

## Arrhythmia surgery for atrial fibrillation associated with atrial septal defect: Right-sided maze versus biatrial maze

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**Background:** Although it has been inferred that a biatrial maze procedure for atrial fibrillation in left-sided heart lesions may lead to better outcomes compared with a limited left atrial lesion set, it remains controversial whether the biatrial maze procedure is superior to the right atrial maze procedure in right-sided heart lesions.

**Methods:** A retrospective review was performed for 56 adults who underwent surgical closure of atrial septal defect and various maze procedures for atrial fibrillation between June 1998 and February 2011. The median age at operation was 59 years (range, 34-79 years). Clinical manifestations of atrial fibrillation were paroxysmal in 8 patients, persistent in 15 patients, and long-standing persistent in 33 patients. A right atrial maze procedure was performed in 23 patients (group 1), and a biatrial maze procedure was performed in 33 patients (group 2). Treatment failure was defined as atrial fibrillation recurrence, development of atrial flutter or other types of atrial tachyarrhythmia, or implantation of a permanent pacemaker. The Cox proportional hazards model was used to identify risk factors for decreased time to treatment failure.

**Results:** During the median follow-up period of 49 months (range, 5-149 months), there was no early death and 1 late noncardiac death. On Cox survival model, group 1 showed a significantly decreased time to treatment failure in comparison with group 2 (hazard ratio, 5.11; 95% confidence interval, 1.59-16.44;  $P = .006$ ). Maintenance of normal sinus rhythm without any episode of atrial fibrillation recurrence at 2 and 5 years postoperatively was 57% and 45% in group 1, respectively, and 82% and 69% in group 2, respectively.

**Conclusions:** Left-sided ablation in addition to a right atrial maze procedure leads to better electrophysiologic outcome in atrial fibrillation associated with atrial septal defect. (*J Thorac Cardiovasc Surg* 2013;145:648-55)

 Supplemental material is available online.

The natural course of an unrepaired atrial septal defect (ASD) is frequently complicated by the development of atrial fibrillation (AF), and the incidence of ASD-associated AF correlates strongly with age.<sup>1,2</sup> Because uncontrolled AF increases the risk of thromboembolism and cerebral stroke, it is of the utmost importance to restore normal sinus rhythm (NSR) on ASD closure for an improved long-term outcome.<sup>3,4</sup> However, there have

been controversies over the appropriate surgical strategies for the elimination of AF in this subset. The Cox-maze procedure, which was originally developed for the treatment of stand-alone AF<sup>5</sup> and AF associated with mitral valvular heart diseases,<sup>3,6-10</sup> began to be used for right-sided heart diseases in the mid-1990s.<sup>3,11</sup> Prompted by a report regarding an exclusive left atrial lesion set for AF associated with mitral stenosis,<sup>6</sup> the Mayo Clinic proposed a new surgical approach (ie, exclusive right atrial lesion set or right atrial maze procedure [RA]) for AF associated with congenital heart diseases affecting the right side of the heart, such as Ebstein's anomaly or ASD.<sup>12</sup> The rationale for an exclusive RA was based on the assumption that the left atrium in right-sided heart diseases is relatively exempt from structural changes caused by pressure and volume overload. It was also asserted that the RA had a number of benefits compared with the cut-and-sew Cox-maze procedure, including shorter operating time, minimal dissection of the heart, avoidance of scar formation in the left atrial wall, and lower risk of postoperative bleeding or systemic thromboembolism from multiple suture lines.

Since the first clinical report in the late 1990s,<sup>12</sup> exclusive right atrial ablation began to be performed for right-sided heart lesions more often than the conventional Cox-maze procedure in many congenital cardiac programs because of

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### Abbreviations and Acronyms

AF	= atrial fibrillation
ASD	= atrial septal defect
BA	= biatrial maze procedure
ECG	= electrocardiogram
NSR	= normal sinus rhythm
PVI	= pulmonary vein isolation
RA	= right atrial maze procedure
TR	= tricuspid regurgitation

institutional bias or individual surgeon's preference. Our program also adopted an exclusive right-sided ablation strategy for AF in ASD starting in 1998. With the frequent use of an exclusive right-sided ablation strategy (Figure E1), we have inferred that the incidence of AF recurrence after the RA for AF associated with ASD seemed higher than after the biatrial maze procedure (BA). Furthermore, the potential advantages of the RA over the cut-and-sew Cox-maze procedure, as listed earlier, have been undermined by the use of alternative energy sources, such as cryothermia and microwave thermal injury. With a brief transitional period of simply adding pulmonary vein isolation (PVI) to the RA, we recently performed a full BA more frequently for AF associated with ASD. In this study, we sought to determine whether a full biatrial lesion set is superior to the exclusive right atrial maze procedure for ASD-related AF.

### PATIENTS AND METHODS

We retrospectively reviewed the medical records of 56 adults who underwent surgical closure of ASD (ostium secundum type in 55 and ostium primum type in 1) and various maze procedures for AF between June 1998 and February 2011. The median age at operation was 59 years (range, 34-79 years). Twenty-eight patients (50%) were male. The clinical manifestation of AF (ie, AF pattern) was paroxysmal in 8 patients, persistent in 15 patients, and long-standing persistent in 33 patients. Significant tricuspid and mitral regurgitation (ie, grade  $\geq$ III) was present in 36 and 8 patients, respectively. The RA was performed in 23 patients (group 1), and the BA was performed in 33 patients (group 2). There was no significant difference in the baseline characteristics between the groups except for a male predominance, a higher incidence of regurgitation of both atrioventricular valves, and longer aortic crossclamping time in the BA group (Table 1). For the retrospective review and collation of the data, an ethics approval of human subject database research was obtained from the institutional review board.

### Surgical Technique

For surgical exposure, the standard median sternotomy approach was used in most patients ( $n = 44$ ). However, a minimally invasive approach using an AESOP system (AESOP 3000 Hermes Ready System Robot, Intuitive Surgical, Inc, Sunnyvale, Calif) and a da Vinci system (IS 3000 da Vinci Si, Intuitive Surgical, Inc) was used in 9 patients (2 in group 1, 7 in group 2) and 3 patients (1 in group 1, 2 in group 2), respectively. Surgical procedures were carried out using cardiopulmonary bypass with moderate hypothermia and antegrade cardioplegia. Two types of alternative energy sources, cryothermia and microwave, were used. For cryoablation, a cardiovascular cryosurgical system (ccs-200; AtriCure, Inc, West Chester, Ohio) was used before 2006, and a long flexible cryoablation probe (ATS

CryoMaze 7-cm surgical Ablation Probe; ATS Medical, Inc, Minneapolis, Minn) plugged into an Argon cryoablation system (ATS CryoMaze Console; ATS Medical, Inc) was used thereafter. For microwave thermal injury, a Guidant Microwave surgical ablation system (Flex 4(10); Boston Scientific Corporation, Natick, Mass) was used. These alternative energy sources were applied endocardially in all patients. The BA comprised 11 ablative lesions (Figure 1). Thus, right-sided ablative lesions (lesions 1 and 2, and 7-11) were made in all patients, whereas lesions 3, 4, 5, and 6 were created in 33 patients (only in group 2). After the right atrial auricle was excised (lesion 1), an oblique incision was made on the right atrial lateral wall from the base of the resected appendage to within 3 to 4 cm of the inferior vena cava (lesion 2). Creation of lesion 1 was deliberately omitted in 29 patients because it was assumed that preservation of the right atrial auricle may be beneficial for postoperative fluid management. Left-sided ablation (group 2) was then performed through lesion 2 and the ASD. The left atrial auricle was isolated (lesion 3) by cutting and sewing ( $n = 9$ ) or using alternative energy sources (cryothermia in 23 patients, microwave in 1 patient). Pulmonary veins were isolated to form a box (lesion 4) by using alternative energy sources for the left half (cryothermia in 30 patients, microwave in 3 patients). The right half of the PVI was performed by cutting and sewing in 19 patients and exclusively using alternative energy sources in 14 patients (cryothermia in 13 patients, microwave in 1 patient). A connection lesion between the left atrial auricle isolation and the PVI box (lesion 5) was created by using alternative energy sources (cryothermia in 30 patients, microwave in 3 patients). Another connection lesion between the PVI box and the mitral valve annulus (lesion 6, left atrial isthmus) was created using alternative energy sources (cryothermia in 30 patients, microwave in 3 patients). Surgical interventions for the mitral valve (repair in 9 patients, replacement in 2 patients) and ASD closure ( $n = 56$ ) were performed at this stage. After vigorous de-airing of the left side of the heart and aortic declamping, the rest of the procedure was performed under a beating heart condition. Lesion 7 was created from the resected margin of the right atrial auricle to the antero-septal commissure of the tricuspid valve. Alternative energy sources were used for the area of the annulus (cryothermia in 44 patients, microwave in 6 patients) or the creation of the whole lesion 7 (cryothermia in 4 patients, microwave in 2 patients). A longitudinal incision was made from the superior vena cava to the inferior vena cava parallel to the plane of the atrial septum (lesion 8). This incision was made exclusively by using alternative energy sources in 7 patients (cryothermia in 4, microwave in 3). Perpendicularly from the inferior portion of lesion 8, a transverse incision was made in the lateral wall of the right atrium, heading to the anterior-posterior commissure of the tricuspid valve (lesion 9). Alternative energy sources were used for the area of the annulus (cryothermia in 44 patients, microwave in 6 patients) or the creation of the whole lesion 9 (cryothermia in 4 patients, microwave in 2 patients). Another lesion from the midportion of lesion 8 was made to the right-side margin of the ASD (or PVI box) (lesion 10) by using cryothermia ( $n = 46$ ), microwave ( $n = 8$ ), or cutting and sewing ( $n = 2$ ). The last lesion (lesion 11, right atrial isthmus) was created from the inferomedial margin of the ASD to the base of the coronary sinus and then to the posteroseptal commissure of the tricuspid valve. Because of anatomic inaccessibility, lesion 11 was exclusively made by using alternative energy sources (cryothermia in 48 patients, microwave in 8 patients). In a patient with primum ASD, lesion 11 was created slightly away from the posteroseptal commissure anteriorly because of the proximity of the atrioventricular node to this commissure. Tricuspid annuloplasty was performed in 42 patients before the repair of cut lesions in the right atrium by using a ring ( $n = 21$ ) or the de Vega technique ( $n = 21$ ). The left atrial auricle was isolated in 18 patients (all in group 2) by excision in 10 and internal obliteration in 8. Cardiopulmonary bypass and aortic crossclamping times were  $137 \pm 44$  minutes and  $82 \pm 31$  minutes, respectively.

### Postoperative Follow-up

Twenty-four patients (24/56, 43%) were given class I or III antiarrhythmic drugs during the postoperative period regardless of immediate

**TABLE 1. Baseline characteristics of each group**

	RA	BA	P value
No. of patients	23	33	
Age, y	58 ± 10	57 ± 11	.849
Male gender, n (%)	7 (30)	21 (64)	.014
AF wave form, n (%)			.398
Fine (<1 mm)	10 (44)	10 (30)	
Coarse (>1 mm)	13 (56)	23 (70)	
AF pattern, n (%)			.704
Paroxysmal	4 (17)	4 (12)	
Persistent	19 (83)	29 (88)	
CT ratio	63 ± 8	62 ± 7	.401
NYHA (≥III), n (%)	8 (35)	6 (18)	.213
Significant MR (≥III), n (%)	0	8 (24)	.016
Significant TR (≥III), n (%)	11 (48)	25 (76)	.048
LVEF, %	61 ± 8	57 ± 9	.148
LAD, mm	49 ± 6	51 ± 7	.437
TR velocity (m/s)	3.3 ± 0.6	3.2 ± 0.6	.398
Operation for MR, n (%)			.076
None	21 (92)	24 (73)	
Repair	1 (4)	8 (24)	
Replacement	1 (4)	1 (3)	
Operation for TR, n (%)	14 (61)	28 (85)	.111
CPB time, min	124 ± 43	150 ± 43	.031
ACC time, min	65 ± 24	96 ± 29	<.001

RA, Right atrial maze procedure; BA, biatrial maze procedure; AF, atrial fibrillation; CT, cardiothoracic; NYHA, New York Heart Association; MR, mitral regurgitation; TR, tricuspid regurgitation; LVEF, left ventricular ejection fraction; LAD, left atrial dimension; CPB, cardiopulmonary bypass; ACC, aortic crossclamping.

postoperative cardiac rhythm (11/23 [47%] in group 1, 13/33 [39%] in group 2). Postoperative electrophysiologic monitoring was intended to abide by the guidelines of the Heart Rhythm Society<sup>13-15</sup> since 2007, that is, postoperative electrocardiograms (ECGs) were taken during the immediate postoperative period; 3, 6, 12, and 18 months postoperatively; and annually thereafter. The follow-up strategy of the patients who had undergone operation before 2007 was left to the discretion of individual surgeons; consequently, standard postoperative electrophysiologic follow-up data could be obtained in 75% of the patients (47/62). Because this study is a retrospective review rather than a clinical trial, postoperative ECG data with inappropriately long intervals were taken for analysis. Event monitoring and a 24-hour recorded Holter monitoring were not undertaken routinely at the time of regular follow-up, but rather were indicated only when patients had specific symptoms (ie, palpitation, cardiac rhythm irregularity, syncope) or when follow-up ECGs were abnormal. AF recurrence was defined as the existence of an AF wave with irregularly irregular cardiac rhythm that persisted more than 30 seconds. AF recurrence during the follow-up period was managed by administering class I or III antiarrhythmic drugs for 3 months, and these drugs were switched to digoxin if AF persisted for more than 3 months.

**Statistical Analysis**

Data are presented as frequencies, medians with ranges, or means with standard deviations. Comparison of patient characteristics between the groups was performed using the Fisher exact test for categorical variables and Mann-Whitney U test for continuous variables. The primary end point of observation was recurrence of AF, development of atrial flutter or other types of atrial tachyarrhythmia, or implantation of a permanent pacemaker, with 3 months of a postoperative blanking period. Freedom from AF recurrence was represented using the Kaplan-Meier method, and stratified survival curves were plotted to explore unadjusted differences between the

procedural groups. The Cox proportional hazards model was fitted for time to the first episode of AF recurrence, development of atrial flutter or other types of atrial tachyarrhythmia, or implantation of a permanent pacemaker, adjusting preoperative and intraoperative risk factors. Variables included were procedural groups, age, sex, preoperative functional class, AF pattern, AF wave form, significant mitral or tricuspid regurgitation (TR), TR flow velocity, left atrial dimension, cardiothoracic ratio on simple chest x-ray, left ventricular ejection fraction, cardiopulmonary bypass time, and aortic crossclamping time. Analyses were conducted using the Statistical Package for the Social Sciences version 18.0 (Korean version; SPSS Inc, Chicago, Ill).

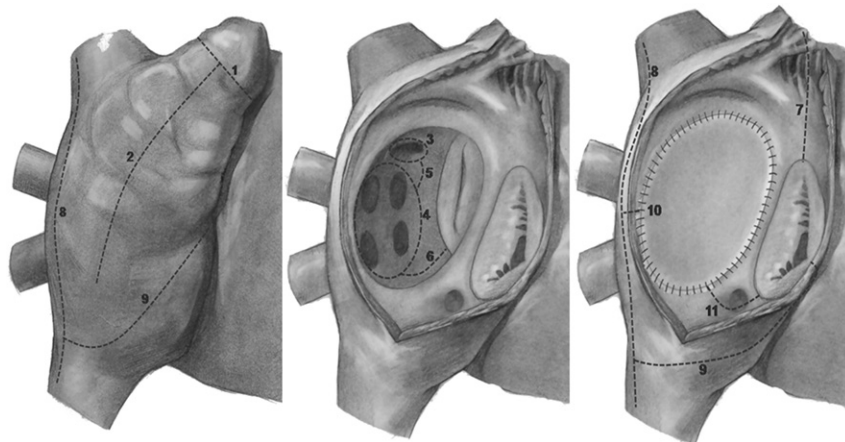
**RESULTS**

There were no early deaths in our cohort. Early postoperative complications developed in 4 patients, which included acute renal failure associated with postoperative bleeding in 1 and wound problem in 3. One patient died of acute fulminant hepatitis at 5 months postoperatively. The median follow-up duration was 49 months (range, 5-149 months). Follow-up was complete in 53 patients (53/56 [95%]). A thromboembolic complication, which was attributed to AF recurrence, developed in 1 patient (in group 1) at 2 months postoperatively. Permanent pacemaker implantation was performed in 2 patients (1 patient in group 1 and 1 patient in group 2) who developed sick sinus syndrome at postoperative 1 and 5 months, respectively.

Univariate analysis revealed that an exclusive RA ( $P = .032$ ), male sex ( $P = .043$ ), a higher TR velocity ( $P = .001$ ), a higher cardiothoracic ratio ( $P = .019$ ), a higher preoperative left ventricular ejection fraction ( $P = .075$ , marginal significance), and the presence of significant preoperative TR ( $P = .076$ , marginal significance) were risk factors for decreased time to the first episode of AF recurrence, development of atrial flutter or other types of atrial tachyarrhythmia, or implantation of a permanent pacemaker. However, on multivariate analysis, only the RA (vs BA) (hazard ratio, 5.11; 95% confidence interval, 1.59-16.44;  $P = .006$ ) and the presence of significant preoperative TR (hazard ratio, 4.67; 95% confidence interval, 1.38-15.87;  $P = .014$ ) remained significant (Table 2). Maintenance of NSR without any episode of AF recurrence, development of atrial flutter or other types of atrial tachyarrhythmia, or implantation of a permanent pacemaker at 2 and 5 years postoperatively were 57% and 45% in group 1, respectively, and 82% and 69% in group 2, respectively (Figure 2).

**DISCUSSION**

ASD is frequently associated with AF, and the incidence of ASD-associated AF is strongly correlated with age.<sup>1,2,16</sup> Although ASD closure alone may lead to the restoration of NSR,<sup>17</sup> it is generally agreed that surgical intervention for AF should be performed on ASD closure, particularly in elderly patients with chronic AF and dilated right atrium.<sup>1,3,4,16,18,19</sup> The question of which is the best lesion set for AF associated with ASD has remained controversial.



**FIGURE 1.** Schematic illustration of the BA. After the right atrial auricle is excised (lesion 1), an oblique incision is made on the right atrial lateral wall from the base of the resected appendage to within 3 to 4 cm of the inferior vena cava (lesion 2). The left atrial auricle is isolated (lesion 3), and the pulmonary veins are isolated to form a box (lesion 4). A connection lesion between the left atrial auricle isolation and the PVI box (lesion 5) is created, and another connection lesion between the PVI box and the mitral valve annulus (lesion 6, left atrial isthmus) is created. Lesion 7 is created from the resected margin of the right atrial auricle to the anteroseptal commissure of the tricuspid valve, and a longitudinal incision is made from the superior vena cava to the inferior vena cava parallel to the plane of the atrial septum (lesion 8). Perpendicularly from the inferior portion of lesion 8, a transverse incision is made in the lateral wall of the right atrium, heading to the anterior-posterior commissure of the tricuspid valve (lesion 9). Another lesion from the midportion of lesion 8 is made to the right-side margin of ASD (or PVI box) (lesion 10), and the last lesion (lesion 11, right atrial isthmus) is created from the inferomedial margin of the ASD to the base of the coronary sinus, and then to the posteroseptal commissure of the tricuspid valve.

Shortly after the development of the Cox-maze procedure for AF, the original cut-and-sew BA also began to be used for AF in ASD. As soon as the maze procedure for left-sided heart diseases began to be confined to the left atrium, the BA for right-sided heart lesions also began to be replaced with the RA.<sup>12,20,21</sup> The rationale for an exclusive right or left atrial lesion set is based on the assumption that the left (or right) atrium in right-sided (or left-sided) heart diseases is relatively exempt from structural changes caused by pressure and volume overload. Therefore, creation of ablative lesions only in the affected atrium seemed sensible. Furthermore, potential drawbacks of the conventional cut-and-sew maze procedure, such as lengthy surgical time and prolonged cardiopulmonary bypass, increased risk of postoperative bleeding, multiple suture lines in the atria resulting in ineffective contraction of the unaffected atria, and the risk of pulmonary vein stenosis,<sup>22</sup> boosted the use of simplified exclusive right- or left-sided ablation. However, with the accumulation of experiences on the left atrial lesion set, it began to be asserted that the BA for AF in left-sided heart lesions may lead to better outcomes compared with the limited left-sided maze procedure.<sup>9,23</sup> A meta-analysis encompassing 69 studies on 5885 patients demonstrated that 3-year freedom from AF was significantly higher after BA than after a limited left atrial lesion set in patients with AF accompanied by mitral valvular heart diseases.<sup>23</sup> Recognition of the superiority of BA over the limited left atrial lesion set in turn led to the idea that BA might also result in a better electrophysiologic outcome compared with the exclusive RA for AF in right-sided heart lesions.<sup>4</sup> In addition, potential advantages of the RA over BA have

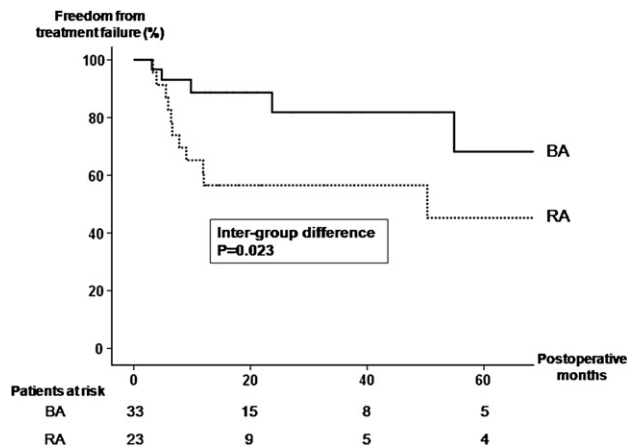
been undermined by the use of alternative energy sources that could substitute for most of the cutting and sewing lesions of the conventional Cox-maze procedure. Various alternative energy sources, such as cryothermia, microwave, radiofrequency energy,<sup>18,19</sup> laser, and high-intensity focused

**TABLE 2. Risk factors for decreased time to treatment failure\***

	Univariate <i>P</i> value	Multivariate		
		Hazard ratio	95% CI	<i>P</i> value
RA vs BA (reference)	.032	5.111	1.589-16.442	.006
Age at operation	.179			
Sex	.043			
Long-standing AF	.255			
Fine AF wave form	.683			
Significant MR	.244			
Significant TR	.076	4.672	1.375-15.873	.014
NYHA (≥III)	.526			
Preoperative TR velocity	.001			
TVP	.666			
LVEF	.075			
LAD	.322			
CT ratio	.019			
CPB	.997			
ACC	.056			

CI, Confidence interval; RA, right atrial maze procedure; BA, biatrial maze procedure; AF, atrial fibrillation; MR, mitral regurgitation; TR, tricuspid regurgitation; NYHA, New York Heart Association; TVP, tricuspid valvuloplasty; LVEF, left ventricular ejection fraction; LAD, left atrial dimension; CT, cardiothoracic; CPB, cardiopulmonary bypass; ACC, aortic crossclamping. \*Treatment failure is defined as recurrence of AF, development of atrial flutter or other types of atrial tachyarrhythmia, or implantation of permanent pacemaker.





**FIGURE 2.** Freedom from the first episode of AF recurrence, atrial flutter, atrial tachyarrhythmias, or permanent pacemaker implantation. BA, Bialtrial maze procedure; RA, right atrial maze procedure.

ultrasound, have been developed and used in practice, and the efficacy of these new ablative modalities is thought to be at least comparable to that of cutting and sewing lesions, provided that they are applied endocardially or in a bipolar fashion.<sup>18,22,24</sup> Cryothermia, which is one of the most frequently used alternative energy sources, does not cause surgical scarring in the atria and therefore would guarantee a normal atrial contraction once NSR is restored. However, it is still uncertain whether the RA is obsolete for AF associated with ASD; thus, an important question arises of whether it is possible to delineate the subset of patients who would best benefit from the RA in terms of left atrial size, AF wave form, or duration of AF. Among the 23 patients undergoing the RA maze procedure in this study, recurrence of AF was observed in 12 patients whose LA dimension was not significantly larger than that of the remaining 9 patients without AF recurrence (Table 3). This finding may be partly attributable to the fact that most of the patients enrolled in this study had advanced disease with older age, larger LA size, and longer history of persistent AF. Thus, it could be argued that the outcome of the RA might have been comparable to that of the BA group if younger patients with a smaller LA and paroxysmal AF had been included in our current study population. However, in a previous report pertaining to the comparison of various lesion sets for the management of AF associated with ASD, AF recurrence after the RA took place regardless of the preoperative LA size, indicating the inherent incompleteness of the procedure.<sup>4</sup>

In previous studies, risk factors for AF recurrence after the maze procedure for AF associated with mitral valvular heart disease included a longer duration of AF,<sup>10</sup> older age at the time of surgical repair, larger preoperative left atrial dimension,<sup>10</sup> fine atrial fibrillatory wave,<sup>8</sup> and limited left atrial lesion set.<sup>9,23,25</sup> With respect to AF associated with ASD, an atrial fibrillatory wave and left atrial diameter were found to be independent predictors of NSR

restoration after the maze procedure, and a BA was recommended for patients with a large left atrial dimension (>59 mm).<sup>4,8</sup> In the current study, the presence of significant TR and high right ventricular pressure were found to be risk factors for AF recurrence, and this result seems plausible given that the pathogenesis of AF in ASD is mainly attributable to right atrial dilatation.

There are several methods to determine the efficacy of arrhythmia surgery for AF. The strictest method, which was adopted in this study, is to fit the time to the first episode of AF recurrence into the survival model, considering it as a treatment failure. Because this method does not take into account the patients with restored NSR after AF recurrence, the success rate is usually underrepresented.<sup>13-15</sup> Another method is to estimate the proportion of patients with NSR who are not taking antiarrhythmic drugs at each postoperative interval. Although this method is useful for the comparison of electrophysiologic outcome between different lesion sets at a certain postoperative period, missing cardiac rhythm information at regular intervals may mislead the practitioners into underestimating or overestimating success rates (Figure E2). Although the majority of our study cohort had undergone operation before the establishment of a standardized postoperative electrophysiologic follow-up protocol proposed by major academic bodies in 2007, 75% of the patients were fortuitously monitored in a standard fashion. However, some may assert that nonstandardized follow-up data should be discarded for fair comparison between the procedural groups. Figure E3 shows freedom from the first episode of AF recurrence in the same cohort with a standard follow-up. Unadjusted comparison between the 2 procedural groups showed an improved electrophysiologic outcome in the BA group. However, it is indisputable that regular electrophysiologic follow-up (ie, ECG and Holter monitoring) and event recording are mandatory for the prospective randomized clinical trial.

**Study Limitations**

Postoperative ECG data with inappropriately long intervals were taken for analysis, and event monitoring and a 24-hour recorded Holter monitor were not undertaken routinely at the time of regular follow-up, which might have overestimated the success rate. Because 5 surgeons operated on the patients included in our study cohort, there were subtle differences in surgical techniques that could not be controlled for in the analysis. The use of alternative energy sources was inconsistent, in terms of the types and extent of their use for creating each ablative lesion. This study was based on the premise that the ablative efficacy of different alternative energy sources was comparable to the cut-and-sew lesion, as long as they were applied endocardially. Because cryothermia and microwave energy were applied endocardially in all patients, variability of the use of alternative energy sources might have been

TABLE 3. Profiles of patients with treatment failure\* (n = 17)

Group	Sex	Age (y)	AF pattern	AF wave	LAD (mm)	LVEF	Vel <sub>TR</sub> (m/s)	Interval (mo)	Follow-up (mo)	Last follow-up rhythm
RA	F	59	LP	Coarse	49	76	3.0	8	129	AF
RA	F	57	LP	Coarse	53	59	3.7	12	53	NSR (off)
RA	F	61	LP	Coarse	54	59	4.0	0.5	94	AF
RA	F	59	P	Coarse	55	63	3.2	7	112	Pacing (DDD)
RA	F	49	LP	Coarse	52	55	3.0	12	48	NSR (on)
RA	F	61	LP	Fine	56	57	4.3	50	50	AF
RA	M	52	LP	Coarse	54	50	2.8	95	100	NSR (off)
RA	F	65	P	Coarse	49	57	3.6	0.3	6	AF
RA	F	59	LP	Fine	46	56	3.4	9	43	NSR (off)
RA	F	69	P	Coarse	55	75	3.6	3	46	AF
RA	F	79	P	Fine	48	66	3.4	0.2	24	AF
RA	M	65	LP	Coarse	54	63	4.4	6	39	AF
BA	F	55	P	Coarse	39	60	4.0	24	117	AF
BA	M	57	LP	Fine	52	69	3.1	10	74	AF
BA	M	44	LP	Coarse	49	50	4.2	55	56	AF
BA	F	74	LP	Fine	59	69	4.5	3	15	NSR (off)
BA	M	43	P	Coarse	56	57	3.5	0.6	13	Pacing (AAI)

Interval is the interval between arrhythmia surgery and the first episode of treatment failure. AF, Atrial fibrillation; LAD, left atrial dimension; LVEF, left ventricular ejection fraction; Vel<sub>TR</sub>, tricuspid regurgitation flow velocity; RA, right atrial maze procedure; BA, biatrial maze procedure; LP, long-standing persistent; P, persistent; NSR (off), normal sinus rhythm without class I and III antiarrhythmic drugs; NSR (on), normal sinus rhythm with class I or III antiarrhythmic drugs; DDD, dual chamber pacing, dual chamber sensing, and dual function (provocative and inhibitory); AAI, atrial pacing, atrial sensing, and inhibited by atrial event. \*Treatment failure is defined as recurrence of AF, development of atrial flutter or other types of atrial tachyarrhythmia, or implantation of permanent pacemaker.

mitigated. However, the efficacy of alternative energy sources in each lesion should be defined in future studies.

## CONCLUSIONS

A biatrial ablation leads to an improved electrophysiologic outcome in AF associated with ASD compared with an exclusive right-sided lesion set. Further prospective randomized study is mandatory to define the efficacy of alternative energy sources in each lesion set.

## References

- Murphy JG, Gersh BJ, McGoon MD, Mair DD, Porter CJ, Ilstrup DM, et al. Long-term outcome after surgical repair of isolated atrial septal defect. Follow-up at 27 to 32 years. *N Engl J Med*. 1990;323:1645-50.
- Gatzoulis MA, Freeman MA, Siu SC, Webb GD, Harris L. Atrial arrhythmia after surgical closure of atrial septal defects in adults. *N Engl J Med*. 1999;340:839-46.
- Sandoval N, Velasco VM, Orjuela H, Caicedo V, Santos H, Rosas F, et al. Concomitant mitral valve or atrial septal defect surgery and the modified Cox-maze procedure. *Am J Cardiol*. 1996;77:591-6.
- Kobayashi J, Yamamoto F, Nakano K, Sasako Y, Kitamura S, Kosakai Y. Maze procedure for atrial fibrillation associated with atrial septal defect. *Circulation*. 1998;98:11399-402.
- Cox JL, Boineau JP, Schuessler RB, Ferguson TB Jr, Cain ME, Lindsay BD, et al. Successful surgical treatment of atrial fibrillation: review and clinical update. *JAMA*. 1991;266:1976-80.
- Brodman RF, Frame R, Fisher JD, Kim SG, Roth JA, Ferrick KJ. Combined treatment of mitral stenosis and atrial fibrillation with valvuloplasty and a left atrial maze procedure. *J Thorac Cardiovasc Surg*. 1994;107:622-4.
- Hornero F, Rodriguez I, Bueno M, Buendia J, Dalmau MJ, Canovas S, et al. Surgical ablation of permanent atrial fibrillation by means of maze radiofrequency: mid-term results. *J Card Surg*. 2004;19:383-8.
- Kamata J, Kawazoe K, Izumoto H, Kitahara H, Shiina Y, Sato Y, et al. Predictors of sinus rhythm restoration after Cox maze procedure concomitant with other cardiac operations. *Ann Thorac Surg*. 1997;64:394-8.
- Kim JB, Bang JH, Jung SH, Choo SJ, Chung CH, Lee JW. Left atrial ablation versus biatrial ablation in the surgical treatment of atrial fibrillation. *Ann Thorac Surg*. 2011;92:1397-405.
- Kosakai Y, Kawaguchi AT, Isobe F, Sasako Y, Nakano K, Eishi K, et al. Cox maze procedure for chronic atrial fibrillation associated with mitral valve disease. *J Thorac Cardiovasc Surg*. 1994;108:1049-55.
- Bonchek LI, Burlingame MW, Worley SJ, Vazales BE, Lundy EF. Cox/maze procedure for atrial septal defect with atrial fibrillation: management strategies. *Ann Thorac Surg*. 1993;55:607-10.
- Theodoro DA, Danielson GK, Porter CJ, Warnes CA. Right-sided maze procedure for right atrial arrhythmias in congenital heart disease. *Ann Thorac Surg*. 1998;65:149-54.
- Calkins H, Brugada J, Packer DL, Cappato R, Chen SA, Crijns HJ, et al. HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for personnel, policy, procedures and follow-up. A report of the Heart Rhythm Society (HRS) Task Force on catheter and surgical ablation of atrial fibrillation. *Heart Rhythm*. 2007;4:816-61.
- Calkins H, Kuck KH, Cappato R, Brugada J, Camm AJ, Chen SA, et al. HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design. *Europace*. 2012;14:528-606.
- Shemin RJ, Cox JL, Gillinov AM, Blackstone EH, Bridges CR. Guidelines for reporting data and outcomes for the surgical treatment of atrial fibrillation. *Ann Thorac Surg*. 2007;83:1225-30.
- Berger F, Vogel M, Kramer A, Alexi-Meskishvili V, Weng Y, Lange PE, et al. Incidence of atrial flutter/fibrillation in adults with atrial septal defect before and after surgery. *Ann Thorac Surg*. 1999;68:75-8.
- Vecht JA, Saso S, Rao C, Dimopoulos K, Grapsa J, Terracciano CM, et al. Atrial septal defect closure is associated with a reduced prevalence of atrial tachyarrhythmia in the short to medium term: a systematic review and meta-analysis. *Heart*. 2010;96:1789-97.
- Giamberti A, Chessa M, Foresti S, Abella R, Butera G, de Vincentiis C, et al. Combined atrial septal defect surgical closure and irrigated radiofrequency ablation in adult patients. *Ann Thorac Surg*. 2006;82:1327-31.
- Giamberti A, Chessa M, Abella R, Butera G, Negura D, Foresti S, et al. Surgical treatment of arrhythmias in adults with congenital heart defects. *Int J Cardiol*. 2008;129:37-41.
- Stulak JM, Dearani JA, Puga FJ, Zehr KJ, Schaff HV, Danielson GK. Right-sided Maze procedure for atrial tachyarrhythmias in congenital heart disease. *Ann Thorac Surg*. 2006;81:1780-5.

21. Greason KL, Dearani JA, Theodoro DA, Porter CB, Warnes CA, Danielson GK. Surgical management of atrial tachyarrhythmias associated with congenital cardiac anomalies: Mayo Clinic experience. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu.* 2003;6:59-71.
22. Shemin JR. Surgical lessons learned from the treatment of atrial fibrillation. *Heart Rhythm.* 2008;5:S40-4.
23. Barnett SD, Ad N. Surgical ablation as treatment for the elimination of atrial fibrillation: a meta-analysis. *J Thorac Cardiovasc Surg.* 2006;131:1029-35.
24. Khargi K, Hutten BA, Lemke B, Deneke T. Surgical treatment of atrial fibrillation; a systematic review. *Eur J Cardiothorac Surg.* 2005;27:258-65.
25. Gillinov AM, Bhavani S, Blackstone EH, Rajeswaran J, Svensson LG, Navia JL, et al. Surgery for permanent atrial fibrillation: impact of patient factors and lesion set. *Ann Thorac Surg.* 2006;82:502-14.

## Discussion

**Dr Christian Pizarro** (*Wilmington, Del.*). The report by Yun and colleagues compares the effectiveness of RA versus BA for the management of AF in a moderate size contemporary cohort of adults with ASD. The article is well written and explains the rationale for a right-sided only approach in these patients on the basis of the assumption that the left atrium is relatively free of structural changes secondary to pressure and volume overload, and therefore a more limited procedure could achieve the same efficacy to restore normal rhythm while reducing the potential for operative morbidity. However, this has not been demonstrated. The authors conclude that at a median follow-up of 54 months, the BA appears to be superior to treat this patient population. I have several questions.

In the technique section you described that lesion 1 was deliberately omitted in 29 patients, which leads to the first question as to how did you select these patients and did this modification result in any benefit as anticipated?

**Dr Yun.** Five surgeons operated on the cohort in this study. One of them is an adult cardiac surgeon who has performed hundreds of maze procedures, and he believes strongly that the right atrial auricle should be preserved for the postoperative fluid management because the right atrial auricle is thought to secrete natriuretic peptide. He operated on 29 patients, and right atrial auricle resection was deliberately omitted in these patients.

**Dr Pizarro.** Did you include this in the analysis to determine if this, in fact, turns out to be true?

**Dr Yun.** No, I did not.

**Dr Pizarro.** By using multivariate analysis, you have shown that the presence of significant TR has an important effect on the time to the first episode of AF recurrence. As previously stated, it is believed that the degree of atrial dilatation secondary to the volume overload is an important contributor to the recurrence of AF. Although closure of the ASD will remove some of the load, it is not surprising that in patients with significant residual volume load secondary to TR the recurrence would be high. Can you tell us what was the incidence of postoperative TR and did this have an impact on the likelihood to maintain NSR?

**Dr Yun.** Patients with significant preoperative TR underwent tricuspid annuloplasty, and TR disappeared postoperatively in most of them. Therefore, we could not analyze the data in terms of the relationship between postoperative TR and the time to the first episode of AF recurrence. However, one thing for sure is that this specific subset of patients is different from the cohort with left heart disease, and right heart parameters (eg, right atrial

size, TR grade, pulmonary artery pressure, or other things that characterize the right heart) should be taken into account when we assess the outcome of arrhythmia surgery in these patients.

**Dr Pizarro.** As you pointed out, this cohort was characterized by advanced disease, older age, large left atrium, and persistent AF. On the basis of these observations and considering the available evidence linking some of these variables to freedom from recurrence, do you think that the choice of procedure, RA versus BA, should be tailored to the presence of these factors? And if so, what would be the thresholds you would suggest to match patient to procedure, for example, left atrial size?

**Dr Yun.** That's a tricky question to answer, and I have to admit that I don't have any idea about that. This study is a retrospective review focusing on the difference of outcome between the 2 procedural groups. To answer that question, we have to conduct a well-designed prospective randomized clinical trial by putting in all the variables including not only the left atrial size but also the right heart parameters, as I pointed out, and produce a statistical model that enables us to predict the benefit of each procedure. However, I wouldn't say that the RA is obsolete. There might be a subset of patients who may benefit from the RA. However, at this point, we don't have an answer for the question of who would best benefit from right-sided only ablation in AF associated with ASD.

**Dr Pizarro.** Would you could comment on the fact that surgeries were performed by 5 surgeons with some differences in surgical technique and inconsistent use of alternative energy sources. How do you think these factors influenced your observation and have you standardized your surgical approach to these patients?

**Dr Yun.** As I said, 5 surgeons were involved in this study, and there were subtle differences in surgical technique between the surgeons in terms of the use of alternative energy sources. For instance, 2 surgeons made the whole lesion 7 or 8 using cryothermia, and others used a cryoprobe for only parts of them. Some surgeons used microwave instead of cryothermia. Because of the complexity of the use of alternative energy sources, I could not control this compounding variable at the time of analysis. Rather, I would say this study is based on the premise that the efficacy of alternative energy sources is equal to that of cut-and-sew, as long as they are applied endocardially. The second premise of this study is that subtle differences in surgical technique did not affect the outcome. This might not be true, but the surgical technique of the maze operation is so diverse that we could not assess the impact of minor technical modification on the long-term outcome.

**Dr Pizarro.** I enjoyed your presentation, and I congratulate you and your colleagues on a well-written article.

**Dr Christopher Caldarone** (*Toronto, Ontario, Canada*). The results you reported are somewhat at odds with the Mayo Clinic report that describes reasonable efficacy with right atrial maze procedures. Now, their patient population was a bit different. They had many more, I believe, intact atrial septa, many more patients with pulmonary insufficiency, right ventricular dilation, and tricuspid insufficiency as their primary pathology. Do you think there is a difference between patients with an intact atrial septum and patients with an ASD in terms of the efficacy of the RA?

**Dr Yun.** Of course, yes. In patients with ASD, especially in patients with a huge ASD, the left atrium is not free from pressure volume overload because the right atrial pressure would be the same as the left atrial pressure. Even if the left atrial size is normal,

the left atrium might be pathologic, and that is the rationale for the BA in this subset. For patients with an intact atrial septum, for instance, in patients with Ebstein's anomaly, the left atrium may be protected, and the right atrial maze operation might be the best way to go.

**Dr Bahaaldin Alsoufi** (*Riyadh, Saudi Arabia*). It's been well shown by the work of Haissaguerre from France and the original work of Dr Cox that AF originates in the left atrium and flutter originates in the right atrium. It's not surprising to me that you had a high failure rate with right atrial ablation only. My question is do you think that those patients are different to justify creating lesions in the right atrium alone?

I need to draw your attention to the presentation at the plenary session yesterday morning from the Columbia University group. They found no advantage of performing right-sided ablation on top of left-sided ablation. It seems to me that left atrial ablation is a must, whereas right atrial ablation should be added in patients with flutter. Many electrophysiologists now would recommend not addressing the right atrium at the time of surgery because it can be easily addressed percutaneously at a later date if needed. So what was your theory to make your group abandon left atrial ablation, which not surprisingly was associated with a low success rate?

**Dr Yun.** The right-sided only concept was developed at the Mayo Clinic, and I learned from them. A lot of congenital cardiac surgeons who are not accustomed to arrhythmia surgery may hesitate to do the original Cox maze procedure for ASD because they may not feel comfortable in cutting all the way down to the left atrial auricle, isolating the left atrial auricle, and creating a cutting lesion to the mitral valve. The concept from the Mayo Clinic that the left atrium might be preserved in right heart disease has led us to choose the right-side only maze procedure instinctively. With the inference that the BA might be superior to the RA in this setting, and, more important, with the development of an alternative energy source, BA has become an easy operation to perform because it takes only 20 or 25 minutes of aortic crossclamping for the left-sided maze operation and the rest of the procedure can be done in the beating-heart condition.

**Dr Alsoufi.** So I think you have to do the left atrial maze.

**Dr Yun.** Right, I agree with that.

**Dr Frederic Jacques** (*Toronto, Ontario, Canada*). In accordance with the Cox studies and others, we know that the substrate (the actual amount of atrial myocardium) influences the result. The stripes of myocardium or the "corridors" organized as a maze have to be small enough to prevent the propagation of the wavelets. You said that right atria were enlarged in your patients, but was the actual size of these atria at the end of the procedure similar between groups? Did you take some of the free wall out to downsize these atria?

**Dr Yun.** Do you mean the size of the right atrium?

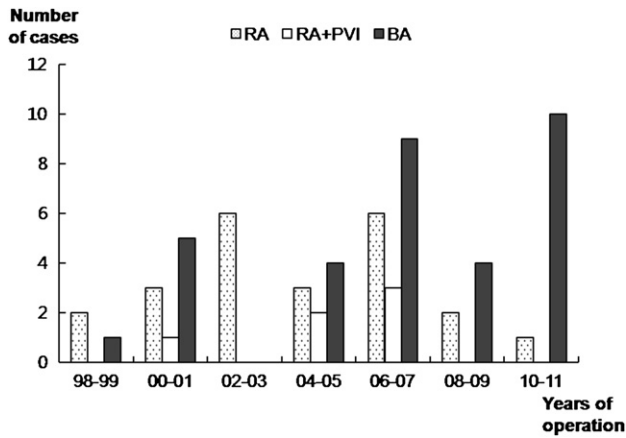
**Dr Jacques.** The right and left atria.

**Dr Yun.** We didn't measure the right atrial size; thus, we cannot compare the outcome in terms of the right atrial size. However, in this patient population, there were several patients who had right atrial wall resection. The rationale for that procedure is based on the experimental study by Dr Cox: To form a macro-reentry circuit, we need 5- or 6-cm strips of atrial wall. Thus, the basic principle of the maze procedure used in this cohort was to make the atrial wall strip narrower than 4 cm. Although there were 5 surgeons involved in this study, the basic surgical principle was the same: Do not make the atrial wall strip wider than 4 cm.

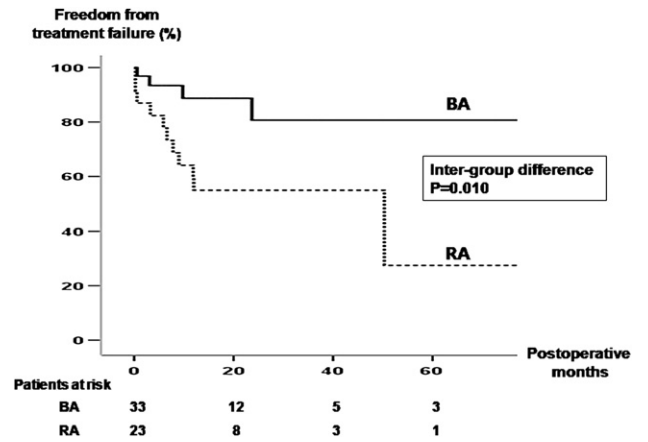
**Dr Jacques.** We know that in the postoperative period after a maze procedure there is an increase in the rate of AF or atrial arrhythmias that affects the atrial electrical remodeling. The use of an antiarrhythmic drug in the early postoperative period may affect this remodeling and influence the recurrence rate in the long run. Can you comment on your perioperative management protocol?

**Dr Yun.** The postoperative antiarrhythmic drug protocol was different from one surgeon to another. Some used prophylactic antiarrhythmic drugs even when NSR was restored. Some did not. Approximately half of the patients had class 1 or 3 antiarrhythmic drugs for 3 months postoperatively. If NSR is restored at 3 months postoperatively, antiarrhythmic medication was no longer used in most patients. In case of AF recurrence during the follow-up period, another 3-month trial of antiarrhythmic medication was attempted, and if this didn't work, antiarrhythmic drugs were switched to digoxin or beta-blockade.

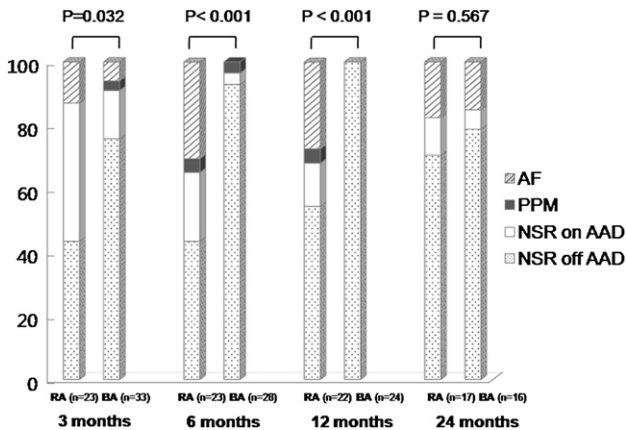




**FIGURE E1.** Annual incidence of various maze procedures. *RA*, Right atrial maze procedure; *PVI*, pulmonary vein isolation; *BA*, biatrial maze procedure.



**FIGURE E3.** Freedom from the first episode of AF recurrence, atrial flutter, atrial tachyarrhythmias, or permanent pacemaker implantation in patients with standard follow-up. *RA*, Right atrial maze procedure; *BA*, biatrial maze procedure; *AF*, atrial fibrillation.



**FIGURE E2.** Freedom from AF with or without antiarrhythmic drugs at 3, 6, 12, and 24 months postoperatively. *RA*, Right atrial maze procedure; *BA*, biatrial maze procedure; *AF*, atrial fibrillation; *PPM*, permanent pacemaker; *NSR*, normal sinus rhythm; *AAD*, antiarrhythmic drugs.