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Cardiovascular Surgery

Fate of Preoperative Atrial Fibrillation After Correction of Atrial Septal Defect

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Background: Atrial fibrillation (AF) is common among adult patients with an atrial septal defect (ASD). Catheter ablation or the Maze procedure can be considered for AF before or concurrently with ASD closure. However, the fate of preoperative AF is not well established. This study examined the postoperative course of patients with AF before undergoing ASD correction.

Methods and Results: The 471 patients (131 men, 42±14 years) underwent transcatheter closure (n=237, 50%) or surgical repair (n=234, 50%) of an ASD. ECG and Holter monitoring were used to document preoperative and postoperative AF. Forty patients had AF before transcatheter closure (n=10) or surgical repair (n=30) of the ASD. During the follow-up period of 44±28 months, excluding 15 patients who had undergone surgical repair with the Maze procedure, sinus rhythm (SR) was maintained in 7 (88%) of 8 patients with paroxysmal AF. However, only 3 (18%) of 17 patients with persistent AF maintained SR. Among the 15 patients treated with the Maze procedure, 12 (80%) maintained SR.

Conclusions: Hemodynamic correction of ASD was effective in conversion to SR in most patients with preoperative paroxysmal AF. However, the Maze procedure or transcatheter ablation before ASD correction needs to be considered for the treatment of AF in patients with persistent AF. (*Circ J* 2013; **77:** 109–115)

Key Words: Atrial fibrillation; Atrial septal defect; Hemodynamic correction; Maze procedure

The natural history of adults with atrial septal defect (ASD) is characterized by an increased risk for the development of atrial arrhythmias, especially atrial fibrillation (AF).[1] AF is the most common arrhythmia related to ASD in patients older than 40 years, and its incidence tends to increase with age.[2–4] The incidence of AF is as high as 52% in patients aged 60 years and older.[4] AF usually causes substantial symptoms in ASD patients because of both tachycardia and the underlying hemodynamics governed by impaired left ventricular (LV) filling and reduced systemic cardiac output. Freedom from postoperative AF can best be achieved when ASD closure is completed before patients reach 40 years of age.[5] Long-term observational studies have shown that early surgical ASD closure (before age 25) can promise a survival similar to that of a normal population.[1] However, many ASDs are discovered late because of the absence of symptoms or physical findings, leading to delay of definite therapy until the patient becomes an adult. Therefore, a significant portion of patients have preoperative AF when they undergo correction of ASD. However, the optimal management for patients with preoperative AF before ASD closure is still open to debate.

Surgical attempts to eliminate AF during ASD closure remain controversial because of the technical complexity of the procedure.[6,7] Recently, Giamberti et al suggested adding intraoperative radiofrequency ablation during surgical closure of ASD in all adult ASD patients with arrhythmias.[8] Instead of a surgical approach, catheter ablation of the AF substrate may be attempted before ASD correction because the bulky occluder device may create a significant disturbance to transseptal intervention through the interatrial septum.[9] However, the prognosis for preoperative AF after correction of ASD has not been completely revealed. This study examined the course of preoperative AF after correction of ASD and/or after a concurrent Maze operation.

Methods

Study Population

We retrospectively analyzed consecutive 471 adult patients ≥18 years old who underwent transcatheter closure (n=237,

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Table 1. Comparison of Baseline Characteristics of ASD Patients With and Without Preoperative AF

	Total (n=471)	No preoperative AF (n=431)	Preoperative AF (n=40)	P value
Male	131 (28%)	109 (25%)	22 (55%)	<0.001
Age (years)	42.4±14.2 (18–76)	41.0±13.5 (18–76)	57.8±12.6 (23–74)	<0.001
Type of ASD correction				0.001
Percutaneous	237 (50%)	227 (53%)	10 (25%)	
Surgical	234 (50%)	204 (47%)	30 (75%)	
Hypertension	93 (20%)	86 (20%)	7 (18%)	0.73
Diabetes mellitus	34 (7%)	29 (7%)	5 (13%)	0.18
Previous stroke	9 (2%)	6 (1%)	3 (8%)	0.08
Qp/Qs	3.0±1.2 (1.6–5.6)	2.7±0.9 (2.0–3.4)	3.1±1.2 (1.6–5.6)	0.21
Echocardiography				
ASD size (mm)	22.1±9.7 (6–53)	22.1±9.0 (6–47)	22.3±12.1 (6–53)	0.93
LA size (mm)	43.7±7.9 (28–61)	40.9±6.5 (28–59)	50.5±6.8 (32–61)	0.001
LVEF (%)	65.6±9.0 (31–84)	66.2±8.9 (31–82)	63.7±9.5 (42–84)	0.12
LVEDD (mm)	41.6±5.7 (30–59)	41.0±5.5 (30–59)	43.4±6.2 (30–58)	0.03
LVESD (mm)	27.1±4.9 (15–45)	26.6±4.5 (17–45)	28.8±5.7 (15–38)	0.03
RVSP (mmHg)	45.4±16.0 (17–117)	45.1±16.7 (17–117)	46.3±14.1 (22–100)	0.67

Numbers in parentheses represent percentage or range.
AF, atrial fibrillation; ASD, atrial septal defect; EF, ejection fraction; LA, left atrial; LV, left ventricular; LVEDD, LV end-diastolic dimension; LVESD, LV end-systolic dimension; Qp/Qs, ratio of pulmonary to systemic blood flow; RVSP, right ventricular systolic pressure.

Table 2. Multivariate Logistic Analysis to Determine Independent Risk Factors for Preoperative AF

	OR	95% CI	P value
Univariate analysis			
Larger LA (>45 mm)	9.1	3.3–24.8	<0.001
Older age (>40 years)	8.8	3.1–25.0	<0.001
Male sex	3.6	1.9–7.0	<0.001
Multivariate analysis			
Larger LA	5.9	1.8–19.2	0.003

AF, atrial fibrillation; CI, confidence interval; LA, left atrium; OR, odds ratio.

50%) or surgical repair of ASD (n=234, 50%) between January 2001 and May 2010 at Severance Cardiovascular Hospital, Seoul, Korea. Among the different types of ASD, only patients with the ostium secundum type of ASD were included in this study. The indication for ASD closure in all patients was a hemodynamically substantial left-to-right atrial shunt [ratio of pulmonary to systemic blood flow (Qp/Qs) >1.5] or the presence of right ventricular (RV) volume overload.[10] The therapeutic modality of ASD correction (percutaneous or surgical) was chosen at the discretion of the physician. Generally, if the defect was too large or the margins of the orifice were not sufficient to accommodate the edges of the closing device, ASD was closed by surgical repair.[11,12] In a patient with a concomitant cardiac lesion, ASD was closed at the time of surgery. Transcatheter closure of ASD was performed using the Amplatzer septal occluder (AGA Medical Corporation; Plymouth, MN, USA). Surgical repair was performed by means of cardiopulmonary bypass with the use of bicaval and ascending aortic cannulation. If the patients had medically refractory symptoms related to AF, the Maze procedure was performed as an additional surgical option in those who were scheduled to undergo surgical repair of ASD with their informed consent.[13] Of the 15 patients undergoing surgical treatment for AF, the biatrial approach (Cox-Maze III procedure) was used in 14 patients and a right-sided Maze procedure (ablation lines on the right atrium only) was carried out in 1 patient. Radiofrequency ablation and cryoablation were performed in 12 and 3 patients, respectively. Transesophageal echocardiography was performed in all patients before the procedure or surgery, and left atrial (LA) thrombi were not detected in any of the patients.

The number of male patients was 131 (28%), and the mean age was 42±14 years (range, 18–76 years); 40 patients had AF before undergoing correction of the ASD. In all patients, preoperative evaluation included clinical history and examination, routine laboratory tests, a standard 12-lead ECG, 24-h ambulatory Holter monitoring, echocardiographic study, and cardiac catheterization. Preoperative AF was confirmed by 12-lead ECG or Holter monitoring. Holter monitoring was performed a mean of 1±2 months before the procedure. The paroxysmal AF (PAF) group included patients with a history of 1 or more episodes of self-terminating AF that lasted less than 7 days. The persistent AF (PeAF) group consisted of patients who had an AF episode that either lasted longer than 7 days or required termination by cardioversion, either with drugs or by direct current cardioversion. The research protocol conformed to the guiding principals of the Declaration of Helsinki and was approved by the institutional review board and informed consent was given by all patients.

Follow-up

All patients had in-hospital continuous ECG monitoring for at least 48 h after transcatheter closure or surgical repair of the ASD. After the ASD correction, all patients were clinically followed up at 1 month with ECG and 24-h ambulatory Holter monitoring and thereafter they had ECG follow-up every 3 months. In patients with arrhythmia before ASD correction, they additionally had 24-h ambulatory Holter monitoring every year. Patients were asked to visit the outpatient clinic at any

Table 3. Comparison of Baseline Characteristics According to the Type of Preoperative AF

	Paroxysmal AF (n=11)	Persistent AF (n=29)	P value
Male	9 (82%)	13 (45%)	0.07
Age (years)	50.7±15.3	60.5±10.5	0.03
Duration of AF (months)	40.4±42.9	48.1±47.4	0.64
Qp/Qs	2.8±1.5	3.2±1.1	0.32
Echocardiography			
LA size (mm)	46.8±4.8	51.9±7.0	0.07
ASD size (mm)	19.0±12.6	23.4±12.0	0.63
LVEF (%)	62.5±12.9	64.1±8.0	0.52
LVEDD (mm)	44.5±4.4	43.0±6.8	0.51
LVESD (mm)	29.8±5.6	28.3±5.7	0.47
RVSP (mmHg)	39.7±10.6	48.8±14.6	0.07
Residual shunt	1 (9%)	2 (7%)	1.00
Medication			
Antiarrhythmic drug	4 (36%)	4 (14%)	0.18
Digoxin	4 (36%)	21 (72%)	0.07
β-blocker	3 (27%)	9 (31%)	1.00
Calcium-channel blocker	5 (46%)	8 (28%)	0.45
ACEI/ARB	6 (55%)	13 (45%)	0.58
Statin	2 (18%)	3 (10%)	0.60

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin-receptor blocker. Other abbreviations as in Tables 1,2.

time if they had any symptoms suspicious of arrhythmia, such as palpitation, chest discomfort or irregular heartbeats, and were checked by 12-lead ECG and 24-h Holter monitoring. In the case of AF recurrence, the patients were referred to electrophysiologists and antiarrhythmic drug (AAD) treatment (class Ic or amiodarone), followed by electrical cardioversion, was instituted. The relevant clinical data and echocardiographic findings were also evaluated at regular visits.

Statistical Analysis

Continuous data are expressed as mean±SD and normality tests were performed for each variable to determine whether or not a data set was well-modeled by normal distribution. The baseline characteristics of the 2 groups were compared using Student's t-test for continuous variables, and the chi-square test and Fisher's exact test for categorical variables. Variables with P<0.10 in the univariate analysis were entered into the multivariate logistic regression model to determine independent predictors for maintaining sinus rhythm (SR) after ASD closure. Statistical significance was established at P<0.05. Statistical analysis was performed by SPSS version 18.0 (SPSS Inc, Chicago, IL, USA).

Results

Baseline Characteristics of Patients With Preoperative AF

A total of 40 (9%) patients had AF before undergoing ASD correction. Table 1 compares the baseline clinical characteristics of the patients with and without preoperative AF. Compared with the patients without preoperative AF, those with preoperative AF were more likely to be male (55 vs. 25%, P<0.001) and older (58±13 vs. 41±14 years, P<0.001). More patients with preoperative AF were treated with surgical repair than those without AF (75 vs. 47%, P=0.001). Patients with preoperative AF also had a larger LA (anteroposterior dimension, 51±7 vs. 41±7 mm, P<0.001), LV end-diastolic dimension (LVEDD, 43±6 vs. 41±6 mm, P=0.03), and LV end-systolic dimension (LVESD, 29±6 vs. 27±5 mm, P=0.03) than those without AF. The ASD size and the prevalence of comorbidities did not differ significantly between the 2 groups.

Table 2 shows the results of the univariate and multivariate analyses of predictors of preoperative AF. In the univariate analysis using clinical and echocardiographic variables and comorbid conditions, larger LA size (anteroposterior dimension >45 mm), older age (>40 years), and male sex were associated with a higher risk of preoperative AF. However, in the multivariate analysis, larger LA was the only significant independent predictor of preoperative AF [odds ratio 5.9, 95% confidence interval 1.8 to 19.2, P=0.003].

Management and Follow-up Results of Patients With AF

Table 3 compares the patients' baseline characteristics according to the type of preoperative AF. Among 40 patients with preoperative AF, PAF and PeAF were observed in 11 (28%) and 29 (72%), respectively. Patients with PeAF were older than those with PAF (61±11 vs. 51±15 years, P=0.03) and tended to have a larger LA (52±7 vs. 47±5 mm, P=0.07) and higher RV systolic pressure (49±15 vs. 40±11 mmHg, P=0.07), although it was not statistically significant.

Figure 1 shows the management and follow-up results in patients with preoperative AF. Patients were clinically followed up postoperatively for a mean duration of 45±28 months (range, 7–107 months). In total, 3 patients with preoperative PAF and 12 patients with PeAF were managed with surgical ASD repair and a concurrent Maze operation. Among the remaining 8 preoperative PAF patients without a Maze operation, 1 (12%) patient was treated with surgical repair, and 7 (88%) patients were treated with transcatheter closure of the ASD. Excluding 12 patients with a Maze operation, 17 patients with preoperative PeAF were managed with surgical repair (n=14, 82%) and transcatheter closure of the ASD (n=3, 18%). After correction of the ASD, SR was maintained in 7 (88%) patients with preoperative PAF, including 3 patients managed with AADs (2 on flecainide and 1 on propafenone). Interestingly, SR was

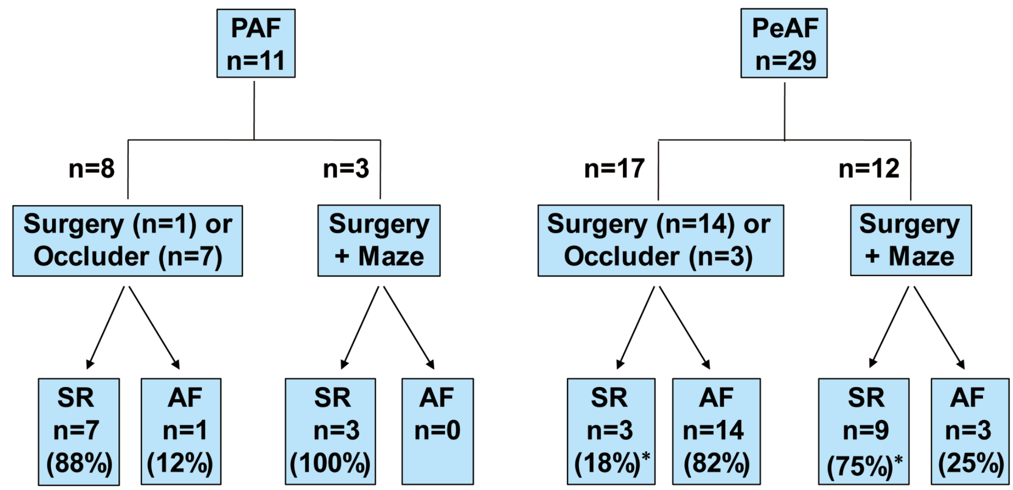

Figure 1. Management and follow-up results in patients with preoperative atrial fibrillation (AF). After correction of an atrial septal defect (ASD) without concurrent Maze procedure, 7 (88%) of 8 preoperative PAF patients maintained sinus rhythm (SR) compared with 3 (18%) of 17 PeAF patients. Meanwhile, 9 (75%) of 12 PeAF patients maintained SR after surgical ASD repair with a Maze procedure. Compared with ASD repair only, concomitant Maze procedure had a higher success rate of maintaining SR in preoperative PeAF patients (*P=0.006). PAF, paroxysmal AF; PeAF, persistent AF; Surgery, surgical ASD repair (non-Maze procedure); Occluder, transcatheter ASD occlusion.

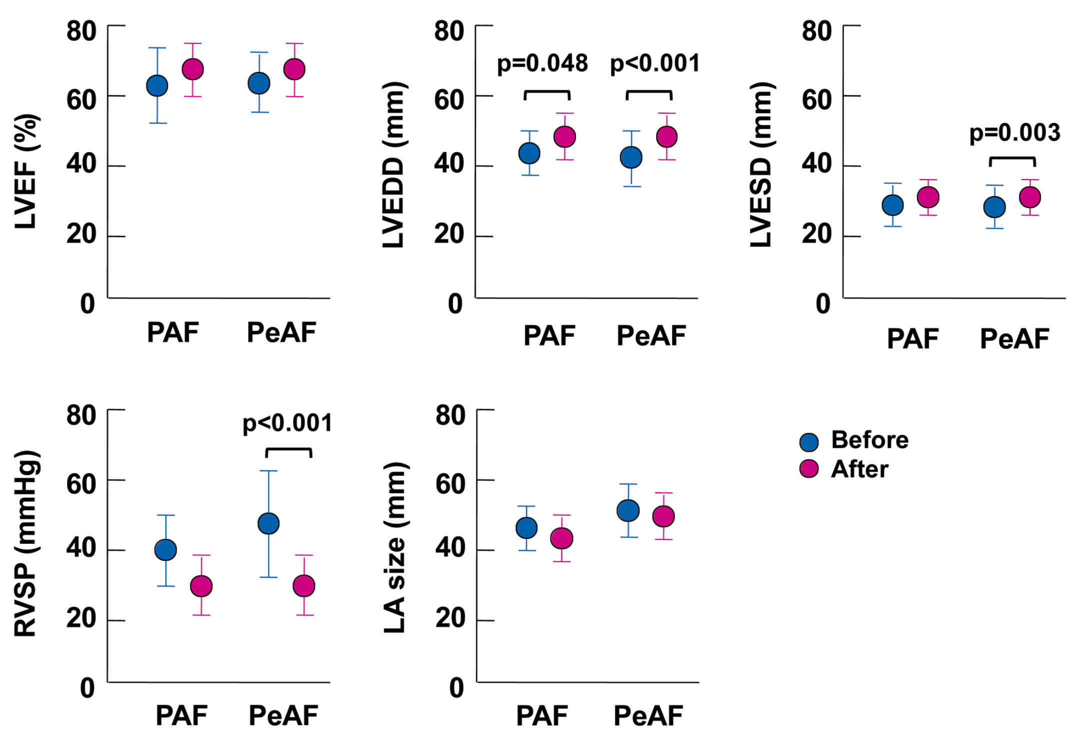

Figure 2. Comparison of echocardiographic parameters before and after atrial septal defect correction according to the type of preoperative atrial fibrillation (AF). PAF, paroxysmal AF; PeAF, persistent AF; LVEF, left ventricular ejection fraction; LVEDD, left ventricular end-diastolic dimension; LVESD, left ventricular end-systolic dimension; RVSP, right ventricular systolic pressure; LA, left atrium.

Table 4. Comparison of Baseline Characteristics Between Patients Maintaining SR and Those With AF During Follow-up After ASD Correction Alone

	SR (n=10)	AF (n=15)	P value
Male	8 (80%)	5 (33%)	0.04
Age (years)	57.1±11.4	62.1±14.0	0.36
Preoperative type of AF (paroxysmal)	7 (70%)	1 (7%)	0.002
Duration of AF (months)	24.6±27.9	60.0±53.7	0.042
Percutaneous closure	7 (70%)	3 (20%)	0.03
Qp/Qs	2.4±0.5	3.2±0.8	0.013
Echocardiographic parameters			
ASD size (mm)	18.9±7.4	19.7±14.2	0.87
LA size (mm)	47.8±6.4	51.6±7.9	0.26
LVEF (%)	63.7±8.3	65.9±7.0	0.49
LVEDD (mm)	42.5±5.7	43.9±5.6	0.56
LVESD (mm)	28.3±5.0	28.7±4.6	0.85
RVSP (mmHg)	43.6±11.7	47.1±18.4	0.60
Residual shunt	0 (0%)	2 (13%)	0.50
Percent change in echocardiographic parameters after ASD correction			
ΔLA size	–7.8±12.1%	–5.0±7.2%	0.54
ΔLVEF	8.9±16.5%	2.2±11.5%	0.28
ΔLVEDD	12.2±13.5%	7.0±11.7%	0.35
ΔLVESD	7.1±15.1%	8.8±15.4%	0.79
ΔRVSP	–16.9±18.9%	–22.1±24.2%	0.59
Medication			
Antiarrhythmic drugs	3 (30%)	0 (0%)	0.052
Digoxin	3 (30%)	14 (93%)	0.002
β-blocker	2 (20%)	5 (33%)	0.66
Calcium-channel blocker	4 (40%)	6 (40%)	1.00
ACEI/ARB	6 (60%)	6 (40%)	0.43
Statin	2 (20%)	2 (13%)	1.00

SR, sinus rhythm. Other abbreviations as in Tables 1,3.

maintained in only 3 (18%) preoperative PeAF patients. Not one of the 14 PeAF patients still remaining with AF experienced a change after ASD repair to the less troublesome condition of PAF.

All 3 PAF patients who were managed with surgical ASD repair and a concurrent Maze procedure maintained SR. Meanwhile, 9 of 12 PeAF patients, who were managed with surgical ASD repair and a concurrent Maze procedure, maintained SR including 5 patients treated with AADs (4 on amiodarone, 1 on flecainide). Compared with ASD repair only, preoperative PeAF patients undergoing a concomitant Maze procedure had a higher success rate of maintaining SR (18 vs. 75%, P=0.006). There was no significant difference in the clinical characteristics of patients treated by ASD repair only and those by concomitant Maze procedure (unpublished data).

Reverse Structural Remodeling After ASD Correction

Figure 2 shows the changes in the echocardiographic parameters after ASD correction according to the type of preoperative AF. Patients showed significant hemodynamic improvements in echocardiography, which was performed 1 month after ASD correction. Although the RV systolic pressure decreased from 39.7±10.6 to 32.0±8.8 mmHg (P=0.078) in PaAF patients, it was decreased from 48.8±14.6 to 31.8±8.8 mmHg (P<0.001) in those with PeAF. The decrease in RV systolic pressure was much larger in patients with PeAF than in those with PAF (−32±19% vs. −15±26%, P=0.03). However, the changes in other parameters showed no difference according to the type of preoperative AF.

Characteristics of Patients With SR

Excluding the 15 patients managed with a Maze procedure, the clinical characteristics of the patients maintaining SR (n=10) and those still in AF (n=15) after correction of ASD are compared in Table 4. Patients maintaining SR were more likely to be male (80 vs. 33%, P=0.04), and to have preoperative PAF (70 vs. 7%, P=0.002), shorter duration of preoperative AF (25±28 vs. 60±54 months, P=0.042) and lower Qp/Qs (2.4±0.5 vs. 3.2±0.8, P=0.013) than those still in AF. However, the changes in the echocardiographic parameters showed no significant difference between patients maintaining SR and those with AF after ASD repair.

Atrial Tachyarrhythmias After ASD Correction

During the follow-up period, among the 15 patients who had undergone ASD surgical repair with the Maze procedure, 2 and 1 patients experienced typical atrial flutter and atrial tachycardia, respectively. These 3 (20%) patients were successfully managed by catheter ablation. Among 25 patients with preoperative AF who had undergone ASD correction only, atrial flutter occurred in 2 (8%) patients and was successfully managed by catheter ablation.

In 431 patients without preoperative AF, 13 (3%) and 2 (0.5%) patients had newly developed AF and atrial flutter, respectively, during the follow-up period. The mean age of these patients was 55±11 years (range, 37–69 years). Surgical repair was performed in 11 (5%) patients and transcatheter closure in 4 (2%) (P=0.04). All cases of atrial flutter occurred in surgical patients.

Discussion

In the present study, we examined the clinical course of preoperative AF after correction of an ASD. The first major finding of this study was that SR was maintained after ASD correction in most patients with preoperative PAF, but not in those with preoperative PeAF. Second, a concurrent Maze procedure helped patients with preoperative PeAF maintain SR. Our findings suggest that in patients with preoperative PeAF a concurrent Maze procedure or transcatheter ablation before ASD correction needs to be considered for the treatment of AF.

ASD and AF

A long-standing left-to-right shunt across an ASD causes volume overload of the RA and RV, subsequently leading to atrial enlargement and RV dilatation and dysfunction.[4,5,14] Chronic atrial enlargement increases vulnerability to atrial arrhythmias and atrial electrical remodeling occurs in response to chronic atrial stretch.[15–17] AF also induces electrical and structural remodeling.[15,18,19] The present study also showed that preoperative AF was closely related to both LA and LV enlargement, consistent with previous studies. These results support early correction of ASD as a preventative strategy against AF.

Reverse Remodeling and SR After ASD Correction

In this study, the type of preoperative AF was associated with recovery of SR in preoperative AF patients. Correction of ASD prevented recurrence of AF in most patients with PAF. This can be explained by the potential antiarrhythmic effect of ASD correction. After ASD correction, the left-to-right shunt ceases and as a result, RA and RV volume overload is relieved, while LV volume is significantly increased and LA volume slightly reduced. Such cardiac remodeling occurs quite quickly; it becomes apparent within 24 h and continues for at least 1 year.[20,21] The correction of hemodynamic abnormalities initiates structural and electrophysiological reverse remodeling processes.[22–25] Most patients with PeAF remained with AF and did not experience a change to the less troublesome condition of PAF even after ASD correction. These findings suggest that hemodynamic correction of ASD alone is not enough to reverse structural and electrical remodeling in patients with preoperative PeAF. However, no difference was observed in the degree of reduction in the size of the LA between PAF and PeAF patients in this study.

Effect of Concurrent Maze Operation on Maintenance of SR

A concurrent Maze operation was highly effective in maintaining SR in patients with preoperative AF, even in those with PeAF. Therefore, this strategy needs to be considered in ASD patients with PeAF, if they are to undergo surgical repair of an ASD. On the other hand, an aggressive concurrent Maze procedure or transcatheter ablation before ASD correction need not be considered in patients with preoperative PAF. However, we could not confirm the effect of catheter ablation before ASD repair because we did not perform it for PeAF before correction of the ASD. The outcome of the Maze procedure and catheter ablation for PeAF is not the same. Compared with catheter ablation, the Maze procedure results in greater freedom from AF during follow-up.[26]

Atrial Tachyarrhythmia After ASD Correction

A study by Silversides et al has shown that patients without a history of arrhythmia have a low incidence of atrial tachycardia during early (6%) and intermediate (1%/year) follow-up after ASD closure.[27] Atrial tachycardia after Maze procedure might be a problem. In the present study, patients who were treated with a Maze procedure showed a tendency toward a higher incidence of newly developed atrial tachycardia than those without a Maze procedure. However, the number of patients with newly developed atrial tachycardia was not enough to define the relationship between the Maze procedure and atrial tachycardia.

Although the accurate mechanism of early postoperative atrial tachyarrhythmia in patients undergoing surgical treatment is still unclear, the atriotomy scar or atrial patches serve as reentrant circuits.[28] After ASD correction with an occluder device, mechanical irritation by the device can account for the development of postoperative atrial tachyarrhythmia.[29,30] The residual shunt and postoperative inflammation also may contribute to new development of atrial tachyarrhythmia.[30] Nevertheless, early postoperative atrial tachyarrhythmias are often transient and usually terminate within the first several weeks after surgery.[31]

Study Limitations

First, although we evaluated a large number of ASD patients with long-term follow-up, the number of patients with preoperative AF was relatively small and all the ASD repairs were performed at a single institution. The types of treatments were also not randomly assigned. Therefore, there might be a selection bias between patients treated with a percutaneous procedure and those with surgical repair. However, this study revealed the clinical course of preoperative AF among patients who underwent ASD correction in a larger population than in previous studies.[32,33] Therefore, our findings need to be confirmed in a larger multicenter trial. Second, the period of continuous monitoring after ASD closure was not long enough to confidently verify the early fate of preoperative AF. Although all patients had in-hospital continuous ECG monitoring for at least 48 h after ASD correction, continuous recording for a longer period would have provided more precise information and insight into the effect of ASD correction on the early occurrence of AF.[34,35] In addition, we often experience asymptomatic cases of AF and to detect these, 24-h Holter monitoring and 3-month visits with standard ECG check-up might not be enough. Finally, medication was not properly controlled in the preoperative stage. Such a therapeutic bias may influence the postoperative AF burden.

Conclusion

Most of the present patients with preoperative PAF maintained SR only after correction of ASD. However, hemodynamic correction of ASD alone was not wholly effective in eliminating AF in patients with preoperative PeAF. A concurrent Maze operation was highly effective in maintaining SR in patients with PeAF. Therefore, concurrent Maze operation or transcatheter ablation before ASD correction needs to be considered in patients with preoperative PeAF.

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Disclosures

None.

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