re-operation in congenital atrioventricular septal defect (AVSD) repair are still unclear. This study analyzed the middle to long-term outcomes of surgical repair for AVSD.

Methods: A total of 150 patients (69 males and 81 females) who underwent AVSD repair at Children's Hospital of Fudan University from January 2013 to December 2021 were divided into complete defect group (C-group, 67 cases), transitional defect group (T-group, 26 cases), and partial defect group (P-group, 57 cases). Outcomes during the peri-operative and 10-year follow-up periods were evaluated.

Results: The total mortality was 5.33% (8/150), including seven early deaths (10.4%) and no late deaths in the C-group, no early deaths (0%) and one late death (1.8%) in the P-group, and no early or late deaths in the T-group. Up to the last follow-up, severe LAVV regurgitation had occurred in 27 patients, including 16 in the C-group, four in the T-group, and seven in the P-group. In total, 12 (12/150, 8.0%) patients received LAVV re-operation, including seven in the C-group, three in the T-group, and two in the P-group. Cox regression analysis showed that pre-operative severe pulmonary hypertension (P=0.006) and severe LAVV regurgitation within 24 hours after the first surgery (P=0.023) were independent risk factors for mortality. ≥ Moderate LAVV regurgitation within the first 24 hours after surgery (P=0.014) was an independent risk factor for LAVV re-operation.

Conclusions: Complete AVSD repair increased the risk of early death, severe LAVV regurgitation and re-operation. Pre-operative severe pulmonary hypertension and residual severe LAVV regurgitation indicated high risk for mortality. ≥ Moderate LAVV regurgitation within 24 hours after the first surgery predicted a high probability of LAVV re-operation.

Keywords: Atrioventricular septal defect (AVSD); pulmonary hypertension; left atrioventricular valve; re-operation; risk factor

Submitted Jun 07, 2022. Accepted for publication Sep 02, 2022.
doi: 10.21037/jtd-22-790
View this article at: https://dx.doi.org/10.21037/jtd-22-790

^ ORCID: 0000-0002-5656-779X.

Introduction

Atrioventricular septal defect (AVSD) is related to severe pulmonary hypertension and heart failure in early childhood. In 1966, Rastelli classified three types of AVSD based on anatomical structure: complete (CAVSD), transitional (TAVSD), and partial (PAVSD) (1). Developed surgical techniques and peri-operative management have reduced AVSD-related mortality in children to about 10% over the past few decades (2,3).

However, despite improved survival, left atrioventricular valve (LAVV) regurgitation may develop as a major event after surgery in 8% to 10% of patients, sometimes requiring re-operation (4,5). The surgical repair for AVSD still remains a great challenge in patients younger than three months, less than four kilograms, or with other genetic disorders (e.g., Down syndrome). This study aimed to evaluate the middle to long-term surgical outcomes in patients with three types of AVSD and identify the risk factors associated with mortality and LAVV re-operation. We present the following article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-790/rc).

Methods

Patients

From January 2013 to December 2021, patients who underwent AVSD repair were recruited from the database of the Cardiovascular Center of the Children's Hospital of Fudan University. Patients who had transposition of the great arteries, double outlet right ventricle, tetralogy of Fallot, or a single ventricle were excluded from the analysis. In total, 150 patients were included and divided into three groups according the Rastelli classification: Complete defect group (C-group), Transitional defect group (T-group), and Partial defect group (P-group). Age (≤3.0 months) and weight (≤4.0 kg) were defined according to the findings reported by other studies (2). Early mortality was defined as death within 30 days after corrective surgery. Echocardiography was regularly used to assess the severity of LAVV regurgitation (mild, moderate, severe) using the color Doppler jet area before and after surgery. The pulmonary arterial pressure was evaluated based on tricuspid regurgitation pressure gradient using echo and further classified as none (PH <30 mmHg), mild (30≤ PH <50 mmHg), moderate (50≤ PH <70 mmHg), and severe (≥70 mmHg) (6). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This retrospective study was approved by the Ethics Review Board of the Children's Hospital of Fudan University [No. (2022)132]. The need for patient consent was waived because of the retrospective nature of the study.

Study endpoints

The primary outcomes were set as time of death, freedom from overall re-operation, and LAVV re-operation. For patients who did not experience these outcomes, times were censored at the last follow-up date (December 31, 2021).

Data collection and follow-up

Demographic and surgical data were obtained from the Center. Follow-up data were collected from clinical examinations and echocardiography during outpatient clinics. The mean follow-up period of the entire cohort was 33.37±27.13 months (range, 1–100 months).

Statistical analysis

Mean ± standard deviation (SD) was used to describe the continuous variables in normal distribution, and median (interquartile range, IQR) to describe data that were not normally distributed. Categorical variables are presented as n (%). Differences among AVSD groups were analyzed using the Chi-squared test and one-way ANOVA analysis. Survival and freedom from LAVV re-operation were assessed using Kaplan-Meier survival analysis. The univariable Cox regression analysis was used to evaluate risk factors for mortality and LAVV re-operation: age ≤3.0 months, weight ≤4.0 kg, gender, Down syndrome, left atrium diameter (LAD) and left ventricular diastolic diameter (LVDD) before surgery, severe pulmonary hypertension before surgery, ≥ moderate LAVV regurgitation before surgery, cardiothoracic ratio (CTR) ≥0.6 before surgery and within 24 hours after surgery, re-operation after AVSD repair, LAVV re-operation, severe LAVV regurgitation within 24 hours after the first surgery, ≥ moderate LAVV regurgitation within 24 hours after the first surgery, and surgery era [2017–2021]. The results of the models are reported as hazard ratios (HR), 95% confidence intervals (CI), and P values. Variables with P<0.1 were then included in the multivariable Cox regression analysis. Statistical significance was set as P<0.05.

All statistical analyses were carried out using the IBM SPSS statistics 25.0 on Windows (SPSS, Inc., Chicago, IL, USA). Figures were created using GraphPad Prism 8 (GraphPad Software, Inc., La Jolla, CA, USA).

Surgical techniques

Surgical repair was performed via median sternotomy with full cardiopulmonary bypass (CPB) at moderate hypothermia. Upon cardiac arrest, the structure of the LAVV was re-observed to determine the type of AVSD and surgical approach. Simple cleft closure, as the dominant approach, was performed in 48 (71.6%), 19 (73.1%), and 40 (70.2%) patients, followed by cleft closure with annuloplasty strategy in 17 (25.4%), 5 (19.2%), and 15 (26.3%) patients, and no repair in two (3%), two (7.7%), and two (3.5%) patients in the C-group, T-group, and P-group, respectively.

CAVSD was repaired using the modified single-patch (MSP) technique in 57 patients and the double-patch (DP) technique in 10 patients. The MSP technique was performed with a patch of glutaraldehyde (GA)-fixed autologous pericardium. The DP technique was performed with a GA-fixed autologous pericardium for the repair of atrial septal defect (ASD), and a Dacron patch (n=5) or a GA-fixed autologous pericardium (n=5) for the repair of ventricular septal defect (VSD). For PAVSD, the ASD was mended using a GA-fixed autologous pericardium. For TAVSD, the VSD was closed directly using a 5-0 proline suture with pledget, and the ASD was closed using a GA-fixed autologous pericardium. As soon as the AVSD was corrected, LAVV function was observed with injection of saline. After releasing from CPB, the degree of LAVV regurgitation was re-assessed using transesophageal echocardiography. If the LAVV regurgitation was graded as severe or the intraoperative echocardiography showed left ventricular outflow tract stenosis, re-exploration was then planned.

Results

Baseline characteristics

The baseline characteristics of the total cohort are summarized in *Table 1*. There were 67 patients with CAVSD, 26 with TAVSD, and 57 with PAVSD. Among the 67 CAVSD patients, 66 patients (98.5%) presented type A (the common superior bridge valve is divided into two halves at the interventricular septum), and one patient (1.5%) presented type C (the superior valve bridge spans the interventricular septum and is not segmented). The median age at surgery was 6 months (IQR, 3–12.5) in the C-group, 20 months (IQR, 9–60) in the T-group, and 33 months (IQR, 11–48) in the P-group. The average weight in these three groups was 6.78±3.82, 12.98±10.04, and 13.88±8.28 kg, respectively. In total, 21 patients under three months old accepted AVSD repair, including 18 in the C-group, one in the T-group, and two in the P-group; 18 patients (10.2%) had Down syndrome (15 in the C-group, two in the T-group, and one in the P-group). The incidence of severe pulmonary hypertension was 34.3% (n=23) in the C-group, 11.5% (n=3) in the T-group, and 7.0% (n=4) in the P-group before surgery. Pre-operative detection showed that LAVV regurgitation was mild in 43, moderate in 45, and severe in 62 patients.

Peri-operative data

The peri-operative data are summarized in *Table 2*. In the entire cohort, the mean CPB time was 95.41±60.54 minutes, the mean cross-clamp time was 56.89±27.36 minutes, and the mean postoperative length of stay (LOS) was 15.61±10.78 days. CPB temperature was controlled at an average of 32.44±1.92 ℃. After surgery, the median mechanical ventilation time was 27.5 (61.63) hours and the median of LOS in the intensive care unit (ICU) was 3.5 [2–7] days. CPB time (111.7±63.3 *vs.* 84.9±22.7, 81.0±64.9 minutes; P=0.011), cross-clamp time (69.5±31.7 *vs.* 52.8±16.4 and 43.7±18.0 minutes; P<0.001), postoperative LOS (20.6±12.6 *vs.* 13.0±7.6 and 10.9±6.4; P<0.001), postoperative mechanical ventilation time {71 [42.75–130] *vs.* 24.5 [19–47.25] and 11.0 [6–24] hours; P<0.001}, and postoperative LOS in the ICU {6 [5–11] *vs.* 3 [2–4] and 2 [1–3] days; P<0.001} were significantly longer in the C-group compared to both the T-group and P-group. Furthermore, the incidence of complications was 28.4% (19/67) in the C-group, which was significantly higher than 7.7% (2/26) in the T-group and 8.8% (5/57) in the P-group (P=0.005). Among the complications, pulmonary hypertensive crisis occurred most frequently, with seven in the C-group, one in the T-group, and two in the P-group.

Survival analysis

The 1-, 3-, and 5-year survival rates were, respectively, 94.5%±1.9%, 94.5%±1.9%, and 94.5%±1.9% in the entire

Table 1 Baseline characteristics of patients

Characteristics	CAVSD	TAVSD	PAVSD	P value
Patient number	67	26	57	
Male, n (%)	30 (44.8)	9 (34.6)	30 (53.6)	0.300
Patient age (months), median [IQR]	6 [3–12.5]	20 [9–60]	33 [11–48]	<0.001
Age ≤3.0 months, n (%)	18 (26.9)	1 (3.8)	2 (3.5)	<0.001
Patient weight (kg), mean ± SD	6.78±3.82	12.98±10.04	13.88±8.28	<0.001
Weight ≤4.0 kg, n (%)	3 (4.5)	1 (3.7)	0 (0)	0.280
Down syndrome, n (%)	15 (22.4)	2 (7.7)	1 (1.8)	0.002
Rastelli classification type, n (%)				
A	66 (98.5)			
B	0 (0)			
C	1 (1.5)			
CTR, mean ± SD	0.650±0.049	0.616±0.059	0.616±0.074	0.004
Previous surgery, n (%)	1 (1.5)	0 (0)	0 (0)	0.536
Pulmonary hypertension, n (%)	60 (89.6)	18 (69.2)	46 (80.7)	<0.001
Mild	11 (16.4)	8 (30.8)	29 (50.9)	
Moderate	26 (38.8)	7 (26.9)	13 (22.8)	
Severe	23 (34.3)	3 (11.5)	4 (7.0)	
Left AV valve regurgitation, n (%)				
Mild	16 (23.9)	9 (34.6)	18 (31.6)	
Moderate	22 (32.8)	6 (23.1)	17 (29.8)	
Severe	29 (43.3)	11 (42.3)	22 (38.6)	

Data are reported as mean ± SD, median [IQR], or n (%). CAVSD, complete atrioventricular septal defect; TAVSD, transitional atrioventricular septal defect; PAVSD, partial atrioventricular septal defect; IQR, interquartile range; SD, standard deviation; CTR, cardiothoracic ratio; AV, atrioventricular.

cohort, 88.9%±4.0%, 88.9%±4.0%, and 88.9%±4.0% in the C-group, 100%, 100%, and 100% in the T-group, and 98.2%±1.7%, 98.2%±1.7%, and 98.2%±1.7% in the P-group. Statistical significance was observed for survival rate among the three groups (P=0.0404). The Kaplan-Meier survival curves for the three AVSD groups are presented in *Figure 1*.

Mortality

The mortality was 5.33% (8/150) in the entire cohort, including seven early deaths (6 in the C-group) and one late death. The 7 (87.5%) deaths included four patients younger than three months in the C-group and 1 (12.5%) in the P-group (*Table 2*, P=0.034). The two major causes of mortality were cardiopulmonary failure (n=5) and heart failure (n=3). In these patients, 5 (62.5%) were diagnosed with severe pulmonary hypertension, and 7 (87.5%) with ≥ moderate LAVV regurgitation prior to surgery. One patient was treated with mechanical ventilation and one with continuous positive airway pressure (CPAP) therapy due to shortness of breath and poor response during preoperative preparation. Five patients showed recurrent pulmonary infection before surgery, and four showed significant developmental delay. The majority of LAVV in these patients were difficult to repair, causing unsatisfied valve function after surgery. Two patients were diagnosed with severe regurgitation within the first 24 hours after surgery, five with moderate, and only one with mild. Three patients underwent re-operation, including one with

Table 2 Perioperative data

Variables	CAVSD	TAVSD	PAVSD	P value
Cleft closure, n (%)				
Simple cleft closure	48 (71.6)	19 (73.1)	40 (70.2)	
Cleft closure + annuloplasty	17 (25.4)	5 (19.2)	15 (26.3)	
Not to repair, n (%)	2 (3.0)	2 (7.7)	2 (3.5)	
CPB time (min), mean ± SD	111.7±63.3	84.9±22.7	81.0±64.9	0.011
Cross-clamp time (min), mean ± SD	69.5±31.7	52.8±16.4	43.7±18.0	<0.001
CPB temperature (℃), mean ± SD	31.2±1.9	32.7±1.3	33.7±1.2	<0.001
Postoperative mechanical ventilation time, median (h), [IQR]	71 [42.75–130]	24.5 [19–47.25]	11.0 [6–24]	<0.001
ICU stay after surgery (days), median [IQR]	6 [5–11]	3 [2–4]	2 [1–3]	<0.001
Postoperative hospital stay (days), mean ± SD	20.6±12.6	13.0±7.6	10.9±6.4	<0.001
Complications, n (%)	19 (28.4)	2 (7.7)	5 (8.8)	0.005
Delayed chest closure	3	0	2	
Respiratory distress	5	0	1	
AV block need pacemaker implantation	3	0	1	
Pulmonary hypertensive crisis	7	1	2	
Pneumothorax	1	0	0	
Peritoneal dialysis/hemodialysis	0	0	1	
Total in-hospital mortality, n (%)	7 (10.9)	0 (0)	1 (1.8)	0.034
LAVV reoperation, n (%)	7 (10.4)	3 (11.5)	2 (3.5)	0.284

Data are reported as mean ± SD, median [IQR], or n (%). CAVSD, complete atrioventricular septal defect; TAVSD, transitional atrioventricular septal defect; PAVSD, partial atrioventricular septal defect; CPB, cardiopulmonary bypass; ICU, intensive care unit; SD, standard deviation; IQR, interquartile range; AV, atrioventricular; LAVV, left atrioventricular valve.

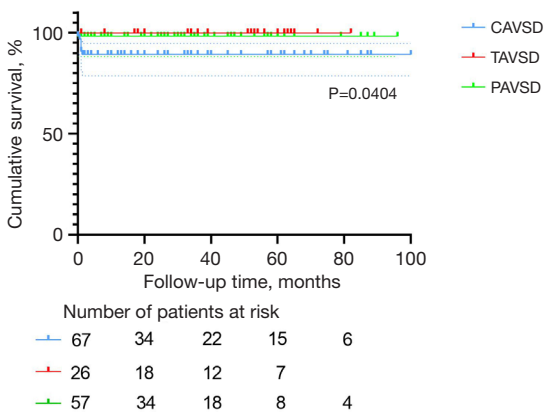

Figure 1 Kaplan-Meier survival for CAVSD group (blue), TAVSD group (red) and PAVSD group (green). Confidence intervals were showed in dotted line. Patients in CAVSD group had higher risk of early mortality and lower overall survival. CAVSD, complete atrioventricular septal defect; TAVSD, transitional atrioventricular septal defect; PAVSD, partial atrioventricular septal defect.

moderate LAVV regurgitation and difficulty weaning off the ventilator, one with postoperative mediastinal infection, and one with left ventricular outflow tract stenosis. The details of in-hospital mortality are listed in *Table 3*.

Predictors of mortality

The univariable Cox regression analysis revealed that age ≤3.0 months, severe pulmonary hypertension before surgery, re-operation after AVSD repair, and severe LAVV regurgitation within 24 hours after the first surgery were predictors of mortality (*Table 4*). In the multivariate Cox regression analysis, severe pulmonary hypertension before surgery (P=0.006) and severe LAVV regurgitation within 24 hours after the first surgery (P=0.023) were independent risk factors for mortality (*Table 4*), while age ≤3.0 months was not (P=0.222).

Table 3 Data of in-hospital mortality

Variables	Age	Weight (kg)	Preoperative PH	Preoperative left AV valve regurgitation	Postoperative left AV valve regurgitation	Cause of reoperation	LAVV regurgitation after reoperation	Death stage	Cause of death
CAVSD									
1	3 mon	5.5	Severe	Moderate	Moderate	No	–	20 days after operation	Cardiopulmonary failure + ventricular fibrillation
2	5 mon	6.6	Moderate	Severe	Moderate	Moderate LAVV regurgitation + difficulty weaning off the ventilator	Moderate	17 days after first operation/2 days after reoperation	Cardiopulmonary failure
3	3 mon	4.8	Severe	Mild	Moderate	No	–	41 days after operation	Cardiopulmonary failure
4	15 mon	8.66	Severe	Severe	Moderate	No	–	28 days after operation	Cardiopulmonary failure
5	1 mon	2.74	Severe	Severe	Mild	Mediastinal infection	Mild	22 days after first operation/7 days after reoperation	Cardiopulmonary failure
6	3 mon	4.3	Moderate	Moderate	Moderate	Left ventricular outflow tract stenosis	Severe	42 days after first operation/41 days after reoperation	Heart failure + fungal sepsis
7	4 mon	6.1	Moderate	Severe	Severe	No	–	10 hours after operation	Heart failure + ventricular fibrillation
PAVSD									
1	24 mon	11	Severe	Severe	Severe	No	–	Intraoperative death	Heart failure

PH, pulmonary hypertension; AV, atrioventricular; LAVV, left atrioventricular valve; CAVSD, complete atrioventricular septal defect; mon, month; PAVSD, partial atrioventricular septal defect.

Overall re-operation and LAVV re-operation

Freedom from re-operation and LAVV re-operation was associated with good outcomes in the entire cohort. Nineteen patients (12.7%) required re-operation after the initial repair of AVSD, including 12 in the C-group, three in the T-group, and four in the P-group. The main reason for re-operation was severe LAVV regurgitation after surgery (n=11, 57.9%). Among these 11 patients, 10 received LAVV repair and one received LAVV repair with annuloplasty. Other indications for re-operations were AV (atrioventricular) block (n=4, 21.1%), mediastinal infection (n=2, 10.5%), moderate LAVV regurgitation with difficulty weaning off the ventilator (n=1, 5.3%), and left ventricular outflow tract stenosis (n=1, 5.3%). The percentages of patients free from overall re-operation at 1, 3, and 5 years were, respectively, 90.9%±2.4%, 87.8%±2.9%, and 81.2%±4.6% in the entire cohort; 85.4%±4.6%, 82.8%±5.1%, and 71.6%±8.6% in the C-group; 96.2%±3.8%, 90.8%±6.3%, and 84.3%±8.6% in the T-group; 94.7%±3.0%, 92.3%±3.7%, and 92.3%±3.7% in the P-group. These percentages did not differ among AVSD types (P=0.1251; *Figure 2*), but the C-group had a relatively higher percentage. The percentages of patients free from LAVV re-operation at 1, 3, and 5 years were, respectively, 95.7%±1.7%, 92.5%±2.5%, and 85.9%±4.4% in the entire

Table 4 Univariable and multivariable risk factors for mortality

Variables	Univariable analysis			Multivariable analysis		
	HR	95% CI	P value	HR	95% CI	P value
Age ≤3.0 months	6.299	1.58–25.19	0.009	2.564	0.57–11.62	0.222
Weight ≤4.0 kg	5.145	0.63–41.83	0.126			
Gender (male =0)	0.869	0.22–3.47	0.842			
Down syndrome	1.000	0.12–8.13	0.999			
LAD before surgery	1.048	0.98–1.12	0.184			
LVDD before surgery	0.930	0.82–1.06	0.263			
Severe pulmonary hypertension before surgery	7.032	1.68–29.45	0.008	12.139	2.03–72.47	0.006
≥ Moderate LAVV regurgitation before surgery	2.886	0.36–23.46	0.322			
CTR ≥0.6 before surgery	35.97	0.07–20,016.56	0.267			
CTR ≥0.6 within 24 hours after surgery	1.030	0.26–4.12	0.966			
Reoperation after AVSD repair	4.686	1.12–19.61	0.034	2.517	0.53–12.01	0.247
LAVV reoperation	2.038	0.25–16.57	0.506			
Severe LAVV regurgitation at first 24 hours after the first surgery	10.63	2.14–52.85	0.004	12.07	1.42–102.90	0.023
Surgical era [2017–2021]	0.498	0.10–2.47	0.394			

HR, hazard ratio; CI, confidence interval; LAD, left atrium diameter; LVDD, left ventricular diastolic diameter; LAVV, left atrioventricular valve; CTR, cardiothoracic ratio; AVSD, atrioventricular septal defect.

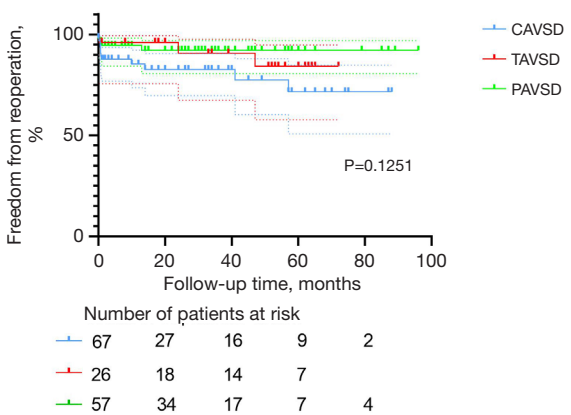

Figure 2 Kaplan-Meier freedom from reoperation for CAVSD group (blue), TAVSD group (red) and PAVSD group (green). Confidence intervals were showed in dotted line. Though the difference among the three groups was not statistically significant, the results reflected a higher reintervention rate in CAVSD group in the follow-up period. CAVSD, complete atrioventricular septal defect; TAVSD, transitional atrioventricular septal defect; PAVSD, partial atrioventricular septal defect.

cohort; 93.1%±3.4%, 90.3%±4.3%, and 79.6%±8.1% in the C-group; 96.2%±3.8%, 90.8%±6.3%, and 84.3%±8.6% in the T-group; 98.2%±1.8%, 95.9%±2.9%, and 95.9%±2.9% in the P-group. These percentages showed no statistical difference related to AVSD type (P=0.2921, *Figure 3*).

Predictors of LAVV re-operation

On the basis of univariable Cox regression analysis, CTR ≥0.6 within 24 hours after surgery, and ≥ moderate LAVV regurgitation within 24 hours after surgery predicted a higher rate of LAVV re-operation (*Table 5*). The multivariable Cox regression analysis showed ≥ moderate LAVV regurgitation within 24 hours after surgery (P=0.014, *Table 5*) was the independent risk factor of LAVV re-operation.

Impact of pulmonary hypertension analyzed at 3 months of age intervals

The results of patients who had severe PH before the first surgery are displayed in *Table 6*. These data reflect

measurements attained at 3 months of age intervals. Severe pulmonary hypertension before surgery was found most frequently in patient under 3 months of age (n=8), between 3–6 months of age (n=5), and beyond 12 months of age (n=13) compared with patients between 6–9 months of age (n=3) and 9–12 months of age (n=1). Among these patients with pre-operative severe pulmonary hypertension, postoperative pulmonary hypertensive crisis occurred in one patient under 3 months of age, two between 3–6 months of age, and three beyond 12 months of age. Three patients under 3 months of age and two beyond 12 months of age eventually died.

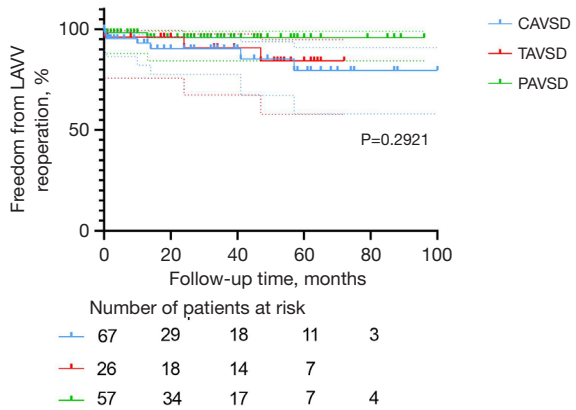

Figure 3 Kaplan-Meier freedom from LAVV reoperation for CAVSD group (blue), TAVSD group (red) and PAVSD group (green). Confidence intervals were showed in dotted line. No significant was found among the three groups. LAVV reinterventions were also common in TAVSD and PAVSD groups. LAVV, left atrioventricular valve; CAVSD, complete atrioventricular septal defect; TAVSD, transitional atrioventricular septal defect; PAVSD, partial atrioventricular septal defect.

Discussion

Our mid to long-term results demonstrated a low mortality (5.44%) and an acceptable overall re-operation rate (12.7%) after AVSD repair, which are consistent with the 2.95–15% mortality (7) and 3.6–22% re-operation rate (8) reported by Hoohenkerk *et al.* and Ginde *et al.* Patients in the CAVSD group had a higher mortality of 10.4% (7/67), including six early deaths. It is interesting to note that no significant difference was found in freedom from LAVV re-operation among three AVSD types. We further evaluated the effect of age (≤3 months), severe pulmonary hypertension before surgery, severe LAVV regurgitation within 24 hours after the first surgery, AVSD type on mortality, and ≥ moderate LAVV regurgitation within 24 hours after the first surgery,

Table 5 Univariable and multivariable risk factors for left AV valve reoperation

Variables	Univariable analysis			Multivariable analysis		
	HR	95% CI	P value	HR	95% CI	P value
Age ≤3.0 months	1.356	0.30–6.20	0.695			
Weight ≤4.0 kg	3.379	0.43–26.45	0.246			
Gender (male =0)	2.062	0.62–6.87	0.239			
Down syndrome	0.040	0.000024–68.17	0.397			
LAD before surgery	1.033	0.96–1.11	0.403			
LVDD before surgery	0.932	0.84–1.04	0.193			
Severe pulmonary hypertension before surgery	0.413	0.05–3.21	0.398			
CTR ≥0.6 before surgery	2.515	0.55–11.50	0.234			
CTR ≥0.6 at first 24 hours after surgery	3.095	0.84–11.44	0.090	2.303	0.62–8.63	0.216
≥ Moderate LAVV regurgitation before surgery	4.571	0.59–35.43	0.146			
≥ Moderate LAVV regurgitation within 24 hours after the first surgery	7.875	1.72–35.98	0.008	6.874	1.49–31.78	0.014
Surgical era [2017–2021]	0.186	0.02–1.47	0.111			

AV, atrioventricular; HR, hazard ratio; CI, confidence interval; LAD, left atrium diameter; LVDD, left ventricular diastolic diameter; CTR, cardiothoracic ratio; LAVV, left atrioventricular valve.

Table 6 Results of patients who had severe PH before first surgery (analyzed by 3 months intervals of age)

Age	<3 months (n=21)	3–6 months (n=31)	6–9 months (n=15)	9–12 months (n=11)	>12 months (n=72)
Severe PH before first surgery, n (%)	8 (38.1)	5 (16.1)	3 (20.0)	1 (9.1)	13 (18.1)
Postoperative pulmonary hypertensive crisis[#], n (%)	1 (12.5)	2 (40.0)	0 (0)	0 (0)	3 (23.1)
Death[#], n (%)	3 (37.5)	0 (0)	0 (0)	0 (0)	2 (15.4)

[#], the number of patients with postoperative pulmonary hypertensive crisis and death were derived from those with severe PH before the first surgery. PH, pulmonary hypertension.

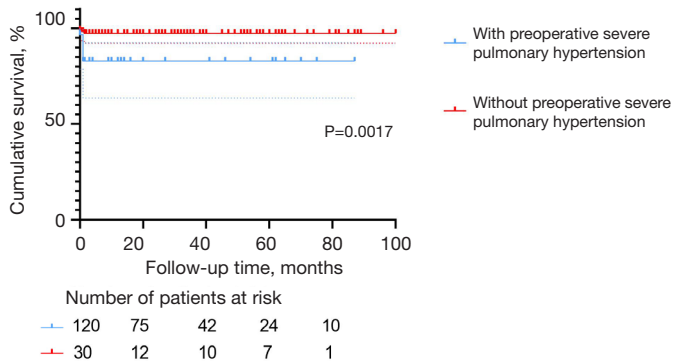

Figure 4 The effect of independent risk factor on survival. Kaplan-Meier survival for patients with (blue) and without preoperative severe pulmonary hypertension (red). Confidence intervals were showed in dotted line.

AVSD types and surgical era [2017–2021] on LAVV re-operation rate. The impact of pulmonary hypertension was also analyzed in patients at 3 months of age intervals.

Mortality

No consensus has been reached about whether AVSD repair can increase mortality in patients ≤3 months of age. It is recommended to perform surgery in children who have symptoms of congestive heart failure at an age of 3–6 months (9). This recommendation is supported by Delmo Walter *et al.*, who pointed out that surgery in younger patients can increase mortality, as their LAVV is relatively fragile and easy to tear, and the surgical exposure during surgery is limited (10). In our cohort, eight patients died after surgery, including four who were ≤3 months of age. The univariable analysis depicted a higher mortality in patients aged ≤3 months (*Table 4*, P=0.009), but this change was not statistically significant in the multivariable analysis (*Table 4*, P=0.222). This result was inconsistent with that reported by Ramgren *et al.* (11), which might be due to the fact that the surgeries in the younger patients were quite difficult, but getting part of these sick patients improved and survived. Fong *et al.* found decreased postoperative mortality over time and a better late survival in patients ≤3 months of age (12). Even for the complex CAVSD repair, complete repair performed on patients ≤3 months of age and weighing ≤3.5 kg was successful, with a 20-year survival rate of 92.0% and 83.8%, respectively, as reported by Buratto *et al.* and Goutallier *et al.* (3,13). On the basis of valvular morphology, individualized surgical strategies can be designed to improve the outcomes of AVSD patients.

In the present study, the multivariable Cox regression analysis revealed severe pulmonary hypertension before surgery as an independent risk factor for postoperative mortality (HR =12.139, P=0.006). This finding was also supported by the Kaplan-Meier survival plot (*Figure 4*, P=0.0017). In our cohort, five of the eight patients who died had pre-operative severe pulmonary hypertension, most of whom also presented with severe LAVV regurgitation. It is also worth noting that pre-operative severe pulmonary hypertension and surgical stimulation may induce intra-operative pulmonary vasospasm, which might increase pulmonary circulatory resistance and, therefore, lead to

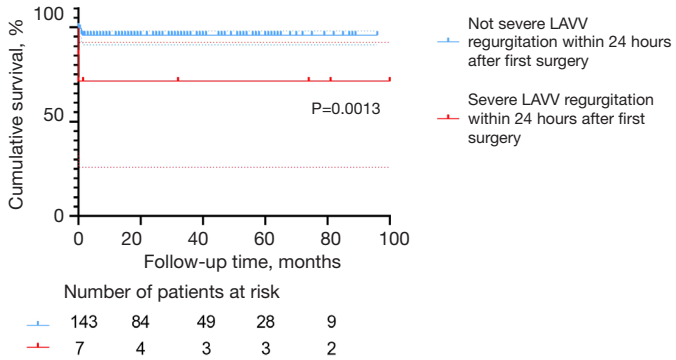

Figure 5 The effect of independent risk factor on survival. Kaplan-Meier survival for patients with (red) and without severe LAVV regurgitation within 24 hours after first surgery (blue). Confidence intervals were showed in dotted line. LAVV, left atrioventricular valve.

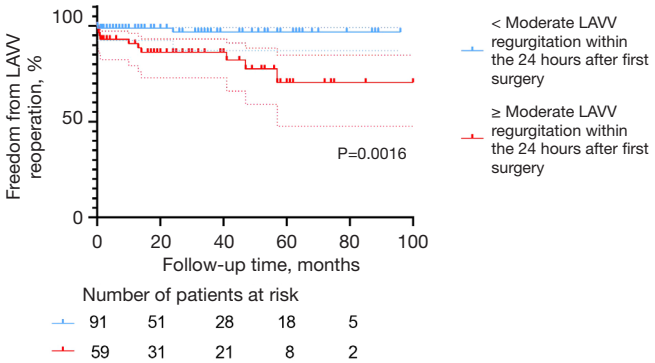

Figure 6 The effect of independent risk factor on freedom from LAVV reoperation. Kaplan-Meier freedom from reoperation for patients with < moderate (blue) and ≥ moderate LAVV regurgitation within the 24 hours after first surgery (red). Confidence intervals were showed in dotted line. LAVV, left atrioventricular valve.

pulmonary hypertensive crisis (2). In our study, incidence of pulmonary hypertensive crisis was significantly higher in the C-group (7/67, 10.4%) than in the T-group (1/26, 3.8%) and P-group (2/57, 3.5%). Preoperative and postoperative management should be further optimized to prevent pulmonary hypertensive crisis, especially in emergencies.

According to the multivariable Cox regression analysis and Kaplan-Meier survival plot, severe LAVV regurgitation within 24 hours after the first surgery remains a major life-threatening event (*Table 4*, P=0.023; *Figure 5*, P=0.0013). Postoperative severe LAVV regurgitation may aggravate pulmonary hypertension, thus leading to cardiac insufficiency, and even early death. Therefore, great caution should be taken in placing traction sutures to achieve good exposure of the surgical field, as well as pulling the valve to avoid severe LAVV regurgitation due to valve rupture. In addition, the operator should repair the valve as delicately as possible to reduce the degree of regurgitation to below moderate levels. Close monitoring of LAVV regurgitation is also required after surgery. As shown in *Table 2* and *Figure 1*, the in-hospital mortality in the C-group was significantly higher than in the other groups, which corroborates the findings by Schleiger *et al.* (2). This difference in mortality could be attributed to the following reasons. First, surgical repair of CAVSD was more technically challenging than TAVSD and PAVSD, resulting in longer CPB time (P=0.011), cross-clamp time (P<0.001), postoperative mechanical ventilation time (P<0.001), LOS in ICU (P<0.001), and postoperative LOS in the hospital (P<0.001). Moreover, complications in seven CAVSD patients who died were much more complex and intractable, characterized by respiratory distress (5/7), pulmonary hypertensive crisis (2/7), arrhythmia (2/7), infections (2/7), delayed chest closure (1/7), and acute renal failure requiring peritoneal dialysis/

hemodialysis (1/7). These findings are in line with those reported by Jacobs, who analyzed 2,882 AVSD operations in the STS Congenital Heart Surgery Database (14). Therefore, early postoperative care should be focused on multiple organ dysfunction and CAVSD complications.

LAVV re-operation

The LAVV re-operation rate increases as LAVV function decreases. The main factor affecting LAVV re-operation is LAVV regurgitation. At the final follow-up, the percentage of patients with severe LAVV regurgitation was higher in the C-group (n=16, 23.9%) than in the T-group (n=4, 15.4%) and P-group (n=7, 12.3%). The re-operation rate of LAVV was 8.0% (12/150) in the entire cohort, with seven patients in the C-group, three in the T-group, and two in the P-group. This result is in accordance with finding by Mery *et al.* and Airaksinen *et al.* (4,5). According to the multivariable Cox regression analysis, ≥ moderate LAVV regurgitation within 24 hours after surgery (P=0.014) was an independent risk factor for LAVV re-operation, which is consistent with the conclusion drawn by Fong *et al.* (12). The finding was also displayed in the Kaplan-Meier survival plot (*Figure 6*, P=0.0016). Interestingly, there was no significant difference in freedom from LAVV re-operation among the three groups (P=0.2921, *Figure 3*), suggesting approximate LAVV re-operation rates of different AVSD types. As suggested by Sarısoy *et al.*, this phenomenon may have arisen from the low incidence of Down syndrome in the T-group and P-group (15-17). In patients without Down syndrome, the morphology of the LAVV is more dysplastic and no redundant valve tissues can be used for LAVV reconstruction (15,16), which may lead to residual regurgitation. During our follow-up period, five patients with TAVSD or PAVSD who underwent LAVV re-operation did not have Down syndrome. Our conclusion was also supported by previous findings of Lange *et al.* (15), who reported a higher rate of freedom from LAVV re-operation in the group with Down syndrome (82%±2.9%) than in the group without Down syndrome (72%±5.3%) during 20 years of follow-up (P=0.004).

Surgical era [2017–2021] was not an independent risk factor for LAVV re-operation in the univariable Cox regression analysis (P=0.111, *Table 5*). In recent years, annuloplasty has been conventionally adopted in our center. In the present study, 15 of 16 patients receiving annuloplasty did not have to undergo LAVV re-operation during the follow-up. In these 16 patients, nine had severe LAVV regurgitation before surgery. At the last follow-up after annuloplasty, 11 patients had mild or moderate LAVV regurgitation, which demonstrates the good outcomes of this technique. According to Komoda *et al.* and Fundarò *et al.*, the application of annuloplasty, especially Wooler annuloplasty, can substantially reduce the risk of LAVV regurgitation, which was confirmed by our statistics (18,19).

Impact of pulmonary hypertension on children of different intervals of age

The proportion of patients with severe pulmonary hypertension before surgery was highest in patients under 3 months of age, which may be related to the large left-to-right shunt, LAVV regurgitation, and the unreduced physiological pulmonary hypertension. It was also interesting to note that the number of patients with pre-operative severe pulmonary hypertension had a bimodal distribution, mostly in those under 6 months and beyond 12 months of age (*Table 6*). Those with pre-operative severe pulmonary hypertension in the two age distributions were more likely to face postoperative pulmonary hypertensive crisis (n=6) and progress to death (n=5), compared with none between 6–9 and 9–12 months of age. This indicates that, due to the evolution of hemodynamics, more positive measures should be taken for children under 6 months and beyond 12 months of age to avoid poor prognosis.

Limitations

The most important limitation of this study lies in that it was a retrospective study carried out in a single center with a limited number of patients. The number of patients ≤3 months of age and weighing ≤4 kg was relatively small, which challenges risk factor analysis, and the results from the analysis might have deviations.

Conclusions

Mortality was higher after surgical repair in CAVSD patients, while freedom from re-operation and LAVV re-operation rates were similar among different AVSD types. Severe pulmonary hypertension before surgery and severe LAVV regurgitation within 24 hours after the first surgery were risk factors for mortality. ≥ Moderate LAVV regurgitation within 24 hours after the first surgery was a risk factor for LAVV re-operation.

Acknowledgments

We would like to thank Medjaden Inc for the help in polishing our paper.
Funding: None.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-790/rc

Data Sharing Statement: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-790/dss

Peer Review File: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-790/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-790/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Review Board of the Children's Hospital of Fudan University [No. (2022)132]. The need for patient consent was waived because of the retrospective nature of the study.

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Cite this article as: Cai Y, Chen R, Chen G, Shi Q, Mi Y, Zhang H, Jia B. Middle to long-term outcomes of surgical repair for atrioventricular septal defect: a single-center study. J Thorac Dis 2022;14(10):3706-3718. doi: 10.21037/jtd-22-790