Risk factors for atrial arrhythmia recurrence after atrial arrhythmia surgery with pulmonary valve replacement

Yuji Tominaga, MD,[a,b] Masaki Taira, MD,[a] Takuji Watanabe, MD,[a] Moyu Hasegawa, MD,[a] Ryoto Sakaniwa, MD, MPH, PhD,[c] Daisuke Yoshioka, MD, PhD,[a] Kazuo Shimamura, MD, PhD,[a] Takayoshi Ueno, MD, PhD,[a] and Shigeru Miyagawa, MD, PhD[a]

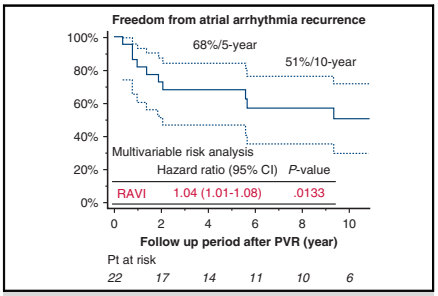
ABSTRACT

Objectives: Atrial arrhythmias are a significant cause of late morbidity and mortality in patients after tetralogy of Fallot repair. However, reports on their recurrence following atrial arrhythmia surgery are limited. We aimed to identify the risk factors for atrial arrhythmia recurrence after pulmonary valve replacement (PVR) and arrhythmia surgery.

Methods: We reviewed 74 patients with repaired tetralogy of Fallot who underwent PVR for pulmonary insufficiency at our hospital between 2003 and 2021. Twenty-two patients (mean age, 39 years) underwent PVR and atrial arrhythmia surgery. A modified Cox-maze III was performed in 6 patients with chronic atrial fibrillation, and a right-sided maze was performed in 12 with paroxysmal atrial fibrillation, 3 with atrial flutter, and 1 with atrial tachycardia. Atrial arrhythmia recurrence was defined as any documented sustained atrial tachyarrhythmia requiring intervention. The influence of preoperative parameters on recurrence was assessed with the Cox proportional-hazards model.

Results: The median follow-up period was 9.2 years (interquartile range, 4.5-12.4). Cardiac death and redo-PVR due to prosthetic valve dysfunction were not observed. Eleven patients had atrial arrhythmia recurrence after discharge. Atrial arrhythmia recurrence-free rates were 68% at 5 years and 51% at 10 years after PVR and arrhythmia surgery. Multivariable analysis revealed that right atrial volume index (hazard ratio, 1.04; 95% confidence interval, 1.01-1.08, $P = .009$) was a significant risk factor for atrial arrhythmia recurrence after arrhythmia surgery and PVR.

Conclusions: Preoperative right atrial volume index was associated with atrial arrhythmia recurrence, which may assist in planning the timing of atrial arrhythmia surgery and PVR. (JTCVS Open 2023;14:123-33)



Right atrial volume index was a risk factor of atrial arrhythmia recurrence.

CENTRAL MESSAGE

Right atrial volume index was a risk factor for atrial arrhythmia recurrence after pulmonary valve replacement and arrhythmia surgery and should be considered when planning the timing of surgery.

PERSPECTIVE

Atrial arrhythmias are major causes of morbidity and mortality in patients late after the repair of tetralogy of Fallot. Right atrial volume index (RAVI) was a significant risk factor for atrial arrhythmia recurrence after arrhythmia surgery and pulmonary valve replacement (PVR). Preoperative RAVI should be considered when planning the timing of PVR and arrhythmia surgery.

From the Departments of [a]Cardiovascular Surgery, and [c]Public Health, Osaka University Graduate School of Medicine, Osaka, Japan; and [b]Department of Pediatric Cardiovascular Surgery, National Cerebral and Cardiovascular Center, Osaka, Japan.

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Address for reprints: Masaki Taira, MD, Department of Cardiovascular Surgery, Osaka University Graduate School of Medicine, 2-2, Yamada-Oka, Suita, Osaka 565-0871, Japan (E-mail: taira@surg1.med.osaka-u.ac.jp).

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Abbreviations and Acronyms

ACHD = adult congenital heart disease
AF = atrial fibrillation
AFL = atrial flutter
AT = atrial tachycardia
CT = computed tomography
IVC = inferior vena cava
LA = left atrium
MRI = magnetic resonance imaging
PVR = pulmonary valve replacement
RA = right atrium
RAVI = right atrial volume index
ROC = receiver operating characteristic
RV = right ventricle
RVESVI = right ventricular end-systolic volume index
TOF = tetralogy of Fallot
TPVI = transcatheter pulmonary valve implantation
TR = tricuspid valve regurgitation
TV = tricuspid valve

Atrial tachyarrhythmia commonly occurs in patients with adult congenital heart disease (ACHD) due to atrial volume, pressure overload, and surgical scars.[1,2] Atrial tachyarrhythmias can cause a deterioration in the quality of life and lead to heart failure and hospitalizations.[3-7] Therefore, it is essential to manage the cumulative lifetime risk of atrial tachyarrhythmia.

Although atrial arrhythmia surgery has been reported to be effective in patients with ACHD, the atrial arrhythmia recurrence rate after arrhythmia surgery is high. Previous studies have reported that the age at the time of arrhythmia surgery, duration of arrhythmia, Ebstein anomaly, and tetralogy of Fallot (TOF) were risk factors for atrial arrhythmia recurrence.[1,8]

In patients with repaired TOF, right ventricular (RV) outflow tract dysfunction is known to cause dilation of the RV and right atrium (RA), biventricular dysfunction, and arrhythmia late after the repair of TOF. Pulmonary valve replacement (PVR) and concomitant arrhythmia surgery were reported to provide beneficial effects in patients with RV outflow tract dysfunction and atrial arrhythmia by reducing the RV volume, improving the RV function, and lowering the risk of adverse outcomes.[1,8,9] Both underlying cardiac disease and atrial fibrillation (AF) promote adverse cardiac remodeling from paroxysmal to persistent. Early therapeutic interventions may prevent this progression.[10]

However, there are limited data on the results of the maze procedure concomitant with PVR, according to the current guidelines, late after the repair of TOF. Furthermore, it has remained unclear which populations among repaired TOF patients are at a greater risk of atrial tachyarrhythmia recurrence after arrhythmia surgery.[1,7,11] To improve the prognosis of patients with repaired TOF, it is important to identify predictors for atrial arrhythmia recurrence and the appropriate timing of surgical intervention. Therefore, this study aimed to identify risk factors for the recurrence of atrial tachyarrhythmia after PVR and simultaneous arrhythmia surgery in patients with repaired TOF.

METHODS

Ethical Statement

This retrospective study was approved by our institutional review board (Osaka University Hospital) on September 15, 2015 (approval number 15241). Written informed consent for using patient records was obtained from the legal guardian of each patient.

Patients

A total of 74 patients underwent PVR for moderate-to-severe pulmonary insufficiency at our institution between 2003 and 2021. During the study period, PVR was indicated for patients with symptoms or signs of RV failure, including arrhythmia, palpitations, and pedal edema. Asymptomatic patients underwent PVR when the right ventricular end-diastolic volume index and right ventricular end-systolic volume index (RVESVI) approached 150 mL/m^2 and 80 mL/m^2, respectively, as assessed by cardiac magnetic resonance imaging (MRI) or cardiac computed tomography (CT).[5,9,12,13] Of these 74 patients, 22 underwent concomitant atrial arrhythmia surgery (18 patients with TOF and 4 patients with pulmonary atresia with ventricular septal defect; mean age at PVR, 39 years; Table 1) before PVR (maze [+] group) due to a history of atrial arrhythmia. The other 52 patients without histories of atrial arrhythmia before PVR did not undergo arrhythmia surgeries (maze [–] group). We performed the modified Cox-maze III procedure in 6 patients with chronic AF and the right-sided maze procedure in 12 patients with paroxysmal AF, 3 with atrial flutter (AFL), and one with atrial tachycardia (AT).

Hemodynamic and Volume Study

All 74 reviewed patients underwent cardiac catheterization, echocardiography, cardiac MRI, and enhanced CT before PVR. The methods for assessing RV and RA volumes using cardiac MRI or CT have been described previously.[13,14] The RA volume at the end-diastolic phase was evaluated, which was identified as 40% of the R-R interval. In patients with contraindications for enhanced CT imaging, the RA volume was measured using MRI and calculated using the method devised by Maceira and colleagues.[15] RA volume was evaluated in 22 patients (100%) in the maze (+) group and 46 (88%) in the maze (−) group.

Definition of Atrial Tachyarrhythmia Recurrence

Atrial tachyarrhythmia recurrence was defined as any documented sustained atrial tachycardia requiring termination by medication, direct cardioversion, or catheter ablation.[1] Cardiac rhythm was confirmed based on symptom reviews, electrocardiography, Holter monitoring, and device interrogation for patients with implantable loop recorders, pacemakers, or implantable cardioverter–defibrillators. Electrocardiograms were performed on all patients during outpatient visits every 2 months and on patients who visited the emergency department with any symptomatic condition. Holter electrocardiography was performed in selected patients with symptoms, and device interrogation was limited to patients after loop recorders or pacemaker implantation.

TABLE 1. Basic patient characteristics

Characteristics	Maze (+)	Maze (−)
Patients, n	22	52
Male, n (%)	10 (45%)	30 (58%)
Diagnosis, TOF:PAVSD	18:4	48:4
Age at PVR, y	39 ± 12	36 ± 14
Previous shunt procedure, n (%)	10 (45%)	12 (23%)
Age at primary repair, y	5.9 [3-11]	2.9 [1.7-4.9]
Type of primary RVOT repair, n (%)		
Commissurotomy	7 (32%)	10 (19%)
Commissurotomy + right ventricular patch	3 (14%)	13 (25%)
Transannular patch	7 (32%)	24 (46%)
Homograft or conduit	5 (23%)	5 (9.6%)
NYHA classification, n (%)		
II/III	9 (41%)/4 (18%)	15 (29%)/3 (5.8%)
Atrial tachyarrhythmia before PVR, n (%)		
Paroxysmal atrial fibrillation	12 (55%)	–
Chronic atrial fibrillation	6 (27%)	–
Atrial flutter	3 (14%)	–
Atrial tachycardia	1 (5%)	–
Sinus node dysfunction, n (%)	4 (18%)	4 (7.7%)
Catheter ablation before PVR, n (%)	5 (23%)	–

Continuous data are shown as mean ± standard deviation or median [interquartile range], whereas categorical data are presented as the number (percentage) of observations. *TOF*, Tetralogy of Fallot; *PAVSD*, pulmonary atresia with ventricular septal defect; *PVR*, pulmonary valve replacement; *RVOT*, right ventricular outflow tract; *NYHA*, New York Heart Association.

Surgical Procedure

PVR was performed using cardiopulmonary bypass. The intraoperative characteristics are summarized in Table 2. Concomitant arrhythmia surgery was performed according to a previous report on managing arrhythmias in patients with ACHD.[2] We performed the modified Cox-maze III procedure in patients with chronic AF and the right-sided maze procedure in patients with paroxysmal AF, AFL, and AT.[16] A bipolar radiofrequency system and a cryoablation device were used for ablation. The device selection was based on the surgeon's preference. The ablation line was based on previous reports.[1,7,13,14]

For the right-sided maze, a vertical incision was made in the RA. The ablation lines of the RA were as follows: (1) from the inferior end of the RA incision toward the superior vena cava and inferior vena cava (IVC); (2) from the RA incision to the RA appendage and the anterior tricuspid valve (TV) annulus; (3) between the IVC and the coronary sinus; and (4) from the TV annulus to the IVC (isthmus line). The right atrial appendage was preserved, and the left atrial appendage was excluded by internal suture through the incision of the atrial septum or by external suture.

For the left-sided maze, the left atrium (LA) was evaluated via a transseptal approach. The base of the LA appendage was sutured internally. The ablation lines in the LA were as follows: (1) a box encircling the pulmonary veins, (2) between the base of the LA appendage and the pulmonary vein box, and (3) a pulmonary vein box to the posterior mitral valve annulus.

Regarding tricuspid valve regurgitation (TR), our strategy was to perform TV surgery for more than moderate TR or dysplastic TV with mild TR. TV surgery included tricuspid annuloplasty and tricuspid valvuloplasty. Concomitant TV annuloplasty and valvuloplasty were performed in patients with greater than moderate TR or a dysplastic valve cusp. A pacemaker was simultaneously implanted for sinus node dysfunction (Table 2).

Definition of End Points and Study Design

The primary end point was defined as all-cause mortality. The postoperative course was reviewed, including the recurrence of atrial tachyarrhythmia and reintervention. We analyzed the preoperative factors that were risks for the recurrence of atrial tachyarrhythmia using the Cox proportional hazards model.

Statistical Analyses

Data are presented as the median and interquartile range or as the mean and standard deviation, according to the distribution pattern. Categorical variables were analyzed using Fisher exact test or Cochran–Armitage trend test, as appropriate. Continuous variables with a normal distribution and continuous variables with non-normal distributions were analyzed using the Student *t*-test and Man–Whitney *U* test, respectively. The incidence of atrial tachyarrhythmia recurrence was estimated using Kaplan–Meier curves. The Cox proportional hazards model was used to adjust for the effects of preoperative variables on the incidence of post-PVR atrial tachyarrhythmia recurrence. To control for type I error in the cause-specific hazard analysis and to increase the power of the analysis, a P value of <.10 was considered statistically significant. Right atrial volume index (RAVI), age at PVR, and chronic AF were imported into the multivariable Cox regression analysis.[17-19] The threshold of RAVI was evaluated using time-dependent receiver operating characteristic (ROC) analysis. Statistical analysis was performed using JMP Pro 14 (SAS Institute Inc) and EZR.[20]

RESULTS

The median follow-up period was 9.2 (interquartile range, 4.5-12) years in 22 patients after PVR and atrial

TABLE 2. Prepulmonary valve replacement demographics and surgical characteristics

Characteristics	Maze (+), n = 22	Maze (−), n = 52	*P* value
RVEDVI, mL/m^2	158 [124-180]	153 [126-190]	.77
RVESVI, mL/m^2	89 [71-114]	86 [68-110]	.84
RV ejection fraction (%)	39 [32-45]	42 [33-50]	.42
RVSP, mm Hg	44 [32-60]	47 [38-59]	.47
RVEDP, mm Hg	10 [8-13]	9 [7-12]	.3
RAVI, mL/m^2	88 [71-107]	72 [58-84]	.018
RAP, mm Hg	9 [7-11]	8 [5.5-10]	.026
pressure gradient (PA-RV), mm Hg	9 [3-20]	11 [5-31]	.18
Tricuspid valve regurgitation moderate or greater, n (%)	11 (50%)	17 (33%)	.19
LVEDVI, mL/m^2	95 [76-118]	98[69-98]	.15
LVESVI, mL/m^2	50 [39-68]	40 [32-48]	.020
LV ejection fraction, %	48 [42-51]	52 [45-57]	.042
PCWP, mm Hg	10 [10-12]	10 [8-13]	.68
RVP/LVP	0.39 [0.28-0.45]	0.39 [0.32-0.51]	.17
QRS duration, ms	170 [150-177]	148 [136-164]	<.001
Intraoperative characteristics at PVR			
Extracorporeal circulation time, min	202 ± 50	152 ± 53	<.001
Aortic crossclamping, n	18 (82%)	24 (46%)	.005
Aortic crossclamping time, min	101 ± 39	84 ± 37	.15
Type of valve			–
Bovine	19 (86%)	32 (62%)	
Porcine	3 (14%)	15 (29%)	
DC		5 (9.6%)	
Valve size, mm	23 [21-25]	23 [21-25]	.81
Concomitant procedure			
Tricuspid valve surgery	18 (82%)	25 (48%)	.010
Pacemaker implantation	4 (18%)	4 (7.7%)	.23

Continuous data are shown as mean ± standard deviation (SD) or median [interquartile range], while categorical data are presented as the number (percentage) of observations. *RVEDVI*, Right ventricular end-diastolic volume index; *RVESVI*, right ventricular end-systolic volume index; *RV*, right ventricular; *RVSP*, right ventricular systolic pressure; *RVEDP*, right ventricular end-diastolic pressure; *RAVI*, right atrial volume index; *RAP*, right atrial pressure; *PA*, pulmonary artery; *LVEDVI*, left ventricular end-diastolic volume index; *LVESVI*, left ventricular end-systolic volume index; *LV*, left ventricular; *PCWP*, pulmonary capillary wedge pressure; *RVP*, right ventricular pressure; *LVP*, left ventricular pressure; *PVR*, pulmonary valve replacement; *DC*, decellularized pulmonary homograft.

arrhythmia surgery (maze [+] group). Tables 1 and 2 summarize the patients' baseline characteristics and the pre-PVR hemodynamic parameters of the study cohort. The patients had atrial tachyarrhythmias, including chronic AF (n = 6 [27%]), paroxysmal AF (n = 12 [55%]), AFL (n = 3 [14%]), and AT (n = 1 [5%]) before PVR. The median duration from the first occurrence of the arrhythmia to surgical intervention was 1.4 (interquartile range, 1.1-2.0) years in the maze (+) group. Ten patients (45%) had a history of shunt palliation. Fifteen patients (68%) required an RV incision at the intracardiac repair.

The post-PVR courses are presented in Table 3. In the maze (+) group, 1 patient died due to a thyroid crisis during the follow-up period, and the overall survival rate was 100% at 5 years and 89% at 10 years after the surgery (Figure 1, *A*). There were no cardiac-related deaths or cases of heart transplantation, and no patient experienced a stroke. After arrhythmia surgery, 22 patients experienced relief from atrial tachyarrhythmia at discharge. Although 20 of 22 patients were on antiarrhythmic medication (beta-blockers, antiarrhythmic drugs, or both) at discharge, 2 patients had to discontinue antiarrhythmic drugs due to bradycardia before discharge. Seven pacemaker implantations after PVR were performed. Two of them had pacemaker implantation early after PVR. The other 5 underwent planned pacemaker implantation at a median of 5.1 years after PVR (IQR, 0.8-5.7). During the follow-up period, there were no cases in which TR worsened to more than moderate in patients with concomitant atrial arrhythmia surgery.

TABLE 3. Postpulmonary valve replacement course

Course details	Maze (+)	Maze (−)
Follow-up period after pulmonary valve replacement, y	9.2 [4.5-12]	7.1 [4.4-11]
All-cause mortality, n	1 (4.5%)	2 (3.8%)
Cardiac-related death or heart transplantation, n	0	1 (1.9%)
Cerebrovascular events, n	0	0
Prosthetic valve dysfunction, n	0	0
Atrial arrhythmia after PVR, n	11 (50%)	8 (15%)
Chronic atrial fibrillation	6 (27%)	1 (1.9%)
Paroxysmal atrial fibrillation	3 (14%)	0
Atrial flutter	1 (4.5%)	5 (9.6%)
Atrial tachycardia	1 (4.5%)	2 (3.8%)
Catheter ablation after pulmonary valve replacement, n	3 (14%)	5 (9.6%)
Ventricular tachycardia, n	3 (14%)	1 (1.9%)
Postoperative pacemaker implantation, n	7 (32%)	2 (3.8%)
Tricuspid valve regurgitation moderate or greater, n (%)	0	2 (3.8%)

Continuous data are presented as median [interquartile range], whereas categorical data are shown as the number of observations. *PVR*, Pulmonary valve replacement.

Recurrence and New Onset of Atrial Tachyarrhythmias

During the follow-up period, there were 11 atrial arrhythmia recurrences (chronic AF: 6, paroxysmal AF: 3, atrial flutter: 1, atrial tachycardia: 1) in the maze (+) group and 8 new-onset atrial arrhythmias (chronic AF: 1, atrial flutter: 5, atrial tachycardia: 2) in the maze (−) group.

In the maze (+) group, 20 patients were on antiarrhythmic medication (Table 4). Freedom from atrial tachyarrhythmia recurrence was 68% at 5 years and 51% at 10 years in the maze (+) group (Figure 1, *B*). No patients required postoperative surgical ablation, and 3 of 11 patients underwent catheter ablation for recurrent atrial tachyarrhythmia. Five of 6 patients with chronic AF before PVR experienced post-PVR recurrences of atrial arrhythmia (chronic AF: 3, paroxysmal AF: 1, and AT: 1). Among the 16 patients who underwent the right-sided maze procedure, 6 patients showed a recurrence of atrial tachyarrhythmia (chronic AF: 3, paroxysmal AF: 2, AFL: 1). Seven patients underwent pacemaker implantation for sick sinus syndrome or atrioventricular block greater than grade II.

Risk Analysis for Atrial Arrhythmia Incidence After PVR and Arrhythmia Surgery

The univariable Cox proportional-hazards model revealed that the factors with $P < .1$ were the RAVI, age at PVR, and a history of chronic AF in the maze (+) group. Right ventricular end-diastolic volume index and RVESVI

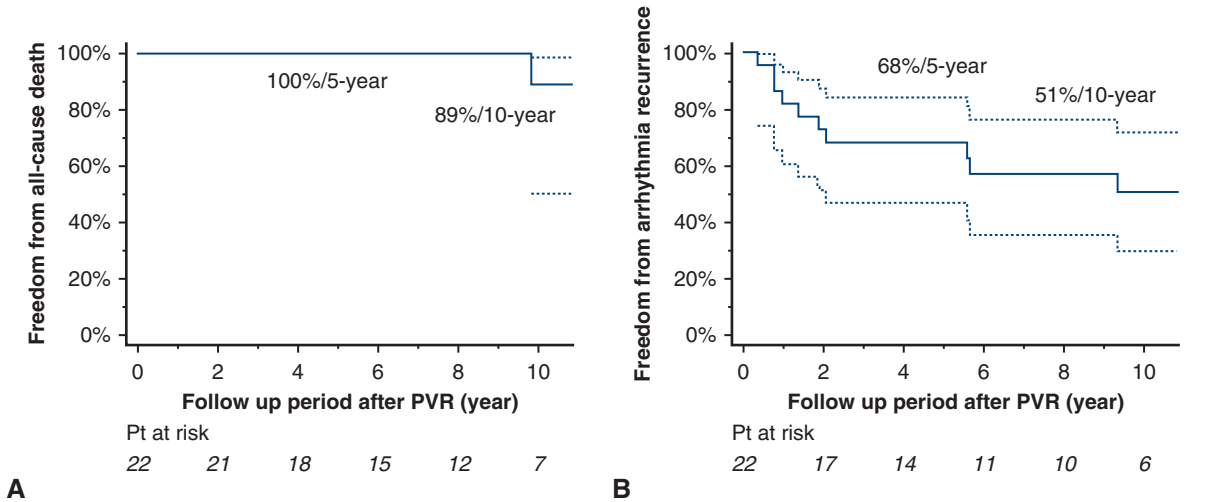

FIGURE 1. Kaplan–Meier analysis of freedom from all-cause death (A) and atrial tachyarrhythmia recurrence (B). The *dotted lines* represent the 95% confidence interval limits. *PVR*, Pulmonary valve replacement.

TABLE 4. Results of arrhythmia surgery in the maze (+) group

	Pre-PVR				At PVR		Post-PVR			
Pt	Atrial arrhythmia	AAD	ABL	SND	Procedure	PMI	Recurrence	AAD	ABL	PMI
1	Chronic AF	+	−	−	Biatrial maze	−	+ Chronic AF	+	−	+
2	Chronic AF	−	−	−	Biatrial maze	−	+ Chronic AF	+	−	+
3	Chronic AF	+	+	−	Biatrial maze	−	+ Chronic AF	+	−	−
4	Chronic AF	+	+	−	Biatrial maze	−	+ Paroxysmal AF	+	−	−
5	Chronic AF	−	−	−	Biatrial maze	−	+ AT	+	+	+
6	Chronic AF	+	+	−	Biatrial maze	−	− −	+	−	−
7	Paroxysmal AF	+	−	−	Rt-sided maze	−	+ Chronic AF	+	+	+
8	Paroxysmal AF	−	−	−	Rt-sided maze	−	+ Chronic AF	+	−	+
9	Paroxysmal AF	+	−	−	Rt-sided maze	−	+ Chronic AF	+	−	−
10	Paroxysmal AF	−	−	−	Rt-sided maze	−	+ Paroxysmal AF	+	−	+
11	Paroxysmal AF	+	−	−	Rt-sided maze	−	+ Atrial flutter	+	+	−
12	Paroxysmal AF	−	−	−	Rt-sided maze	−	− −	+	−	−
13	Paroxysmal AF	−	−	+	Rt-sided maze	+	− −	−	−	−
14	Paroxysmal AF	−	−	+	Rt-sided maze	+	− −	−	−	−
15	Paroxysmal AF	+	+	−	Rt-sided maze	−	− −	+	−	+
16	Paroxysmal AF	−	−	−	Rt-sided maze	−	− −	+	−	−
17	Paroxysmal AF	−	−	−	Rt-sided maze	−	− −	+	−	−
18	Paroxysmal AF	+	−	−	Rt-sided maze	−	− −	+	−	−
19	Atrial flutter	−	−	+	Rt-sided maze	+	+ Paroxysmal AF	+	−	−
20	Atrial flutter	−	−	−	Rt-sided maze	−	− −	+	−	−
21	Atrial flutter	−	−	−	Rt-sided maze	−	− −	+	−	−
22	AT	+	−	+	Rt-sided maze	+	− −	+	−	−

PVR, Pulmonary valve replacement; *Pt*, patient; *AAD*, anti-arrhythmic durg; *ABL*, catheter ablation; *SND*, sinus node dysfunction; *PMI*, pacemaker implantation; *AF*, atrial fibrillation; *AT*, atrial tachycardia; *Rt*, right.

were not associated with atrial arrhythmia recurrence in the maze (+) group. In the maze (–) group and in total 74 patients, RVESVI and RAVI were associated with atrial arrhythmia incidence after PVR (Table E1).

According to a multivariable Cox proportional-hazards model in the maze (+) group, RAVI was a significant risk factor for atrial arrhythmia recurrence (hazard ratio, 1.04; 95% confidence interval, 1.01-1.08, $P = .0133$; Table 5). RAVI did not correlate with RVEDP ($P = .34$).

A time-dependent ROC curve at 1 year after PVR revealed that the threshold of RAVI was 88 mL/m^2 (area under the curve = 0.861, sensitivity = 1, and specificity = 0.667). The median value of RAVI in 22 patients was 88 mL/m^2. The probability of atrial tachyarrhythmia recurrence, stratified by the value of the RAVI threshold, revealed that patients with a RAVI <88 mL/m^2 had a significantly greater recurrence-free rate of 83% at 5 years after surgery (Figure 2).

DISCUSSION

The main findings of this retrospective study are summarized herein. First, atrial tachyarrhythmia recurrence-free rates were 68% at 5 years and 51% at 10 years after PVR and concomitant arrhythmia surgery in patients with atrial arrhythmia history. Second, a multivariable Cox proportional-hazards model showed that a large RAVI was a significant risk factor for atrial tachyarrhythmia recurrence. Patients with a RAVI <88 mL/m^2 had a significantly greater recurrence-free rate of 83% at 5 years after surgery. Age at PVR, history of chronic AF, QRS duration, and TR grade were not risk factors for atrial tachyarrhythmia recurrence in this study (Figure 3, Video Abstract).

In patients late after TOF repair, not only ventricular but atrial arrhythmias are a major cause of morbidity and mortality and a common reason for hospitalization.[1,2,7,9,12-14,21] There are limited data on the results of the maze procedure simultaneous with PVR, according to the current guidelines, late after TOF repair.[2,6,9,12,22] Suture lines, areas of scar tissue, cannulation sites, and prosthetic materials from previous surgery might provide the anatomical substrate for re-entry tachyarrhythmias. Recent reports on the long-term results of the maze procedure in patients with ACHD, including TOF cases, revealed that freedom from atrial arrhythmias was 67% to 76% at 5 years' post-maze.[1,7] Although it is difficult to directly compare the

TABLE 5. Risk analysis for atrial tachyarrhythmia recurrence in maze (+) group

Characteristics	Univariable		Multivariable	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
RAVI	1.04 (1.01-1.08)	.0120	1.04 (1.01-1.08)	.0133
Age at PVR	1.05 (0.99-1.12)	.0636	1.05 (0.99-1.13)	.13
Chronic AF	3.0 (0.91-9.8)	.0724	2.3 (0.66-8.3)	.19
RVEDP	1.1 (0.96-1.25)	.13		
RVESVI	1.02 (0.99-1.04)	.15		
TR moderate or greater	2.4 (0.69-8.3)	.17		
LVEF <50%	0.47 (0.14-1.6)	.22		
RVEF <40%	2.1 (0.60-7.4)	.24		
Age at primary repair	1.06 (0.92-1.2)	.37		
QRS duration	0.99 (0.96-1.03)	.6		
RVEDVI	1.0 (0.99-1.02)	.65		

There are no missing values in the variables that were subjected to multivariable analysis. *HR*, Hazard ratio; *CI*, confidence interval; *RAVI*, right atrial volume index; *PVR*, pulmonary valve replacement; *AF*, atrial fibrillation; *RVEDP*, right ventricular end-diastolic pressure; *RVESVI*, right ventricular end-systolic volume index; *TR*, tricuspid regurgitation; *LVEF*, left ventricular ejection fraction; *RVEF*, right ventricular ejection fraction; *RVEDVI*, right ventricular end-diastolic volume index.

results due to differences in the proportion of diseases included in the study, atrial arrhythmia management strategy, and age of the target population, the results were comparable with our report, which included patients late after TOF repair only.

It remained unclear which parameters are risk factors for atrial arrhythmia recurrence in patients with late repair of TOF. In this study, the multivariable analysis revealed that RAVI enlargement was a risk factor for atrial tachyarrhythmia in patients with late repair of TOF who underwent PVR and atrial arrhythmia surgery. RAVI enlargement seems to be a phenotype of atrial remodeling in response to long-standing atrial volume and pressure loading. Although previous reports revealed a relationship between RAVI and arrhythmia late after PVR,[13,14,21] this is the first report stating that preoperative RAVI enlargement is associated with a risk of arrhythmia recurrence after PVR and arrhythmia surgery. It is preferable to plan for atrial arrhythmia surgery before increasing the RAVI for a better prognosis. This study suggested that concomitant maze procedures in patients with small RAVI might have a greater recurrence-free rate than the previously reported rate.

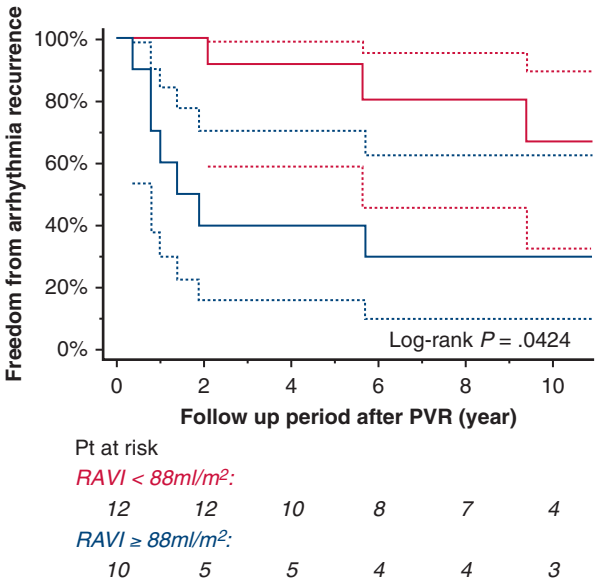

FIGURE 2. Kaplan–Meier analysis of freedom from the atrial tachyarrhythmia recurrence stratified by median right atrial volume index (*RAVI*). The *dotted lines* represent the 95% confidence interval limits. *PVR*, Pulmonary valve replacement.

This study showed that concomitant arrhythmia surgery was found to be more effective in patients with smaller RAVIs when PVR is required. RAVI should be included as an evaluated variable during follow-up, and PVR and concomitant arrhythmia surgery prior to excessive RAVI enlargement may reduce the incidence of morbidity. Not performing the maze procedure is an important treatment option for patients with excessive RAVI enlargement. The number of transcatheter pulmonary valve implantation (TPVI) procedures performed has been increasing in recent years. Maze procedures and surgical PVRs were effective in patients with smaller RAVIs. However, as shown in the results of this study, one strategy is to minimally invasively improve pulmonary valve function by performing TPVI in cases with excessive RAVI enlargement because a maze procedure is not expected to be effective. Therefore, a prospective multicenter study with a larger sample is needed to validate this study's results or to establish a better treatment strategy: the threshold regarding the degree of RAVI enlargement at which the maze procedure should not be performed, and TPVI is preferred.

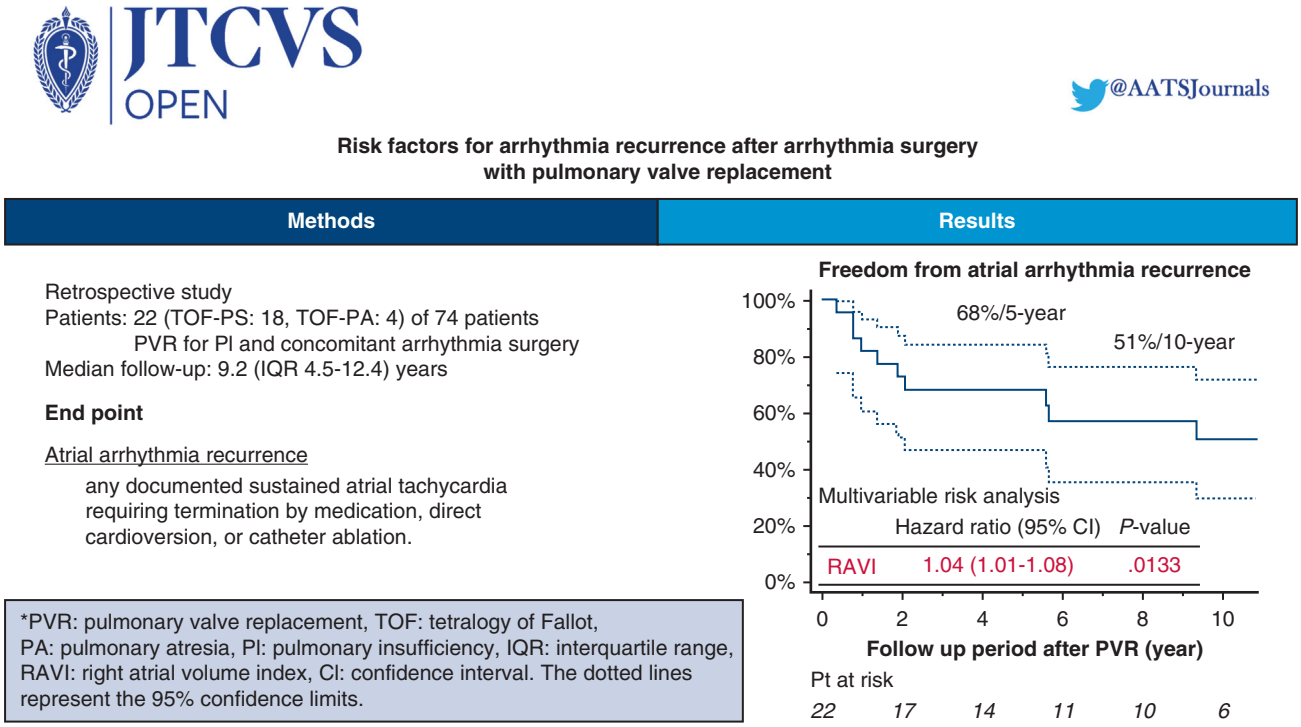

FIGURE 3. Summary of the study. The *dotted lines* represent the 95% confidence interval limits. *TOF*, Tetralogy of Fallot; *PS*, pulmonary stenosis; *PA*, pulmonary atresia; *PVR*, pulmonary valve replacement; *PI*, pulmonary insufficiency; *IQR*, interquartile range; *CI*, confidence interval; *RAVI*, right atrial volume index.

The etiology of RA dilation is important. Increased RA size has been reported to correlate with TR.[14] TR grade itself was not a significant risk factor in this study. The TR grade, as well as a duration of TR greater than moderate, may have a significant impact on RAVI. However, in this study, we evaluated only the TR grade in the preoperative PVR data, not including the duration. As for RV diastolic dysfunction, only RVEDP and right atrial pressure are shown in Table 2. For other RV diastolic dysfunction markers, it is difficult to evaluate further due to the lack of accurate data. RVEDP was not a significant risk factor and did not correlate with RAVI in this study. Other markers of RV diastolic dysfunction and duration of TR greater than moderate or high RVEDP should be examined in the future to determine the relation to RAVI and their impact on atrial arrhythmia recurrence.

In acquired cardiac disease, AF coexists with mitral valve disease or aortic valve disease. It has been reported that preoperative AF has a significantly greater risk of late mortality and adverse events, including heart failure and stroke.[10,23,24] A preoperatively enlarged LA dimension was associated with an increased risk of postoperative AF recurrence independently. Chronic pressure and volume load lead to LA remodeling and fibrosis in the atrium.[23] The same mechanism may be applied to the right side of the heart.

Regarding RA enlargement and the incidence of atrial fibrillation, AF generally originates from the pulmonary veins in the LA. LA dilatation was important for the incidence of atrial fibrillation. However, the LA volume index could not be evaluated because cardiac MRI was not performed in the dimensions necessary for estimating LA volume at our institution. In this study, left ventricular ejection fraction was lower, and the LVESVI was enlarged in the maze (+) group compared with the maze (−) group. Then, we can assume that LA was also affected to a certain extent. In contrast, there is a possibility of non-PV–triggered atrial fibrillation development. Previous studies have addressed the importance of non-PV triggers for AF initiation, and the reported incidence of non-PV triggers in PAF ranged from 3.2% to 62%.[25] A distinguishing feature of AF in patients with ACHD is the suspected presence of AF which is of right atrial origin, in contrast to typical adult-onset AF, which is of LA origin.[26] A possible cause could be adverse remodeling of atrial muscle due to the effects of RA pressure/volume loading associated with elevated RVEDP or volume loading such as TR. The mechanism should be evaluated by further research.

For patients with right-sided congenital heart disease, the right-sided maze procedure was proposed based on the idea that the LA was relatively unaffected in patients with right-sided congenital heart disease.[16,27] The limitation of the creation of ablation lines to the supposedly affected atrium led to simplification, shortening of the original procedure, and reduced complication risk.[16,27] In patients with atrial septal defect, the biatrial maze procedure was preferred in previous studies.[28] However, there are limited data on patients with repaired TOF, and we could not conclude whether the biatrial maze should be performed in all patients. In this study, we performed a biatrial maze procedure for chronic AF and a right-sided maze procedure for paroxysmal atrial tachyarrhythmia considering operation time, concomitant procedures, and anatomical features. Six of 16 patients who underwent a right-sided maze procedure experienced atrial tachyarrhythmia recurrence after surgery. Further large-scale studies are warranted to determine the optimal selection of whether the biatrial maze procedure may be the preferred strategy for the surgical treatment of paroxysmal or chronic AF in this population.

Catheter ablation for atrial tachyarrhythmia in patients with ACHD is one of the most important treatment options. However, previous reports demonstrated that catheter ablation for patients with ACHD had a limited success rate for a single procedure (1 year: 63%; 5 years: 22%) and that multiple procedures were necessary.[29] One possible reason for this is that patients with ACHD have a continuous load on the ventricles and atria due to residual region and anatomical predisposition. It is essential to understand the characteristics of both catheter ablation and surgical ablation and perform the treatment for arrhythmia appropriately in patients with repaired TOF.

This study had several limitations, particularly its small sample size and retrospective, long-term, single-center design. The RAVI threshold was determined using time-dependent ROC analysis with a small sample size. Therefore, there may be insufficient statistical power to provide robust evidence. This study included patients who underwent different arrhythmia surgeries: full maze or right-sided maze procedures. We used 2 imaging methods for RAVI evaluation: contrast-enhanced CT imaging or MRI in patients with contraindications to CT imaging.

In addition, patients who required pacemaker implantation were included in this study. The possibility that this inclusion increased the recurrence-free survival cannot be ruled out. Holter electrocardiography was performed in selected patients with symptoms, and device interrogation was limited to patients after PM implantation. Therefore, the incidence of arrhythmia recurrence may be underestimated. Multicenter prospective studies with a larger sample are required to validate the risk factors for atrial arrhythmia recurrence after surgery and the prognostic importance of the presented cut-off points.

In conclusion, after PVR with atrial arrhythmia surgery, the atrial arrhythmia recurrence rates were high in patients late after TOF repairs. Preoperative RAVI needs to be considered when planning the timing of PVR with atrial arrhythmia surgery.

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: tetralogy of Fallot, atrial tachyarrhythmia, maze procedure, recurrence rate, pulmonary valve replacement

TABLE E1. Analysis of the association between the incidence of atrial arrhythmia and RA size or RV indexed size

	RVEDVI		RVESVI		RAVI	
Patients category	**HR (95% CI)**	***P* value**	**HR (95% CI)**	***P* value**	**HR (95% CI)**	***P* value**
n = 74						
Total	1.01 (0.99-1.002)	.1	1.02 (1.00-1.03)	.007	1.04 (1.02-1.06)	<.001
n = 52						
De novo	1.01 (0.99-1.03)	.052	1.02 (1.00-1.04)	.034	1.04 (1.02-1.07)	<.001
n = 22						
Recurrence	1 (0.99-1.02)	.65	1.02 (0.99-1.04)	.15	1.04 (1.01-1.08)	.012

RVEDVI, Right ventricular end-diastolic volume index; *RVESVI*, right ventricular end-systolic volume index; *RAVI*, right atrial volume index; *HR*, hazard ratio; *CI*, confidence interval.