



Mid-Term Results of Totally Thoracoscopic Ablation in Patients with Recurrent Atrial Fibrillation after Catheter Ablation

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Background: We investigated the impact of previous catheter ablation (CA) on the mid-term outcomes of totally thoracoscopic ablation in patients with lone atrial fibrillation (AF).
Methods: Between February 2012 and July 2018, 332 patients underwent totally thoracoscopic ablation for the treatment of AF (persistent AF; n=264, 80%). The patients were stratified into CA (n=47, 14%) and non-CA (nCA; n=285, 86%) groups according to their CA history.

Results: All the baseline clinical characteristics and risk factors were similar between the groups except for age, percentage of male patients, prevalence of paroxysmal AF, prior percutaneous coronary intervention, and left atrial volume index (LAVI). No significant intergroup differences were observed in the incidence of early and late complications. At late follow-up, normal sinus rhythm was observed in 92% (43 of 47) of the patients in the CA group and 85% (242 of 285) of the patients in the nCA group (p=0.268). The rate of freedom from AF recurrence at 5 years was 55.3%±11.0% in the CA group, which was similar to that in the nCA group (55.7%±5.1%, p=0.690). In Cox regression analysis, preoperative brain natriuretic peptide levels and LAVI were associated with AF recurrence, but CA history was not significant.

Conclusion: Totally thoracoscopic ablation was safe and effective in treating AF irrespective of CA history. A history of CA did not appear to affect the procedural complexity.

Keywords: Atrial fibrillation, Radiofrequency catheter ablation, Totally thoracoscopic ablation

Introduction

Atrial fibrillation (AF), which is the most common cardiac arrhythmia, is associated with significant complications such as heart failure and stroke. The overall incidence rate of AF is 9.9 per 1000 person-years [1]. For patients with AF that is refractory to antiarrhythmic drugs, the Cox maze III operation has been proven to be the most effective procedure, with a high success rate [2]. Radiofrequency catheter ablation (CA) has been a primary choice of treatment for AF owing to its safety and low invasiveness. However, a major concern is the high AF recurrence rate, which has been reported to be up to 43% within 12 months after CA [3-5]. Recurrent symptomatic AF or atrial tachycardia after a CA procedure necessitates repeated ablation in 20%–40% of patients [6]. With repeated procedures, com-

plications may occur in up to 6% of cases [7]. The most common finding in cases of repeated CA is high pulmonary vein reconnection through the previously targeted pulmonary veins, reflecting the undesirable capability of CA to achieve transmural ablation [8]. In addition, repeated ablation could result in a scar burden in the atrial tissue, which can be problematic and even promote the formation of a proarrhythmic substrate in the atria, which subsequently leads to new non-pulmonary vein triggers or atypical atrial flutter in the future [9]. Totally thoracoscopic ablation (TTA) may be a good choice of treatment owing to its high capability of achieving transmural ablation in patients with refractory AF. According to recent reports, this technique eliminates AF in 80% to 91% of patients [10]. The number of patients referred for TTA is increasing because of its advantages after failed CA; however, the efficacy of



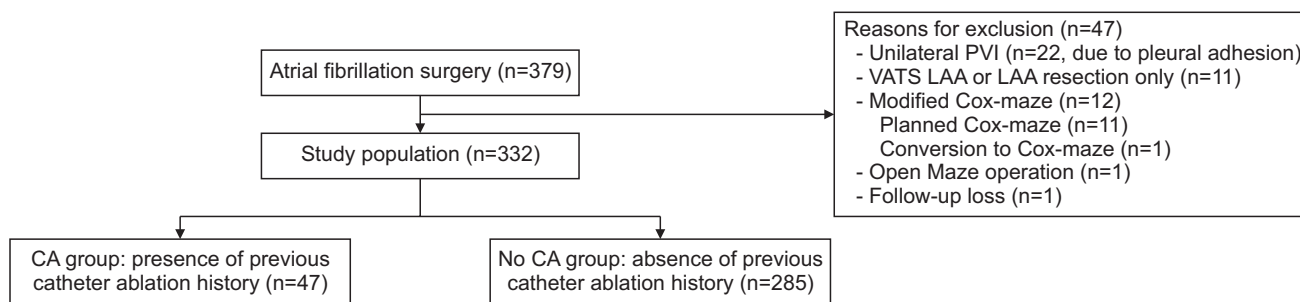


Fig. 1. Flow diagram of patient selection. PVI, pulmonary vein isolation; VATS, video-assisted thoracoscopic surgery; LAA, left atrial appendage; CA, catheter ablation.

TTA in these patients remains unknown. Herein, we investigated the impact of previous CA on the outcomes of TTA.

Methods

Study population

We applied the definitions of terms used in the 2012 Heart Rhythm Society/European Heart Rhythm Association/European Cardiac Arrhythmia Society consensus document for catheter and surgical ablation of AF. Patients with paroxysmal, persistent, or long-standing persistent AF refractory to at least 1 antiarrhythmic drug or direct current cardioversion were eligible candidates for TTA. The indications for TTA also included patient preference for surgery, a history of stroke, or a relative contraindication to warfarin therapy. TTA was contraindicated in patients with left atrial thrombi or intolerance to one-lung ventilation. Transthoracic echocardiography, pulmonary function testing, and chest computed tomography were performed in all patients preoperatively.

Between February 2012 and July 2018, 379 patients underwent surgery solely for arrhythmia at Samsung Medical Center. Forty-seven patients who had a Cox maze operation or incomplete pulmonary vein isolations were excluded from the study (Fig. 1). Consequently, 332 patients who underwent TTA for the treatment of AF were retrospectively evaluated. The patients were grouped according to the presence (CA group; n=47, 14%) or absence (nCA group; n=285, 86%) of a CA history. We compared the rhythm outcomes and complications between the 2 groups. The study was approved by the Institutional Review Board of Samsung Medical Center (IRB approval no., SMC 2019-12-011-001). Informed consent was obtained from all individual participants included in the study.

Operative technique

After general anesthesia induction and double-lumen endotracheal intubation, selective ventilation of the contralateral lung was performed. TTA is a video-assisted thoracoscopic surgical technique without the aid of the Da Vinci system and cardiopulmonary bypass. A bilateral approach is required, and the right-side procedure is performed first with a 12-mm port inserted in the fourth intercostal space at the anterior axillary line. Two additional ports are placed, a 5-mm port in the third intercostal space at the anterior axillary line and a 5-mm port in the sixth intercostal space at the midaxillary line, after carbon dioxide insufflation to expand the operative field and depress the diaphragm. The pericardium is opened, and pericardial tenting is performed. A rubber band is then fixed to an AtriCure Isolator Transpolar Clamp (AtriCure Inc., Mason, OH, USA), and the bipolar clamp is opened and secured around the antrum of the right pulmonary veins to perform bipolar radiofrequency ablation for at least 6 overlapping lesions. On the left side, a 12-mm port is inserted in the fourth intercostal space at the midaxillary line. Like on the right side, a 5-mm port is inserted in the third intercostal space at the anterior axillary line and a 5-mm port is inserted in the sixth intercostal space at the midaxillary line. The left atrial roof and floor lesions connecting both pulmonary veins are created with a linear pen device (AtriCure Inc.). Next, the ganglionated plexuses are ablated because they are composed of autonomic fibers and can initiate AF when excess activity at these sites occurs [11]. An AtriCure Cooltip pen (AtriCure Inc.) is used to confirm the placement of the ablation lines, and a pacing test is subsequently conducted. The ligament of Marshall (LOM), which might be a source of adrenergic atrial tachycardia, is also divided. The left atrial appendage (LAA) is either removed by stapling with an endoscopic stapling de-

vice (Endo GIA; Tyco Healthcare Group, North Haven, CT, USA) or clipped (AtriClip; AtriCure Inc.). The sequence of the procedures has been discussed in more detail in a previously published article [10].

Electrophysiological study

In our early practice, we performed an endocardial procedure 3 months after surgery on the basis of the finding that during this window period, even with bidirectional block confirmation, several patients showed late cavo-tricuspid-isthmus (CTI)-dependent atrial flutter [10]. However, we currently perform a staged hybrid procedure only in patients with recurrent atrial tachyarrhythmia refractory to thoracoscopic epicardial ablation.

Pulmonary vein potentials were assessed using Lasso catheters (Biosense Webster) with a diameter of 15–25 mm. The intra-atrial, atrio-His, and His-ventricular conduction intervals were measured. CTI ablation was performed in patients with long-standing AF or in those who had episodes of atrial flutter after TTA.

Postoperative care and follow-up

The patients were monitored in the intensive care unit for the first 24 hours. Postoperatively, heparin was administered, and conversion to either warfarin or edoxaban was performed on postoperative day 1. Oral amiodarone was prescribed if the heart rate was >80 beats/min at rest. All the patients were followed up at 3, 6, and 12 months, and annually thereafter with 24-hour Holter monitoring and echocardiography to evaluate rhythm and atrial activity. Electric or chemical cardioversion was performed in patients with AF, atrial flutter, or atrial tachycardia within the 3-month blanking period during follow-up. All antiarrhythmic drugs were discontinued once patients recovered sinus rhythm at 3 months or up to 6 months.

Statistical analysis

The independent t-test was used to compare continuous variables, which are presented as medians and interquartile ranges, between the 2 groups. The chi-square test was used to compare categorical data, which are presented as proportions. Freedom from AF recurrence at 5 years was analyzed using curves derived from a Kaplan-Meier analysis. A p-value of <0.05 was considered to indicate statistical significance. Cox regression analysis was performed to identify predictors of AF recurrence after TTA. The vari-

ables that were included in the univariate analysis were age, body mass index, hypertension, congestive heart failure, AF duration, preoperative brain natriuretic peptide, left atrial volume index, left ventricular ejection fraction, and history of CA. Variables with p-values of <0.20 in the univariate analysis were entered into the multivariate analysis.

Results

Baseline characteristics of the patients

The baseline characteristics of the patients are shown in Table 1. The median age of all the patients was 56 years, and the patients in the nCA group were older than those in the CA group. The proportion of male patients was higher in the nCA group than in the CA group. The patients in the CA group had significantly smaller left atrial volume index (49 versus 39 mL/m², p=0.001) and were more likely to have paroxysmal AF than those in the nCA group (34.0% versus 18.2%, p=0.01). In addition, the patients in the nCA group had higher preoperative BNP levels (414.3 versus 322.5 pg/mL, p=0.017). Concerning comorbidities, more patients had a history of prior percutaneous coronary intervention in the CA group (8% versus 1%, p=0.001). The other baseline characteristics and risk factors were similar between the groups. In the CA group, 29 (62%), 14 (29%), and 4 (9%) patients had a history of 1, 2, and 3 previous CAs, respectively. All the patients underwent isolation of both pulmonary veins. LAA resection or clipping was performed in 323 patients (97%). Additionally, 134 patients (40%) underwent ablation of a circular lesion made in the superior vena cava with a bipolar clamp, when the right atrium was significantly enlarged in the thoracoscopic view. The proportions of the surgical techniques used were similar between the groups (Table 1). Thirty-two patients, of whom only 1 was from the CA group, underwent post-procedural electrophysiological confirmation after TTA.

Postoperative complications

Postoperative adverse outcomes are listed in Table 2. No mortality was reported during hospitalization or follow-up. Regarding thromboembolism, only 3 cases of stroke occurred in the nCA group. Pulmonary complications, including prolonged pleural effusion and mild pneumonia, occurred in 12 patients in the nCA group and in 1 patient in the CA group (p=0.495).

One patient experienced subconjunctival hemorrhage.

Table 1. Baseline and procedural characteristics

Characteristic	No CA group (n=285)	CA group (n=47)	Total (N=332)	p-value
Baseline characteristics				
Age (yr)	57.0 (51–62)	52.9 (44–59)	56.3 (51–62)	0.004
Male sex	258 (90.5)	37 (78.7)	295 (88.9)	0.017
Body mass index (kg/m ²)	25.7 (23–27)	25.1 (23–26)	25.7 (23–27)	0.147
AF duration (mo)	62.7 (11–70)	84.2 (39–122)	65.7 (13–79)	0.317
Type of AF				
Paroxysmal	51 (17.8)	16 (34.0)	68 (20.5)	0.010
Persistent or long-standing	234 (82.1)	31 (66.0)	265 (79.9)	
Procedural characteristics				
Left atrial appendage resection or clipping	277 (97.1)	46 (97.8)	323 (97.2)	0.790
Superior ablation	246 (86.3)	40 (85.1)	286 (86.1)	0.824
Posterior ablation	282 (98.9)	46 (97.8)	328 (98.7)	0.531
Superior vena cava ablation	116 (40.7)	18 (38.2%)	134 (40.3)	0.756
Left atrial volume index (mL/m ²)	49.3 (34–52)	39.9 (28–40)	48.0 (33–50)	0.001
Left ventricular ejection fraction (%)	59.9 (60–61)	59.0 (60–60)	59.8 (60–60)	0.383
Preoperative brain natriuretic peptide (pg/mL)	414.3 (68–529)	322.5 (85–444)	401.0 (158–521)	0.017
Comorbidities				
Congestive heart failure	20 (7.0)	1 (2.1)	21 (6.3)	0.202
Prior stroke	53 (18.6)	6 (12.8)	59 (17.8)	0.333
Prior percutaneous coronary intervention	3 (1.1)	4 (8.5)	7 (2.1)	0.001
Peripheral vascular disease	6 (2.1)	1 (2.1)	7 (2.1)	0.992
Hypertension	105 (36.8)	12 (25.5)	117 (35.2)	0.133
Diabetes mellitus	28 (9.8)	3 (6.4)	31 (9.3)	0.452

Values are presented as median (interquartile range) or number (%). CA, catheter ablation; AF, atrial fibrillation.

Table 2. Major complications

Variable	No CA group (n=285)	CA group (n=47)	p-value
Stroke	3 (1.0)	0	0.480
Postoperative bleeding	6 (2.1)	2 (4.2)	0.373
Pacemaker insertion	4 (1.4)	0	0.414
Prolonged pleural effusion	12 (4.2)	1 (2.1)	0.495
Sinus node dysfunction	8 (2.8)	2 (4.2)	0.590

Values are presented as number (%). CA, catheter ablation.

However, the symptom resolved spontaneously without any treatment. Minor chest tube bleeding that required no intervention occurred in 4 cases. Chest tube drainage was needed for pleural hematoma that developed 2 days after removal of the original chest tube in 1 case. Two cases needed bleeding control operation for the left hemothorax on postoperative day 1 for a sustained large amount of chest tube bleeding. In one of the cases, we could not find the specific bleeding focus solely on the basis of the diffuse oozing. The bleeding focus in the other case was from the arterial bleeding of the apex side of the left pleural space, where we initially performed adhesiolysis for pleural adhe-

sion. Neither patient showed any postoperative complications.

Rhythm outcomes

The median follow-up duration was 24.3 months, and all the patients were followed up with 24-hour Holter monitoring. The median follow-up duration was 22.8 months in the CA group and 24.8 months in the nCA group. At the latest follow-up, normal sinus rhythm was observed in 92% (43 of 47) of the patients in the CA group and in 85% (242 of 285) of the patients in the nCA group ($p=0.268$). Of the 285 patients, 75 (27%) and 210 (73%) attained sinus rhythm with and without taking antiarrhythmic drugs, respectively. The rate of freedom from AF recurrence at 5 years was $55.3\pm 11.0\%$ in the CA group, which was similar to that in the nCA group ($55.7\pm 5.1\%$, $p=0.690$) (Fig. 2). In the Cox regression analysis, preoperative brain natriuretic peptide levels (hazard ratio, 1.001; $p=0.006$) and the left atrial volume index (hazard ratio, 1.028; $p=0.001$) were associated with AF recurrence after TTA (Table 3).

Discussion

In this study, we compared the outcomes of patients who underwent TTA with and without a history of CA. No previous study in the current literature has investigated the effect of CA on TTA. The mechanisms of AF are known to be complex and are not fully understood despite extensive research. The pulmonary veins are considered the most important treatment target, as they function as triggers for the development of AF. However, the sources of recurrent AF, especially permanent AF, are often difficult to identify. In patients with refractory AF, re-entrant activities induced

by atrial remodeling are another possible causative factor [12]. In a previously published study, AF recurrence after PVI was predicted on the basis of the extent of fibrosis, and atrial fibrosis was present in all the cases [13]. Fibrosis identified on cardiac magnetic resonance imaging was proven to be an independent factor associated with AF recurrence after CA [13]. Furthermore, a left atrial scar burden after multiple extensive CA was reported [14]. Therefore, we anticipated that the patients in the CA group would be in a more advanced atrial remodeling state with repeated CA, which might lead to a lower chance of normal sinus rhythm recovery than those in the nCA group.

Surgical complexity was sometimes observed in patients with a CA history, including pericardium adhesion due to hemopericardium, left atrial contractions, and dimpling. Infrequently, some patients had left atrial stenosis or occlusion after repeated radiofrequency CA, which increased the operative time, but did not affect the surgical outcomes. Our data also showed that the 2 groups had no significant differences in AF recurrence.

The 2016 European Society of Cardiology/European Association for Cardiothoracic Surgery guidelines for AF indicate TTA as a class 2A recommendation for the treatment of symptomatic and drug-refractory AF. This recommendation is based on the FAST trial, which showed that surgical ablation is better than CA for patients with an enlarged left atrium and hypertension, or in whom prior CA has failed [15]. Recent studies have reported additional long-term outcomes of CA and surgical ablation. Castella et al. [16] reported that surgical ablation was associated with higher rates of sinus rhythm maintenance and lower

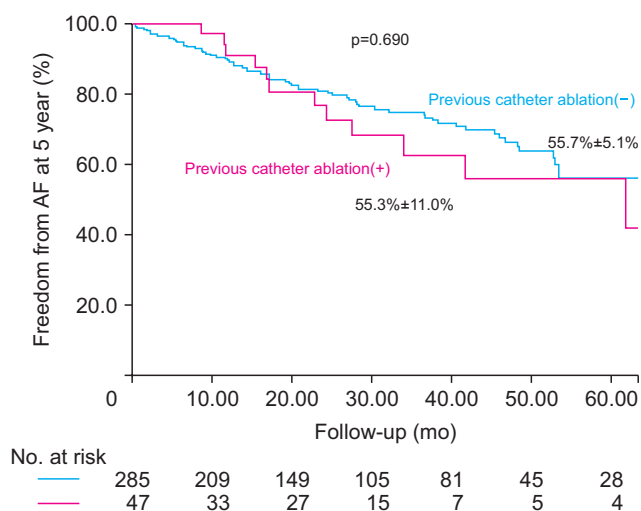


Fig. 2. Freedom from AF recurrence at 5 years. Kaplan-Meier curves of AF recurrence and antiarrhythmic drug use are shown. AF, atrial fibrillation.

Table 3. Predictors of recurrent AF

Variable	Univariate p-value	Multivariate p-value	Hazard ratio (95% confidence interval)
Age	0.335		
Female sex	0.040		
Body mass index	0.053		
AF duration	0.465		
Persistent or long-standing AF	0.012		
Left atrial volume index	0.005	0.001	1.028 (1.012–1.044)
Left ventricular ejection fraction	0.640		
Preoperative brain natriuretic peptide	0.002	0.006	1.001 (1.000–1.002)
Congestive heart failure	0.913		
Prior stroke	0.195	0.050	0.396 (0.157–0.999)
Prior percutaneous coronary intervention	0.629		
Peripheral vascular disease	0.541		
Hypertension	0.189		
Diabetes mellitus	0.280		
Previous catheter ablation history	0.179		

AF, atrial fibrillation.

rates of additional ablation or antiarrhythmic drug use.

The other advantages of TTA over CA include its capability to ablate ganglionated plexuses, to divide the LOM, and to resect the LAA. The LOM is an arrhythmogenic source located in the epicardium between the LAA and the left pulmonary veins. The LOM is a remnant tissue of the left superior vena cava that contains nerves, muscle bundles, and fibrous tissues. Ablation of the LOM is helpful for patients with AF, as it can eliminate accessory pathway conduction [17]. Furthermore, the LAA can be excluded using a clip or stapler. Doing so is important for preventing embolic stroke and eliminating the trigger site of AF [18]. We expected that these advantages of TTA would have an additive effect on patients in the CA group.

However, TTA alone cannot treat AF, especially persistent AF. In our previously reported study that included part of the dataset in the present study, 19% of the patients required additional cardiac ablation because mitral annulus and septal line ablations are difficult to ablate using only a thoracoscope [10]. Moreover, pulmonary vein isolation is sometimes not perfect in the presence of a very large left atrium. In addition, as demonstrated in another study that included part of the same dataset in the present study, arrhythmia cannot be perfectly treated with any single procedure [19]. Therefore, a hybrid procedure (combination of epicardial and endocardial ablations) is expected to be the standard treatment for AF, especially persistent or long-standing persistent AF. However, evidence is still lacking about the ideal timing of postoperative electrophysiological confirmation and additional ablation after TTA. Recent studies on simultaneous TTA and hybrid ablation and sequential ablation were mostly either retrospective in nature or had small sample sizes [20].

We anticipated that the outcomes of the CA group would be better than those of the nCA group for a number of other reasons. According to many published studies, one of the main causes of AF recurrence after CA is recanalization of a pulmonary vein isolation lesion [3,5]. Meanwhile, a major advantage of TTA is the achievement of durable pulmonary vein isolation. Furthermore, ablation of CTI and creation of a mitral isthmus lesion, which are not possible during TTA, can be performed with CA. Therefore, hybrid ablation can be anticipated to have favorable effects. However, in this study, CA history did not affect the mid-term outcomes of TTA. A possible explanation is that the long-term use and over-prescription of antiarrhythmic drugs led to similar results between the groups. Following the guidelines on the use of antiarrhythmic drugs and conducting long-term follow-up of patients are necessary.

Our study has some limitations. First, this is a small-scale retrospective study investigating the impact of previous CA on the short-term outcomes of TTA. Studies of long-term outcomes in more patients are needed. Moreover, no standardized protocol has been established for AF treatment. The time of thoracoscopic ablation after radiofrequency CA should be confirmed. Moreover, the use of medications should be included in future studies.

In conclusion, CA history did not affect the procedural complexity or success rate of thoracoscopic ablation. TTA after CA is safe and effective.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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