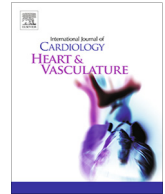




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Long-term outcome of totally thoracoscopic surgical ablation in atrial fibrillation: A single-center experience



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ABSTRACT

Background: Totally thoracoscopic ablation (TTA) is a minimally invasive and safe alternative to radiofrequency catheter ablation (RFCA) for patients with atrial fibrillation (AF). It has evolved over the last decades, but data are limited. The aim of this study was to report the long-term efficacy and safety of TTA through a single center experience.

Methods: We retrospectively analyzed all consecutive patients who underwent TTA for AF from February 2012 to December 2018. All patients were followed every 3 months after operation with 12-lead ECG and 24-hour Holter ECG monitoring. The late recurrence of AF was defined as any atrial tachyarrhythmia (ATA) sustained more than 30 s from 3 months after surgery.

Results: Of the total 408 patients undergoing TTA, 265 were analyzed in this study (17% paroxysmal, persistent or long standing persistent 83%, mean age 56 ± 9 years). During the mean follow-up duration 23 ± 18 months, ATA-free survival rate was 74%, 64%, 58%, 51% and 51% at 1,2,3,4 and 5 years, respectively. At the last follow-up, 75% of patients had sinus rhythm with or without additional intervention. The overall complication rate was 4.5% (12 events) and four patients (1.5%) had a stroke during follow-up.

Conclusions: TTA could be effective treatment option for AF. It had a very low risk of complication and could reduce stroke incidence. Further studies are needed to improve treatment strategy.

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1. Introduction

In patients with drug refractory symptomatic atrial fibrillation (AF), pulmonary vein (PV) isolation with catheter ablation is a well-established standard treatment [1]. This approach improved the quality of life of patients with atrial fibrillation and reduced the incidence of ischemic stroke and mortality of heart failure patients [2,3]. However, despite many advances such as development of three-dimensional mapping systems, catheter innovation, and advancement of ablation strategies, a certain degree of recurrence remains. In addition, catheter ablation is challenging in

patients with persistent or long-standing persistent AF, with success rate ranging from 20 to 60% [4].

Surgical ablation represented by the Cox-Maze procedure was very effective and showed a high success rate [5,6]. However, as a highly invasive procedure with sternotomy and cardiopulmonary bypass (CPB), the risk of complications was high, and it was difficult to perform in patients with stand-alone AF. Totally thoracoscopic ablation (TTA) is a minimally invasive and safe alternative method that has evolved over the last decade. Off-pump epicardial ablation through mini-thoracotomy or thoracoscopy approach has been attempted, and there have been many studies on optimal lesion set such as PVI alone, additional ganglion plexus (GP) ablation or Dallas lesion set. Recently, there has been much interest in the hybrid approach that performs both epicardial ablation and endocardial ablation. It is performed in the beating heart, and effective PV isolation is possible through direct epicardial application. There are additional advantages of ablation of epicardial structures, such as the GP or ligament of Marshall, and exclusion

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of left atrial appendages (LAAs). The GP, ligament of Marshall or LAA has been implicated as a driver of AF arrhythmogenesis. The current guidelines recommend surgical ablation in patients with prior failed catheter ablation or drug-refractory atrial fibrillation and prefer surgical ablation [1,7].

Studies on TTA are increasing, but data are limited. The procedure success rate varies widely from 38 to 83% due to heterogeneous patient or procedural characteristics, and most prior studies are small. The aim of this study was to report the long-term efficacy and safety of TTA through our experience with a relatively large number of patients.

2. Materials and methods

2.1. Study population

All consecutive patients who underwent TTA for AF from February 2012 to December 2018 were retrospectively analyzed. TTA were indicated in patients with longstanding persistent AF, persistent AF with larger left atrium (LA) size or long AF duration, previous failed catheter ablation, or history of stroke with paroxysmal AF. The following patients were excluded from this study: 1) patients who underwent combined hybrid ablation during index admission and 2) those with failed or incomplete bilateral pulmonary vein isolation due to severe intrathoracic adhesion. In the first 70 cases, hybrid ablation was performed at the same admission to confirm the integrity of the epicardial ablation lesion. After that, it was performed at the same admission only when atrial flutter recurred in the early period. Demographic, procedure, and follow-up data were retrospectively collected through a review of medical records. The definitions of AF, procedure success, and complications followed the current guidelines. The Institution Review Board of Samsung Medical Center approved the study protocol, and informed consent was waived (IRB No. 2020-06-159).

2.2. Surgical procedure

Totally thoracoscopic ablation (TTA) refers to a video-assisted thoracoscopic surgical ablation technique without assistance of the Da Vinci system (Intuitive Surgical, Sunnyvale, CA, USA) or cardiopulmonary bypass. This is a bilateral approach, requiring only 3 holes per each side: a 5-mm port introduced in the fourth intercostal space at the midaxillary line and two ports placed in the third intercostal space at the anterior axillary line and at the sixth intercostal space at the midaxillary line, respectively. After pericardial tenting, a lighted dissector (AtriCure LumitipDissector, Atricure, Inc., Cincinnati, OH, USA) was used to pass a rubber band under the pulmonary vein (PV) antrum through the oblique sinus. An AtriCure Isolator Transpolar Clamp was positioned around the PV antrum through connection to the rubber band. Bipolar radiofrequency energy was delivered six times to the clamps for PV isolation. Superior and inferior lines connecting both PV isolation lines were created using a linear pen device (Atricure, Inc.). Ganglionated plexuses were ablated with bipolar energy under high-frequency pacing. After PV and ganglionated plexus ablation, the ligament of Marshall was dissected and ablated. Once ablations were complete and conduction block was confirmed, the left atrial appendage was removed with an endoscopic stapling device. All procedures were performed by a single experienced cardiac surgeon (DSJ).

2.3. Follow-up

All patients took oral anticoagulants for at least 4 weeks before surgery, and transesophageal echocardiogram was performed to

rule out thrombus in LA and LAA. After surgery, all patients were monitored in the intensive care unit. After excluding pericardial effusion by transthoracic echocardiography, heparin injection was started 4 h after surgery and titrated according to the activated partial thromboplastin time (target 60–80 s). An oral anticoagulant (such as warfarin or a non-vitamin K antagonist oral anticoagulant) was started the day after the procedure. Antiarrhythmic drugs were continued after surgery unless contraindicated.

All patients were followed postoperatively at two weeks, three months, six months, and every six months thereafter. At every visit, 12-lead electrocardiography (ECG) and 24-hour Holter monitoring were performed with evaluation of any symptom of AF recurrence. The primary outcome was the late recurrence of AF (LRAF). The LRAF was defined as any atrial tachyarrhythmias (ATa) including AF, atrial flutter (AFL), or atrial tachycardia (AT) for more than 30 s after a three-month blanking period. Cardioversion was performed as needed during the blanking period. In patients with recurrence of ATa, additional intervention such as antiarrhythmic drugs, catheter ablation, or DC cardioversion was performed in consideration of patient status. In general, antiarrhythmic drugs (AADs) were discontinued after three months if there was no evidence of recurrence. Oral anticoagulants (OACs) were continued postoperatively; in some patients with no history of stroke, low CHAD₂-VASc score, and well-maintained sinus rhythm, it was discontinued at the decision of the attending physician.

2.4. Statistical analysis

Categorical variables are reported as number and percentage, while continuous variables are presented as mean \pm standard deviation (SD). For comparison between the two groups based on late recurrence, a chi-square test or Fisher's exact test was used for categorical variables, and an independent sample T-test was used for continuous variables. ATa-free survival were estimated according to the Kaplan-Meier method. Cox proportional hazard analysis was used to identify predictors of AF recurrence. A two-sided P-value < 0.05 was considered statistically significant. All statistical analysis was conducted using commercial software, SPSS (Version 23.0; IBM, Armonk, NY).

3. Results

3.1. Baseline demographics

Of the total 408 patients undergoing TTA, 265 were analyzed according to the above criteria. The mean patient age was 56 ± 9 years, and male was 87%. Most patients were persistent AF (40%) or long-standing persistent AF (42%), and only 17% were paroxysmal AF. Patients with prior failed catheter ablation represented 21% of the population. Forty-three patients (16%) had history of prior stroke. Congestive heart failure was 12% of patients. The mean CHAD₂-VASc score was 1.3 ± 1.4 , and 55 patients (25%) had more than two points. The mean LV ejection fraction was $60 \pm 8\%$, which was within the normal range, and the mean LA diameter was 46 ± 7 mm (range 26–69). Baseline characteristics are shown in Table 1. When comparing the two groups according to the recurrence of ATa during follow-up, there were no significant difference between the two groups in age, sex and comorbidities. However, non-paroxysmal AF was significantly more in the recur group and showed a larger LA size.

Table 1
Baseline characteristics.

Variables	Value (n = 265)	No recur (n = 163)	Recur (n = 102)	p-value
Gender, Female (%)	35 (13)	19 (12)	16 (16)	0.357
Age, year	56 ± 9	56 ± 9	56 ± 8	0.909
Body mass index, kg/m ²	26 ± 3	25 ± 3	26 ± 3	0.057
Comorbidities				
Hypertension (%)	97 (37)	60 (37)	37 (36)	0.930
Diabetes mellitus (%)	30 (11)	20 (13)	10 (10)	0.538
Prior stroke/TIA (%)	43 (16)	31 (19)	12 (12)	0.119
Congestive Heart failure (%)	31 (12)	19 (12)	12 (12)	0.979
Coronary artery disease (%)	8 (3)	7 (4)	1 (1)	0.125
CHA ₂ DS ₂ VASc score	1.3 ± 1.4			
Prior catheter ablation (%)	55 (21)	24 (15)	17 (17)	0.670
Type of AF (%)				
Paroxysmal	46 (17)	40 (25)	6 (6)	
Persistent	107 (40)	65 (40)	42 (42)	
Long standing persistent	112 (42)	58 (35)	54 (52)	
LV EF, %	60 ± 8	60 ± 8	58 ± 8	0.073
LA diameter, mm	46 ± 7 (26–69)	44 ± 7	49 ± 7	<0.001
LA volume index, ml/m ²	49 ± 17 (17–156)	45 ± 7	56 ± 19	<0.001

*TIA, transient ischemic attack; AF, atrial fibrillation; LV, left ventricular; EF, ejection fraction; LA, left atrial.

3.2. Procedure characteristics

The mean procedure time was 159 ± 55 min, and the mean length of hospital stay was 6.5 days. Bilateral pulmonary vein isolation was performed in all patients. In more than 90% of patients, additional ablation of the LA posterior wall box lesion and ligament of Marshall were performed. Ganglionic plexus ablation was performed in 88% and LAA resection was performed in 99% of patients. About half of the patients underwent SVC ablation (Table 2). There were no significant difference between two groups according to ATa recurrence.

3.3. Follow-up

The mean follow-up duration was 32 ± 17 months (range: 3–60 months). The ATa-free survival rate was 74% at 1-year and 51% at 5-years, respectively (Fig. 1A). In subgroup analysis, patients with paroxysmal AF had significantly better ATa-free survival rates compared to those with persistent and long-standing persistent AF at five years (81%, 50%, and 37%, respectively, *P* < 0.001, Fig. 1B), Supplementary Fig. 1. Sixty-two percent of all patients were maintained in sinus rhythm after TTA procedure. Of the 102 patients who recurred ATa, 26% patients received additional intervention such as catheter ablation or electrical cardioversion. Based on the last outpatient visit, 75% of all patients maintained sinus rhythm (Fig. 2). Both univariate and multivariate analyses showed that persistent AF, long-standing persistent AF, and LA diameter predicted recurrence of AF (Table 3).

3.4. Complications

During the mean follow-up of 32 ± 17 months, the overall complication rate was 4.5% (12 events) (Table 4). There was no case of

Table 2
Procedural characteristics.

Variables	Value (n = 265)	No recur (n = 163)	Recur (n = 102)	p-value
Pulmonary vein isolation (%)	265 (100)	163 (100)	102 (100)	
Ganglionic plexus ablation (%)	234 (88)	139 (86)	95 (93)	0.067
Roof line ablation (%)	246 (93)	149 (91)	97 (95)	0.452
Inferior line ablation (%)	261 (99)	159 (98)	102 (100)	0.281
Division of ligament of Marshall (%)	253 (96)	156 (96)	97 (96)	0.895
LAA resection or clipping (%)	261 (99)	160 (98)	101 (99)	0.576
SVC circular ablation (%)	124 (47)	73 (45)	51 (50)	0.408
SVC-IVC linear ablation (%)	29 (11)	17 (10)	12 (12)	0.735

conversion to open heart surgery due to intraoperative injury. One patient died one month after TTA for reasons not directly related to the operation. Four patients (1.5%) experienced minor stroke or transient ischemic attack (TIA) during follow-up (Table 5). One patient was an early phase of TTA and suffered embolic stroke in the left middle cerebral artery territory on postoperative day 4 with AF and no anticoagulation. Another patient suffered recurrent stroke before surgery and developed embolic stroke on postoperative day 2 despite heparin infusion. The other two patients developed minor stroke for different reasons such as atherosclerosis without recurrence of atrial fibrillation. Four patients developed pericarditis requiring medical treatment, and two patients had pleural effusion. Two patients received a permanent pacemaker because of sick sinus syndrome after surgery.

4. Discussion

4.1. Main findings

In this study, we presented our experience with the long-term efficacy and safety of TTA in patients with AF. After single TTA procedure, 51% of patients were free from ATa at five years. With additional treatment such as catheter ablation, DC cardioversion, or pharmacologic medication, three-quarters of patients maintained sinus rhythm over a mean follow-up of 23 months. During the follow-up period, stroke occurred in 1.5% of patients, and one died from a cause unrelated to the procedure.

The ATa-free survival rate of our study showed a similar trend to that of the previous study [8]. It has been hypothesized that direct application of TTA via epicardial access leads to a more constant and uniform transmural lesion. Early TTA studies have shown promising outcomes compared to catheter ablation. In a FAST study, surgical ablation was found to have better AF-free survival

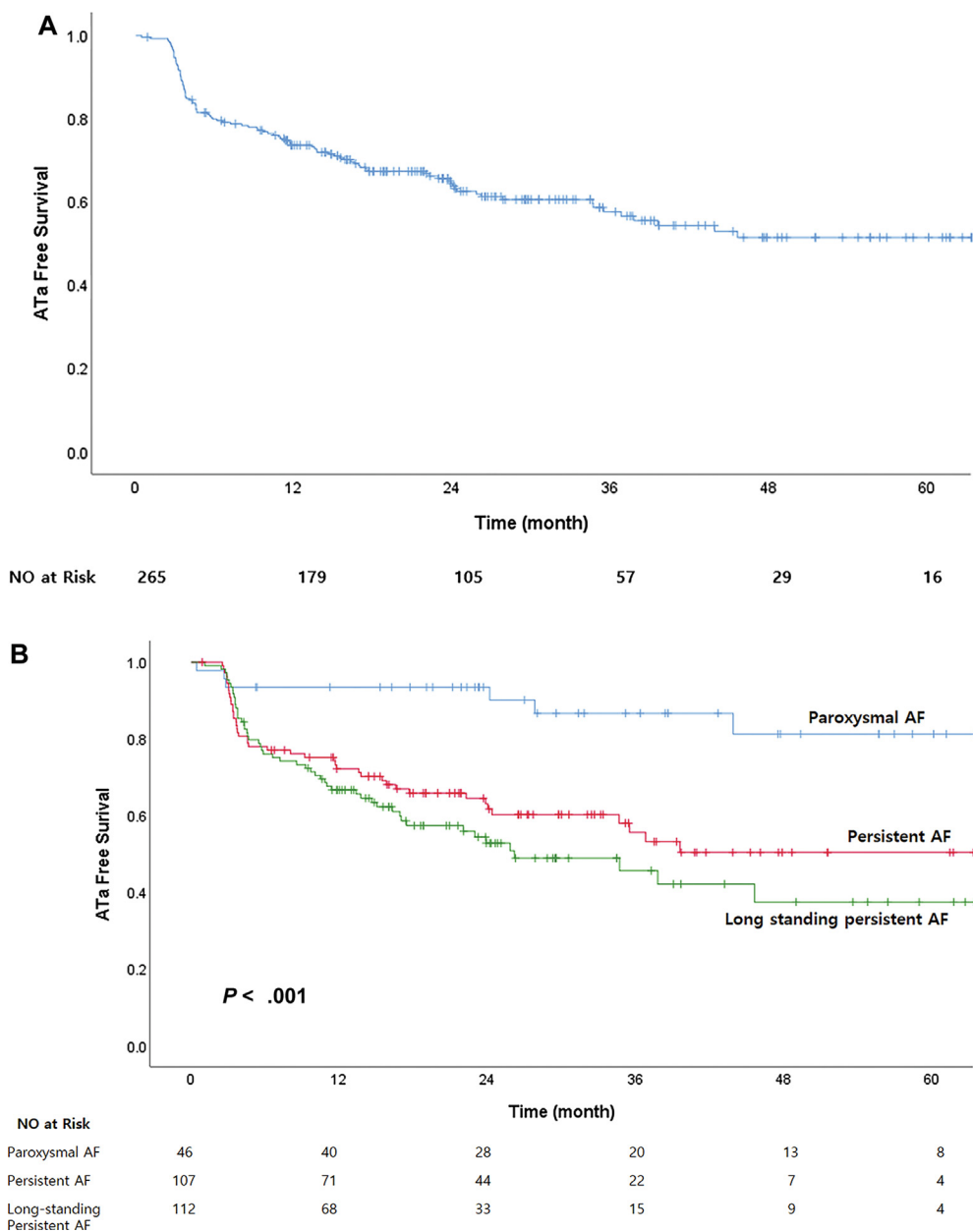


Fig. 1. Kaplan-Mayer curve for atrial tachyarrhythmia free survival. (A) Kaplan-Meier curve of freedom from atrial tachyarrhythmia in all patients. (B) Kaplan-Meier curve of freedom from atrial tachyarrhythmia according to AF type.

at 12 months than did catheter ablation (65.6% vs. 36.5%, $P = 0.002$) [9]. In another study of patients without previous ablation, the ATa-free survival was 91%, – significantly better than that of the catheter ablation group at 62% [10]. In two recent randomized studies of early persistent atrial fibrillation and longstanding persistent atrial fibrillation, there was no difference in efficacy between catheter ablation and surgical ablation. Catheter ablation was not inferior to surgical ablation in terms of efficacy and resulted in fewer complications (26% vs. 28%, $P = 0.83$) [11,12]. These studies were able to confirm asymptomatic AF recurrence using continuous ECG monitoring such as implantable loop recorder. Development of sophisticated 3D mapping system or advanced catheters has improved efficacy of catheter ablation, and continuous ECG monitoring has improved the diagnosis rate of recurrence. Next, in our study, although the five-year AF-free survival rate was about 50%, 75% of patients maintained sinus rhythm at the last follow-up with or without additional interven-

tion, including catheter ablation or DC cardioversion. These results mean that staged hybrid ablation may further improve efficacy outcomes.

The additional benefit of TTA is that it can enforce LAA exclusions simultaneously. Because LAA is the main site of intracardiac thrombus formation, LAA occlusion can reduce the risk of thromboembolism [13]. During the mean follow-up, the occurrence of stroke or TIA was very low, about 1.4%, which was much lower than expected based on CHA₂DS₂-VASc score, and half of stroke cases could be attributed to cerebral atherosclerosis. These are the results of the combined effects of rhythm control, anticoagulation, and LAA closure. However, evidence on the efficacy of LAA occlusion for stroke prevention is lacking, and the results of large-scale randomized studies currently in progress need to be confirmed [14]. In addition, the overall complication rate was very low at 4.5%. One patient died because of a medical problem not related to surgery, and there were no other serious complications.

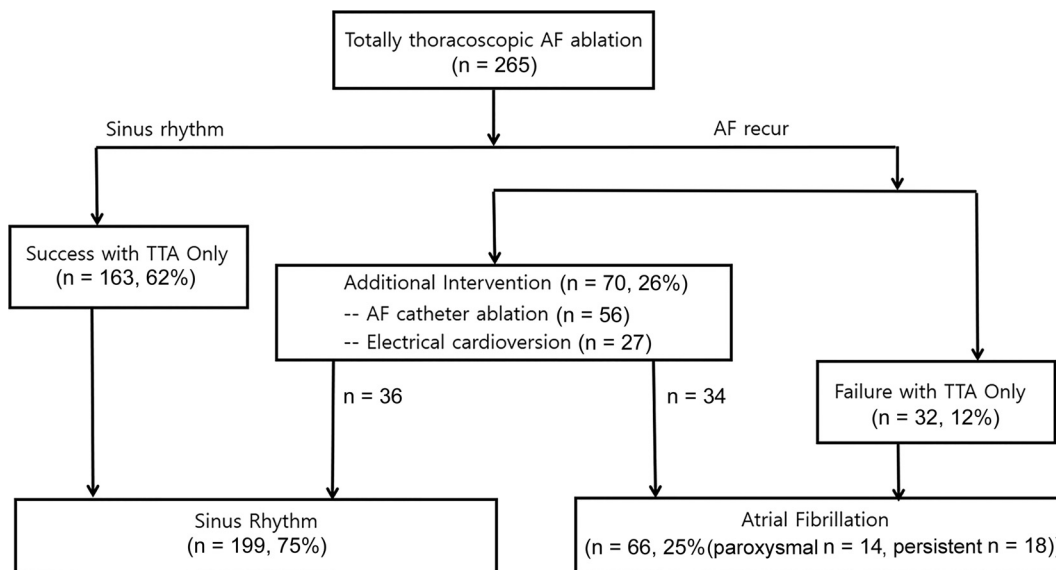


Fig. 2. Outcome of totally thoroscopic ablation in Samsung medical center. The mean follow-up duration was 23 ± 18 months (range: 3–60 months).

Table 3 Predictors for recurrence of atrial tachyarrhythmia.

Variables	Univariate analysis			Multivariate analysis*		
	HR	95% CI	P-value	HR	95% CI	P-value
Age	1.005	0.984–1.027	0.618	1.000	0.975–1.026	0.985
Sex	0.818	0.480–1.395	0.462	–	–	–
HTN	1.031	0.689–1.545	0.881	0.769	0.493–1.198	0.769
DM	0.833	0.433–1.600	0.583	–	–	–
BMI	1.060	1.003–1.119	0.038	1.017	0.953–1.086	0.611
Previous HF	1.081	0.578–2.021	0.808	–	–	–
Prior RFCA	1.250	0.741–2.107	0.403	–	–	–
Type of AF				–		
Paroxysmal		Reference			Reference	
Persistent	4.031	1.715–9.477	0.001	2.970	1.243–7.094	0.014
Long standing persistent	5.206	2.227–12.171	<0.001	3.958	1.660–9.434	0.002
LA diameter	1.081	1.050–1.114	<0.001	1.068	1.033–1.104	<0.001

* Multivariate analysis; adjusting age, HTN, BMI, AF type and LA diameter.

Table 4 Perioperative complications.

Variables	Value (n = 265)
Total complications (%)	12 (4.5)
Death (%)	1 (0.4)
Stroke or TIA (%)	4 (1.5)
Perioperative (in-hospital) (%)	2 (0.8)
During the follow-up (%)	2 (0.8)
Cardiac tamponade (%)	0
Pacemaker implantation (%)	2 (0.8)
Underlying sinus node dysfunction (%)	1 (0.4)
Postoperatively detected sinus node dysfunction (%)	1 (0.4)
Pericarditis (%)	4 (1.5)
Pleural effusion/Pleuritis (%)	1 (0.4)
Infection (%)	0

*TIA, transient ischemic attack.

Table 5 Characteristics of patients with stroke after TTA.

No	Sex	Age	C-V score	Onset	AC	Etiology	AF recur	
1	F	62	1	4 days	(–)	CE	(–)	Post op heparin discontinuation
2	M	65	3	2 days	(+)	CE	(+)	Perioperative recurrent stroke history
3	M	69	1	23 months	(–)	SAO	(–)	Cerebral atherosclerosis
4	F	62	1	9 months	(–)	CE	(–)	ASD closure, TCD shunt test (+)

**All patient underwent TTA with LAA exclusion.

Onset, stroke onset after TTA; AC, anticoagulation, CE, cardioembolism; SAO, small artery occlusion; mo, months; ASD, atrial septal defect; TCD, trans-cranial Doppler.

These results are significantly lower than Cox-maze, which has a 30-day mortality rate of 1% or more and a PPM insertion rate of 7% after surgery [15].

4.2. Study limitations

Study limitations include the single-center design. Further, there may be selection bias due to inclusion of only patients undergoing surgical ablation, and a few patients were lost to follow-up. However, compared to previous studies, a relatively large number of patients was included. In addition, this study could not evaluate the reconnection of surgical ablation lesions in patients with late recurrence. Further studies evaluating the durability of the lesion several months after ablation are needed. Finally, there is a possibility that recurrence of AF was underestimated using intermittent

ECG monitoring instead of continuous monitoring, and the burden of AF could not be measured.

5. Conclusion

TTA could be an effective treatment option for atrial fibrillation. It had a very low risk of complication and could reduce stroke incidence. Further studies are needed to improve treatment strategy.

Declaration of Competing Interest

The authors report no relationships that could be construed as a conflict of interest.

Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ijcha.2021.100861>.

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