Original Article

Risk factors for the recurrence of left atrioventricular valvular regurgitation after surgical repair of partial and transitional atrioventricular septal defect

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Background: Left atrioventricular valvular regurgitation (LAVVR) recurrence after partial and transitional atrioventricular septal defect (AVSD) repair is the main risk factor associated with reoperation or mortality. The purpose of this study was to identify risk factors associated with the recurrence of LAVVR after surgical repair of transitional and partial AVSD at a single institution.

Methods: A hundred and fifty-seven patients who underwent anatomical repair for partial and transitional AVSD from January 2013 to December 2021 were included in our institutional database. Demographic characteristics, operative information, comorbidities, complications, and outcomes were retrieved from electronic medical records. Echocardiographic evaluations included cardiac dimensions, the degree of LAVVR, and the anatomy of the atrioventricular valve.

Results: After a median follow-up period of 5.8 years, 40 patients had recurrent moderate or even more severe LAVVR. Compared with patients without recurrent LAVVR, those experiencing LAVVR recurrence were more likely to have larger preoperative left atrial (LA) size and larger left ventricular (LV) size after standardization, larger left atrioventricular valve (LAVV) cleft width, higher proportions of preoperative moderate or even more severe LAVVR, and immediately postoperative mild to moderate or even more severe LAVVR. Univariate Cox regression analysis showed that age at first repair, height, LA size after standardization, LV size after standardization, the severity of preoperative LAVVR, immediately postoperative LAVVR, and the LAVV cleft width more than 1cm were risk factors for recurrent LAVVR ($P<0.05$ for all). Multivariable Cox regression analysis showed that mild to moderate or even more severe LAVVR postoperatively [hazard ratio (HR) 9.53, 95% confidence interval (CI): 3.78–24.01; $P<0.001$], the width of LAVV cleft more than 1 cm (HR: 3.90, 95% CI: 1.80–8.48; $P<0.001$) and age at first repair (HR: 0.45, 95% CI: 0.31–0.66; $P<0.001$) were independently associated with the recurrence of LAVVR.

Conclusions: The width of LAVV cleft, mild to moderate or even more severe LAVVR immediately after surgery, and age at initial surgery are risk factors for recurrent LAVVR. The presence of recurrent LAVVR

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necessitates proactive surveillance to facilitate timely reintervention.

Keywords: Atrioventricular septal defect (AVSD); left atrioventricular valve (LAVV); recurrent regurgitation; congenital heart disease

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Introduction

Atrioventricular septal defect (AVSD) represents a spectrum of the atrial and ventricular septal defect (VSD) along with a common or partially separate atrioventricular valve (1), which accounts for almost 5% of congenital heart anomalies. AVSD is further classified into distinct subtypes, namely complete, partial, and transitional AVSD. Partial AVSD is characterized by the presence of an ostium primum atrial septal defect (ASD), along with distinct atrioventricular valves that share a common junction. Additionally, it typically includes the occurrence of a cleft mitral valve. Transitional AVSD extends beyond the features of partial AVSD and encompasses the presence of a small and restrictive VSD (2,3). Children with partial and transitional AVSD are largely asymptomatic, which leads to the deferral of surgical referral until the preschool or older age stage (4-6). Surgical intervention for uncomplicated incomplete AVSD is generally characterized by its simplicity and overall positive outcomes. The mortality after 30 days following the repair of incomplete AVSD is rare, ranging from 0% to 4% of patients (7-9). However, as with complete AVSD, left atrioventricular valve regurgitation (LAVVR) emerges as a primary cause of late morbidity following incomplete AVSD repair. Despite low early mortality and excellent long-term survival, prior investigations have demonstrated that reoperation for significant postoperative LAVVR is required in 3% to 13% of patients who undergo repair for partial and transitional AVSD (10,11). Repair during infancy (12) and unsutured clefts (13,14) are reported to be risk factors influencing late LAVVR. Abbruzzese and his colleague have elucidated that preoperative left atrioventricular valve insufficiency and associated valvular malformations are major determinants of late left atrioventricular valve insufficiency in partial AVSD (15). Furthermore, the study conducted by Kobayashi *et al.* (4) demonstrated LAVVR as a major cause of late morbidity. Specifically, the postoperative grade of LAVVR is the only independent risk factor for late LAVVR. Consequently, it is imperative to emphasize the optimization of left atrioventricular valve repair to minimize residual regurgitation, even mild regurgitation. The surgical repair for left atrioventricular valve (LAVV) remains a challenge in patients younger than 3 months, less than four kilograms, or with other genetic disorders. Repair during infancy has been reported to carry high mortality and morbidity (16), yet the ideal age at repair continues to be a matter of debate (17-19). The presence of postoperative LAVVR is a common phenomenon in such patients. Postoperative LAVVR increases volume overload, leading to further left atrioventricular (LV) remodeling and exaggerating the severity of LAVVR. Recurrent LAVVR has been found to be associated with adverse clinical outcomes, sometimes requiring reoperation (4,15,20-23). However, the risk factors of LAVVR recurrence after partial

Highlight box

Key findings

- The presence of mild to moderate or even more severe left atrioventricular valve regurgitation (LAVVR) postoperatively, the width of LAVV cleft ≥1 cm, and younger age at first repair are independently associated with increased risk of recurrent LAVVR after partial and transitional atrioventricular septal defect (AVSD) repair.

What is known and what is new?

- Mortality after partial and transitional AVSD repair is low, yet reoperation due to recurrent LAVVR remains a significant problem.
- Mild to moderate or even more severe LAVVR immediately after surgery, the width of left atrioventricular valve cleft and age are independent predictors of recurrent LAVVR.

What is the implication, and what should change now?

- As the morphologic heterogeneity of the left atrioventricular valvular apparatus, more effort should be focused on personalized valve repair to minimize residual regurgitation.
- Recurrent LAVVR necessitates proactive surveillance to facilitate timely reintervention.

and transitional AVSD repair have not been well clarified. Therefore, the aim of this study was to determine the risk factors for recurrent LAVVR in a consecutive single-center patient cohort. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1694/rc).

Methods

Study population and study design

Consecutive patients with partial and transitional AVSD who had undergone surgical repair of at Union Hospital, Tongji Medical College, Huazhong University of Science and Technology from January 2013 to December 2021, were included. Echocardiography was performed for all patients as preoperative and postoperative evaluation of cardiac dimensions and function, as well as the severity of LAVVR. Patients with heterotaxy and genetic syndromes were also included, whereas those with the complete form of AVSD, and if there was inadequate preoperative imaging, no postoperative transthoracic echocardiography, or with major additional congenital heart defects such as transposition of the great arteries were excluded. We included a total of 157 consecutive patients with partial and transitional AVSD who underwent surgical repair. These patients were divided into two groups according to the presence of at least moderate recurrent LAVVR: recurrent LAVVR group and no recurrent LAVVR group. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the institutional ethics board of Union Hospital, Tongji Medical College, Huazhong University of Science and Technology (No. 20230803) and individual consent for this retrospective analysis was waived. The records of these patients were reviewed for demographic, echocardiographic, perioperative features, and clinical data. Baseline and surgical characteristics, echocardiographic data, and clinical outcomes were evaluated for all patients.

Surgical technique

A comprehensive surgical approach was undertaken with full cardiopulmonary bypass (CPB) and moderate hypothermia. The intervention involved a median sternotomy, allowing access for surgical repair. After cardiac arrest, a thorough reassessment of the LAVV structure was conducted to determine the type of AVSD and appropriate surgical strategy. AVSD closure of the ASD was begun with a running proline suture to fix an autologous pericardial patch, starting in the commissure between the right mural leaflet and the inferior bridging leaflet, following the hinge-point level of the leaflet. In cases of partial AVSD (PAVSD), an autologous pericardium was used to repair the ASD. For patients with transitional AVSD (TAVSD), the ASD was closed with autologous pericardium. In addition to ASD closure, the VSD was directly closed with a 5-0 proline suture, which was reinforced with pledgets. The LAVV function was assessed by saline injection after the correction of AVSD. Subsequently, echocardiography was performed to reevaluate the LAVV regurgitation severity after the patient was released from CPB. Re-exploration was then planned if the LAVV regurgitation was graded as severe or the intraoperative echocardiography revealed the presence of LV outflow tract stenosis.

Clinical data

Patients' demographic characteristics, medical histories, laboratory examinations, echocardiographic findings and outcomes were retrieved from electronic medical records. Follow-up was obtained by a combination of clinic notes review and telephone interviews of patients, families, and referring physicians. These data were independently reviewed and entered into the computer database by two analysts.

Echocardiography

Two-dimensional and Doppler transthoracic echocardiography was performed preoperatively, intraoperatively, before discharge and at follow-up period for all patients using a standard protocol. LA and LV dimensions were measured in parasternal long-axis view. Right atrial (RA) and right ventricular (RV) dimensions were determined from the apical 4-chamber view. Left ventricular ejection fraction (LVEF) was measured by the modified biplane Simpson's method. The short-axis view of the LV at the level of mitral valve, and the apical four-chamber view were obtained to evaluate the geometry and function of LAVV. The cleft width of LAVV was measured. Estimation of LAVVR incorporated color Doppler imaging and contour of the jet on continuous-wave Doppler imaging. The LAVVR was graded as none/trace, mild, mild to moderate, moderate, moderate to severe and severe according to American College of Cardiology/American

Heart Association (ACC/AHA) guideline (24). Pulmonary artery systolic pressure (PASP) was assessed from the peak velocity of the tricuspid regurgitation (TR) jet, using the modified Bernoulli equation plus RA pressure evaluated from the inferior vena cava size and its collapsibility.

Study follow-up

The primary outcome of this study was moderate or even more severe LAVVR recurrence. Reoperation included any cardiac surgery after initial AVSD repair, excluding pacemaker implantation. Early mortality was defined as death within 30 days of the first operation. Late mortality was defined as death after 30 days of the first operation. The final follow-up data were collected on December 31, 2022.

Statistical analysis

Continuous data were described as mean ± SD or median [interquartile range (IQR)] and compared using Student's *t*-test (for normally distributed data) or the Mann-Whitney *U* test (for non-normally distributed data). Categorical variables were expressed as frequencies and percentages and compared using the Chi-squared test or the Fisher exact test. The Kaplan-Meier method was used to assess hazard probability of recurrent LAVVR. Univariable and multivariable Cox regression analyses were performed to identify variables associated with the recurrent LAVVR. All potential risk factors of recurrent LAVVR were entered into univariate analyses. Variables with P values <0.01 in univariate analysis were entered into multivariate Cox regression models. Statistical analysis was performed using SPSS statistical software version 27.0 (SPSS, Inc., Chicago, IL, USA). A level of P value <0.05 was considered statistically significant.

Results

Study population

One hundred and fifty-seven patients who underwent AVSD repair between 2013 and 2022 were included, which was consisted of 118 (75.2%) patients with partial AVSD repair and 39 (24.8%) patients with transitional AVSD repair. Baseline patient characteristics are summarized in *Table 1*. The median age and median weight of patients underwent AVSD repair was 19.47 years (2.33–39.66 years) and 49.50 kg (10.63–59.75 kg), respectively. The overall study cohort included 100 female (63.7%) and 57 male (36.3%) patients. Patients were classified according to age at repair as 13 (8.3%) <90 days, 16 (10.2%) 90 days to <1 year, 46 (29.3%) 1–18 years, and 82 (52.2%) above 18 years (P=0.01). Compared with patients without postoperative recurrent LAVVR, patients with recurrent LAVVR were more likely to have lower body weight (P=0.02), lower height (P=0.02), and were more likely to be accompanied with other cardiac abnormalities (P=0.03). The incidence of being accompanied with cardiac abnormalities was 30% (12/40) in the recurrent LAVVR group, which was significantly higher than the 14.5% (17/117) in the no recurrent LAVVR group. Patients coexisted with cardiac abnormalities are presented in *Table 1*, including patent ductus arteriosus in 5 patients, persistent left superior vena cava in 11 patients,, pulmonary valve stenosis in 9 patients, single atrium in 1 patients, right-sided aortic arch in 1 patient, partial anomalous pulmonary venous connection in 1 patient, unroofed coronary sinus in 2 patients, LV dysplasia in 1 patient, RV outflow tract stenosis in 1 patient, and double orifice mitral valve in 1 patient. There were no significant differences in sex, the type of AVSD, pulmonary arterial hypertension and combined atrioventricular block.

Surgical data are summarized in *Table 1*. In the entire cohort, the median CPB time was 86.50 minutes (IQR, 71.00–108.00 minutes), the median cross-clamp time was 57.00 minutes (IQR, 43.00–74.00 minutes), the rate of temporary pacemaker implantation was 30.6% and the rate of small incision endoscopic surgery was 5.7%.

Echocardiographic characteristics

The echocardiographic characteristics of patients at baseline are presented in *Table 2*. Preoperative echocardiography showed that LAVV regurgitation was mild in 26, mild to moderate in 22, moderate in 20, moderate to severe in 21, and severe in 62 patients. Mean LVEF was 64.2%±0.6% in the overall study cohort. Comparisons of echocardiographic characteristics of patients with and without recurrent LAVVR demonstrated that patients with recurrent LAVVR exhibited larger LA dimension index, larger LV end-diastolic dimension index and larger cleft width. The incidence of pulmonary hypertension was 54.7% (n=64) in the no recurrent LAVVR group and 65.0% (n=26) in the recurrent LAVVR group before surgery. RA size, and RV size after standardization, LVEF and pulmonary artery hypertension (PAH), were similar between two groups. There was no difference in whether it was combined with

Table 1 Patient characteristics of partial and transitional atrioventricular septal defect repair (n=157)

Patient characteristics	Whole cohort (n=157)	No recurrent LAVVR (n=117)	Recurrent LAVVR (n=40)	P value
Demographics				
Female	100 (63.7)	73 (62.4)	27 (67.5)	0.56
Age (years)	19.47 (2.33–39.66)	16.99 (1.66–37.92)	25.59 (5.55–47.50)	0.01
<90 days	13 (8.3)	5 (4.3)	8 (20.0)	
90 days to <1 year	16 (10.2)	11 (9.4)	5 (12.5)	
1–18 years	46 (29.3)	34 (29.1)	12 (30.0)	
Above 18 years	82 (52.2)	67 (57.3)	15 (37.5)	
Body weight (kg)	49.50 (10.63–59.75)	50.50 (13.25–63.75)	16.00 (6.63–52.5)	0.02
Height (cm)	155.50 (85.5–165.00)	157.5 (95.25–165.75)	109.00 (64.25–160.00)	0.02
TAVSD	39 (24.8)	29 (24.8)	10 (25.0)	0.98
Atrioventricular conduction block	87 (55.4)	67 (57.3)	20 (50.0)	0.43
Pulmonary hypertension	75 (47.8)	57 (48.7)	18 (45.0)	0.26
Company with cardiac abnormalities	29 (18.5)	17 (14.5)	12 (30.0)	0.03
Patent ductus arteriosus	5 (3.2)	2 (1.7)	3 (7.5)	
Persistent left superior vena cava	11 (7.0)	6 (5.1)	5 (12.5)	
Pulmonary valve stenosis	9 (5.7)	4 (3.4)	5 (12.5)	
Single atrium	1 (0.6)	0 (0)	1 (2.5)	
Partial anomalous pulmonary venous connection	1 (0.6)	1 (0.9)	0 (0.0)	
Right-sided aortic arch	1 (0.6)	1 (0.9)	0 (0.0)	
Unroofed coronary sinus	2 (1.3)	2 (1.7)	0 (0.0)	
Left ventricular dysplasia	1 (0.6)	0 (0.0)	1 (2.5)	
Right ventricular outflow tract stenosis	1 (0.6)	1 (0.9)	0 (0.0)	
Double-orifice mitral valve	1 (0.6)	1 (0.9)	0 (0.0)	
Surgical data				
CPB time (min)	86.50 (71.00–108.00)	87.00 (74.00–110.25)	84.50 (62.00–97.75)	0.69
Aortic cross-clamp time (min)	57.00 (43.00–74.00)	55.50 (45.25–74.75)	61.00 (38.5–73.5)	0.68
Temporary pacemaker implantation	48 (30.6)	37 (31.6)	11 (27.5)	0.60
Small incision endoscopic surgery	9 (5.7)	9 (7.7)	0 (0.0)	0.07

Values are n (%) or median (interquartile range). TAVSD, transitional atrioventricular septal defect; CPB, cardiopulmonary bypass; LAVVR, left atrioventricular valvular regurgitation.

preoperative valve cleft between the two groups (P=0.20). Patients with recurrent LAVVR exhibited more likely to have moderate or even more severe preoperative LAVVR and right atrioventricular valve regurgitation (RAVVR), and mild to moderate or even more severe immediately postoperative LAVVR and RAVVR (P<0.001).

Recurrence of LAVVR

Echocardiographic follow-up was performed in alive patients for each defined time interval at a median of 5.8 years (IQR, 2.4–6.6 years) postoperatively. Recurrence of moderate or even more severe LAVVR was diagnosed

Table 2 The echocardiographic characteristics in patients at baseline (n=157)

Patient characteristics	Whole cohort (n=157)	No recurrent LAVVR (n=117)	Recurrent LAVVR (n=40)	P value
Preoperative data				
LAD (mm)	31.02±1.24	32.03±1.28	27.39±2.67	0.04
LADI (mm/m^2)	27.95±1.13	24.64±1.53	30.10±1.34	0.045
LVEDD (mm)	36.52±1.08	36.91±1.21	35.02±3.0	0.13
LVEDDI (mm/m^2)	32.90±1.21	28.39±1.76	38.48±1.91	0.03
RAD (mm)	43.88 (29.47–49.04)	45.00 (33.29–50.65)	34.45 (22.27–47.02)	0.04
RADI (mm/m^2)	39.53 (26.55–44.18)	34.62 (25.61–38.97)	37.86 (24.45–51.67)	0.08
RVEDD (mm)	44.48 (29.29–52.03)	45.99 (32.01–54.02)	34.98 (22.04–48.58)	0.09
RVEDDI (mm/m^2)	40.07 (26.39–46.87)	35.38 (35.18–59.36)	38.44 (24.22–53.38)	0.051
PAD (mm)	2.55 (1.63–3.28)	2.60 (1.80–3.28)	1.90 (1.50–3.28)	0.33
LVEF (%)	64.18±0.60	64.43±0.70	63.35±1.19	0.36
PAH	90 (57.3)	64 (54.7)	26 (65.0)	0.27
LAVV cleft width (≥1 cm)	76 (48.4)	49 (41.9)	27 (67.5)	0.005
Preoperative LAVV cleft	132 (84.1)	97 (82.9)	35 (87.5)	0.20
Preoperative LAVVR (moderate or even more severe)	104 (66.2)	69 (59.0)	35 (87.5)	<0.001
Preoperative RAVVR (moderate or even more severe)	76 (48.4)	55 (47)	21 (52.5)	<0.001
Postoperative data				
Immediately postoperative LAVVR (mild to moderate or even more severe)	56 (35.7)	22 (18.8)	34 (85.0)	<0.001
Immediately postoperative RAVVR (mild to moderate or even more severe)	6 (3.8)	1 (0.9)	5 (12.5)	<0.001

Values are mean ± SD, n (%), or median (interquartile range). LAD, left atrial diameter; LADI, left atrial diameter index; LVEDD, left ventricular end-diastolic diameter; LVEDDI, left ventricular end-diastolic diameter index; RAD, right atrial diameter; RADI, right atrial diameter index; RVEDD, right ventricular end-diastolic diameter; RVEDDI, right ventricular end-diastolic diameter index; PAD, pulmonary artery diameter; LVEF, left ventricular ejection fraction; PAH, pulmonary artery hypertension; LAVV, left atrioventricular valve; LAVVR, left atrioventricular valve regurgitation; RAVVR, right atrioventricular valve regurgitation; SD, standard deviation.

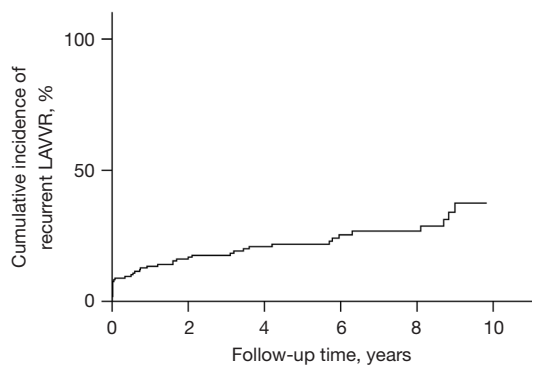

Figure 1 Cumulative incidence of recurrent LAVVR. LAVVR, left atrioventricular valve regurgitation.

in 40 patients (25.5%). Sixteen patients (10.2%) with recurrent moderate LAVVR progressed to severe LAVVR. The cumulative incidence of recurrent LAVVR was 13.4% at 1-year, 17.6% at 3-year, 21.8% at 5-year, 26.8% at 7-year follow-up as shown in *Figure 1*.

Risk factors for recurrent LAVVR

Risk factors for recurrent LAVVR are presented in *Table 3*. A univariate Cox regression analysis showed that mild to moderate or even more severe LAVVR on immediately postoperative echocardiography [hazard ratio (HR): 12.828, 95% confidence interval (CI): 5.376–30.614; P<0.001] , the

Table 3 Risk factors for LAVVR recurrence after atrioventricular septal defect repair by univariable and multivariable proportional hazards analysis (Cox regression)

Risk factors for LAVVR recurrence	Univariate Cox regression		Multivariate Cox regression	
	HR (95% CI)	P value	HR (95% CI)	P value
Age			0.453 (0.313–0.656)	<0.001
<90 days	Reference	<0.001		
90 days to <1 year	0.277 (0.089–0.860)	0.03		
1–18 years	0.242 (0.097–0.601)	0.002		
Above 18 years	0.168 (0.07–0.403)	<0.001		
Gender	1.195 (0.616–2.316)	0.56		
Height	0.989 (0.981–0.997)	0.01		
Body weight	0.987 (0.973–1.000)	0.051		
CPB time	0.999 (0.989–1.010)	0.93		
Aortic cross-clamp time	1.005 (0.991–1.018)	0.49		
Atrioventricular conduction block	0.765 (0.411–1.422)	0.40		
Temporary pacemaker implantation	1.036 (0.515–2.082)	0.92		
Surgical approach	0.046 (0.000–20.026)	0.32		
LADI	1.375 (1.005–1.362)	0.048		
LVEDDI	1.321 (1.131–1.517)	0.03		
RADI	1.215 (0.967–1.829)	0.64		
RVDI	1.041 (0.892–1.075)	0.27		
PAD	0.834 (0.565–1.230)	0.35		
LVEF	0.963 (0.902–1.029)	0.27		
PAH	1.457 (0.760–2.793)	0.26		
Immediate postoperative LAVVR (mild to moderate or even more severe)	12.828 (5.376–30.614)	<0.001	9.526 (3.780–24.007)	<0.001
Preoperative LAVVR (moderate or even more severe)	3.946 (1.545–10.079)	0.004	1.272 (0.459–3.525)	0.64
Preoperative RAVVR (moderate or even more severe)	1.288 (0.692–2.397)	0.43		
With LAVV cleft	2.191 (0.673–7.140)	0.19		
LAVV cleft width (≥1 cm)	2.626 (1.353–5.096)	0.004	3.904 (1.798–8.479)	<0.001

LAVVR, left atrioventricular valve regurgitation; CPB, cardiopulmonary bypass; LADI, left atrial diameter index; LVEDDI, left ventricular end-diastolic diameter index; RADI, right atrial diameter index; RVDI, right ventricular diameter index; PAD, pulmonary artery diameter; LVEF, left ventricular ejection fraction; PAH, pulmonary artery hypertension; RAVVR, right atrioventricular valve regurgitation; LAVV, left atrioventricular valve; HR, hazard ratio; CI, confidence interval.

width of LAVV cleft more than 1 cm (HR: 2.626, 95% CI: 1.353–5.096; P=0.004), age at first repair (HR: 0.453, 95% CI: 0.313–0.656; P<0.001), preoperative LAVVR (moderate or even more severe) (HR: 3.946, 95% CI: 1.545–10.079; P=0.004), height (HR: 0.989, 95% CI: 0.981–0.997; P=0.01), LA diameter index (LADI) (HR: 1.375, 95% CI: 1.005–1.362; P=0.048), LV end-diastolic diameter index (LVEDDI) (HR: 1.321, 95% CI: 1.131–1.517; P=0.03) were associated with higher risk for LAVVR recurrence (*Table 3*). However, gender, CPB time, aortic cross-clamp time, atrioventricular conduction block, temporary pacemaker implantation, surgical approach, RADI, RVDI, LVEF,

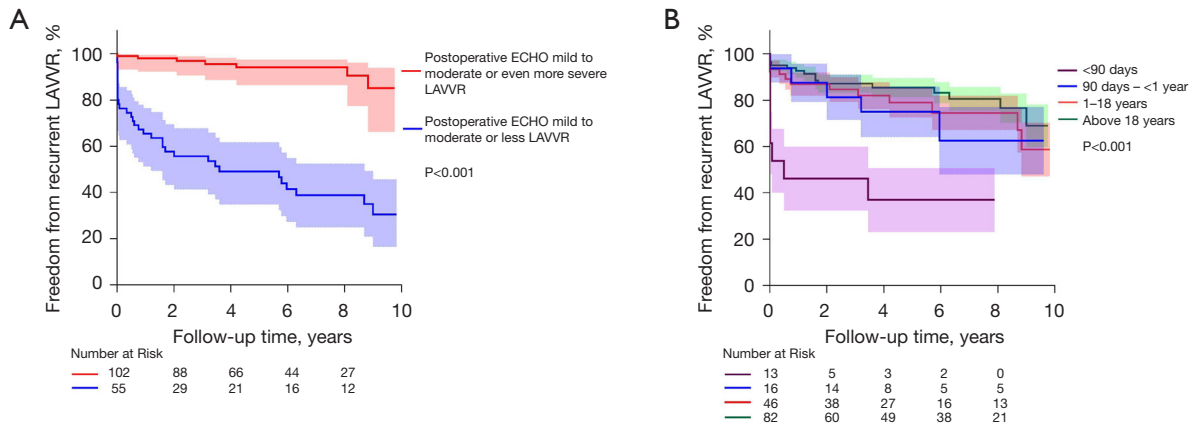

Figure 2 The effect of independent risk factor on recurrent LAVVR. (A) Freedom from recurrent LAVVR by mild to moderate or even more severe LAVVR/mild to moderate or less LAVVR immediately after surgery; (B) freedom from recurrent LAVVR by age categories. ECHO, echocardiography; LAVVR, left atrioventricular valve regurgitation.

Table 4 Reoperation and mortality data (n=157)

Patient characteristics	Whole cohort (n=157)	No recurrent LAVVR (n=117)	Recurrent LAVVR (n=40)	P value
Reoperation	10 (6.4)	1 (0.9)	9 (22.5)	<0.001
Total mortality	4 (2.5)	1 (0.9)	3 (7.5)	0.051
30-day mortality	3 (1.9)	1 (0.9)	2 (5.0)	0.16

Values are n (%). LAVVR, left atrioventricular valve regurgitation.

and PAH were not the risk factors of LAVVR recurrence in univariate analysis. In multivariate cox analysis models, age (HR: 0.453, 95% CI: 0.313–0.656; P<0.001), mild to moderate or even more severe LAVVR on immediately postoperative echocardiography (HR: 9.526, 95% CI: 3.780–24.007; P<0.001), and the width of LAVV cleft (HR: 3.904, 95% CI: 1.798–8.479; P<0.001) were found to be risk factors associated with recurrent LAVVR.

These findings were confirmed by Kaplan-Meier curves (*Figure 2*), which demonstrated that mild to moderate or even more severe LAVVR postoperatively and age were able to differentiate the recurrent LAVVR group and the no recurrent LAVVR group. Mild to moderate or even more severe LAVVR immediately after surgery group had a relatively higher percentage of recurrent LAVVR, the percentage of recurrent LAVVR at 10 years was 60.00% in the mild to moderate or even more severe LAVVR immediately after surgery group and 6.86% in the mild to moderate or less LAVVR immediately after surgery group (P<0.0001; *Figure 2A*). And the clinical impact of age at repair on recurrent LAVVR is displayed in *Figure 2B*. The percentage of recurrent LAVVR at 10 years in each of the four age-based groups was 61.5%, 31.3%, 26.1%, and 18.3%, respectively (P<0.001).

Reoperation and mortality

Eleven patients (7.0%) underwent reoperation at a median of 7.2 years (IQR, 3.2–9.1 years) post-operatively. The subsequent reoperations were performed due to recurrent LAVVR (10/11, 90.9%) and LVOTO (1/11, 9.1%). For those who required reoperation for LAVVR, there were 6 patients who underwent LAVV repair, and 4 patients underwent mechanical valve replacement. The freedom from reoperation rate at 1,3, 5, and 7 years from the date of initial repair was 100%, 99.27%, 96.81% and 92.75%, respectively. The mortality was 2.5% (4/157) in the entire cohort, including three early deaths and one late death (*Table 4*). The two major causes of mortality were multiple organ failure due to severe sepsis, and heart failure due to recurrent LAVVR.

Discussion

Our study has several important findings. (I) Compared with patients without recurrent LAVVR, those experiencing LAVVR recurrence were more likely to have larger preoperative LADI and larger preoperative LVEDDI, larger LAVV cleft width, higher proportions of preoperative moderate or even more severe LAVVR, and immediately postoperative mild to moderate or even more severe LAVVR; (II) mild to moderate or even more severe LAVVR immediately after surgery, the width of LAVV cleft and age at initial surgery indicated high risk for recurrent LAVVR. There was no observable correlation between the severity of preoperative LAVVR and recurrent LAVVR in our study, which was similar to the study of Kwon *et al.* (25).

Despite improved outcomes of partial and transitional AVSD repair overtime, the occurrence of postoperative LAVVR during the follow-up duration of left atrioventricular valve repair was reduced (26-28). The cumulative incidence of recurrent LAVVR of moderate or serious degree observed in this investigation was 13.4% at 1-year, 17.6% at 3-year, 21.8% at 5-year, 26.8% at 7-year follow-up. The LAVVR recurrent rate is lower than the rate reported by Fortuna and his colleagues (29). The estimated overall mortality and re-operation rate were 2.5% and 6.4% in our study, which were similar to previous studies (30-32).

Our findings demonstrated that recurrent LAVVR was associated with the width of the LAVV cleft. The wider the LAVV cleft indicates the greater loss of the leaflet, which is necessary for reattachment of leaflet. The reattachment of leaflet may result in subtle, complex geometric changes that increase tension on the cleft closure and thus the risk of cleft dehiscence (29). This may explain why abnormality of the LAVV is a strong risk factor for recurrent LAVVR. As patients with larger LAVV cleft tend to have recurrent LAVVR postoperatively, surveillance of these patients is essential to reduce the risk of late morbidity and mortality.

Another finding is that patients with mild to moderate or even more severe LAVVR immediately after surgery were more likely to have recurrent LAVVR in late follow-up. Similarly, Murashita *et al.* (33) showed that the postoperative LAVVR at hospital discharge was associated with the late deterioration of LAVVR after partial AVSD repair. Postoperative LAVVR may aggravate pulmonary hypertension, leading to cardiac insufficiency and worsening LAVVR. Therefore, we suggest that more effort should be focused on valve repair to minimize residual regurgitation, as even mild postoperative LAVVR might develop. Previous studies demonstrated that the severity of preoperative LAVVR was an independent predictor of recurrence of LAVVR (34,35). However, our study found that the preoperative LAVVR was not an independent risk factor. The explanation of this inconsistent finding may probably be a higher incidence of LAVV abnormality in their studies than in our series (34).

In addition, age at initial surgery was proved to be a risk factor in this investigation. We discovered that those who underwent surgery during infancy were more vulnerable to LAVVR recurrence. These results are in line with the findings of Buratto *et al.*, which indicated a tendency for increased reoperation in 75 infants compared with 355 older children (19). A possible mechanism is that the surgical exposure is restricted in younger individuals and the LAVV is particularly brittle and easily torn (36). In addition, Mery *et al.* (22) found that repair during infancy is most likely a marker of more severe disease rather than the cause of reoperation. This probably reflects the fact that patients who undergo operation at younger ages have more severe malformation of LAVV than those who reach an older age before operation.

This present study is limited by its observational and retrospective nature, which may therefore bear associated biases. LAVV anomalies were retroactively examined and gathered. It was challenging to determine the impact of some of the intricate atrioventricular valve morphology on the incidence of long-term reintervention due to the retrospective evaluation of echocardiographic variables. Moreover, our study is limited by being a single-center study with a relatively limited sample size. The patients included may not represent the populations in other areas. Furthermore, we enrolled patients who were hospitalized with AVSD, and patients who had not been admitted to the hospital were not included. Therefore, future multicenter studies with larger sample sizes are needed to determine the prognostic value of echocardiographic characteristics.

Conclusions

Mild to moderate or even more severe LAVVR immediately after surgery, the width of LAVV cleft and age at initial surgery indicated high risk for recurrent LAVVR in late follow-up. The close surveillance of recurrent LAVVR is essential to allow timely reintervention.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1694/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1694/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 institutional ethics board of Union Hospital, Tongji Medical College, Huazhong University of Science and Technology (20230803) and individual consent for this retrospective analysis was waived.

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