Electrical isolation of the left atrial appendage in East Asian patients with atrial fibrillation

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BACKGROUND The left atrial appendage (LAA) is a source of non–pulmonary vein triggers in patients with atrial fibrillation (AF). Electrical isolation of the LAA (EILAA) improves rhythm outcome with an inherent risk of embolism unless lifelong anticoagulation is continued. However, evidence of the efficacy and safety of EILAA in the East Asian population remains lacking.

OBJECTIVE The purpose of this study was to evaluate the efficacy and safety in East Asian patients who underwent EILAA.

METHODS Using the data from a single center, we identified patients who underwent EILAA for AF between January 2009 and August 2023. Clinical and procedural data were analyzed.

RESULTS We included a total of 41 patients who underwent EILAA. EILAA was unsuccessful in 2 patients. The median duration of AF was 5.0 years (interquartile range 4.0–10.0 years). Twenty-five patients (65.8%) underwent more than 1 previous ablation for AF before the index procedure. The mean CHA_2DS_2-VASc score was 2.8 ± 1.6. The mean left atrial dimension was 50.6 ± 8.7 mm. The 1-year recurrence rate of atrial arrhythmia after EILAA was 42.0% (21 patients during follow-up). Six patients (14.6%) underwent redo ablation, and 5 of them had durable isolation of the LAA. One patient had cardiac tamponade, which was drained with pericardiocentesis. All patients had taken lifelong anticoagulation, and 3 of them had stroke or systemic embolism during the follow-up period.

CONCLUSION EILAA could be a safe and effective strategy for patients with long-standing AF with a history of failed ablation, especially with a high CHA_2DS_2-VASc score. Lifelong anticoagulation is mandatory for patients undergoing EILAA.

KEYWORDS Atrial appendage; Atrial fibrillation; Catheter ablation; Stroke; Left atrium; Anticoagulants

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Introduction

Catheter ablation is the criterion standard strategy for treating rhythm control in atrial fibrillation (AF), and pulmonary vein (PV) isolation is a key component.[1,2] However, the recurrence rate of AF after PV isolation remains substantial, particularly in patients with long-standing AF.[3] The role of non-PV triggers and substrate modification in these patients has been extensively investigated and discussed from various perspectives.[4–7] Since the left atrial appendage (LAA) serves as a non-PV trigger in patients with AF, electrical isolation of the LAA (EILAA) improves rhythm outcome, especially in persistent AF.[8–12] However, the concern of an inherent risk of stroke and systemic thromboembolism exists unless lifelong oral anticoagulation (OAC) therapy is maintained.[13,14]

In previous studies, the proportion of East Asian participants was either minimal or absent. Considering the genetic, environmental, and lifestyle factors specific to the East Asian population, there is insufficient evidence regarding the safety and efficacy of EILAA in East Asians. Therefore, in this study, we evaluated clinical characteristics and stroke or thromboembolism in East Asian patients with AF who underwent EILAA by using real-world data.

Methods

Data sources and study population

In this retrospective analysis, we included patients with AF who underwent radiofrequency ablation along with EILAA or subsequently underwent EILAA in a single center (Division of Cardiology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea) between January 2009 and August 2023 (Figure 1).

AF-related clinical variables, including demographic factors, medical history, and clinical characteristics and

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KEY FINDINGS

- Patients undergoing electrical isolation of the left atrial appendage (EILAA) primarily presented with advanced atrial fibrillation (AF), characterized by long-standing persistent AF, an enlarged left atrial dimension, and a history of multiple failed surgical or catheter ablation procedures.
- EILAA proved to be an effective strategy in this high-risk population, achieving favorable clinical outcomes despite the advanced nature of their AF.
- Lifelong anticoagulation was administered to all patients, leading to a low incidence of stroke or systemic embolism when maintained with appropriate oral anticoagulation therapy, even during extended follow-up.
- EILAA was particularly effective for patients with super-long-standing persistent AF who were refractory to previous ablation procedures or had a high recurrence risk, as indicated by elevated CHA_2DS_2-VASc scores.
- For patients undergoing EILAA, lifelong anticoagulation is critical, and early consideration of left atrial appendage closure may further enhance clinical outcomes.

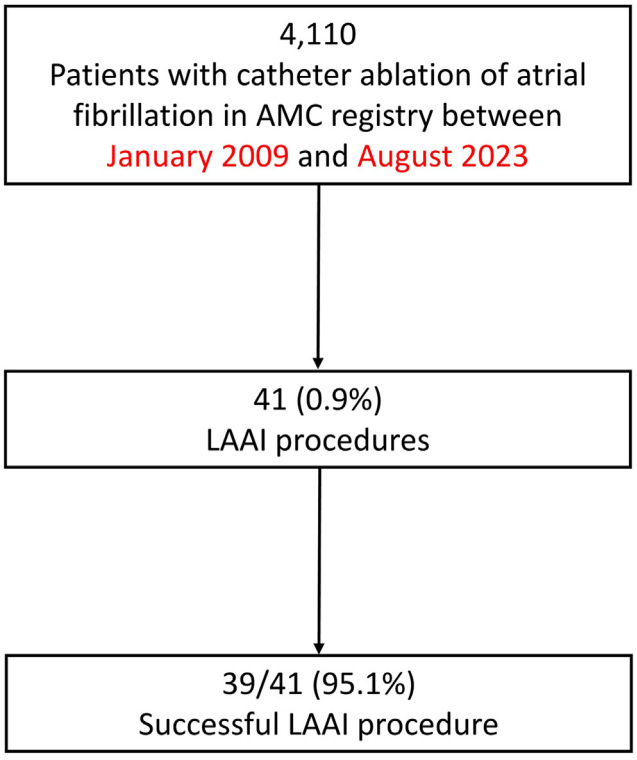

Figure 1 Flow diagram.

procedure-related variables, were obtained from the hospital records.

This study adhered to the ethical principles outlined in the Declaration of Helsinki and was approved by the Institutional Review Board of Asan Medical Center. All patients provided their written informed consent before inclusion in the Asan Medical Center-atrial fibrillation ablation registry.

Preprocedural anatomic evaluation

All patients underwent transthoracic echocardiography before radiofrequency ablation. Computed tomography or magnetic resonance imaging was performed to assess the anatomic features and variations in the PVs as well as to exclude the presence of a thrombus in the left atrium.

Standard ablation procedure

The ablation procedure was performed under deep sedation using infusion of propofol with fentanyl or remifentanil. A double transseptal puncture was performed using a modified Brockenbrough technique with or without intracardiac echocardiography. Unfractionated heparin was administered before transseptal catheterization, and the activated clotting time was monitored. According to the ablation protocol, the circumferential PV was isolated, guided by a mapping catheter and 3-dimensional electroanatomic mapping system (Carto, Biosense Webster, Lake Forest, CA; Rhythmia, Boston Scientific, Marlborough, MA; and EnSite, Abbott, Chicago, IL). Ablation was performed with a contact force–sensing irrigated tip catheter. For redo cases, conduction gaps of prior linear ablation procedures were closed and bidirectional block was verified. If a trigger from the LAA was found or no other trigger was found after 2 additional prior ablation procedures, empirical EILAA was performed. EILAA was performed using 2 techniques (Figures 2A and 2B). The first method was circumferential ablation at the level of the ostium (power 40 W, 20–30 seconds at each point, target contact force 5–25 g). The second approach involved creating a line around the LAA, achieved by performing linear ablation along the anterior part of the left ridge line, a posterolateral mitral isthmus line, and an anterolateral line (Figure 2B) (40 W, 20–30 seconds).[10,15] In both methods, the end point of ablation was entrance and exit block to the LAA (Figure 2C).

Outcomes

The primary efficacy outcome was freedom from all atrial arrhythmia recurrence lasting more than 30 seconds during follow-up. Events that occurred during the first 3 months after the procedure were not considered recurrence (blanking period). The primary safety outcomes included procedure-related complications, and the secondary safety end point was symptomatic ischemic stroke or systemic thromboembolic event.

Postablation treatment and follow-up

All patients had taken lifelong OAC therapy irrespective of CHA_2DS_2-VASc score. The maintenance of antiarrhythmic drugs after the index procedure was at the physician's discretion.

Twelve-lead electrocardiography was performed immediately after ablation and between 1, 3, and 6 months after the

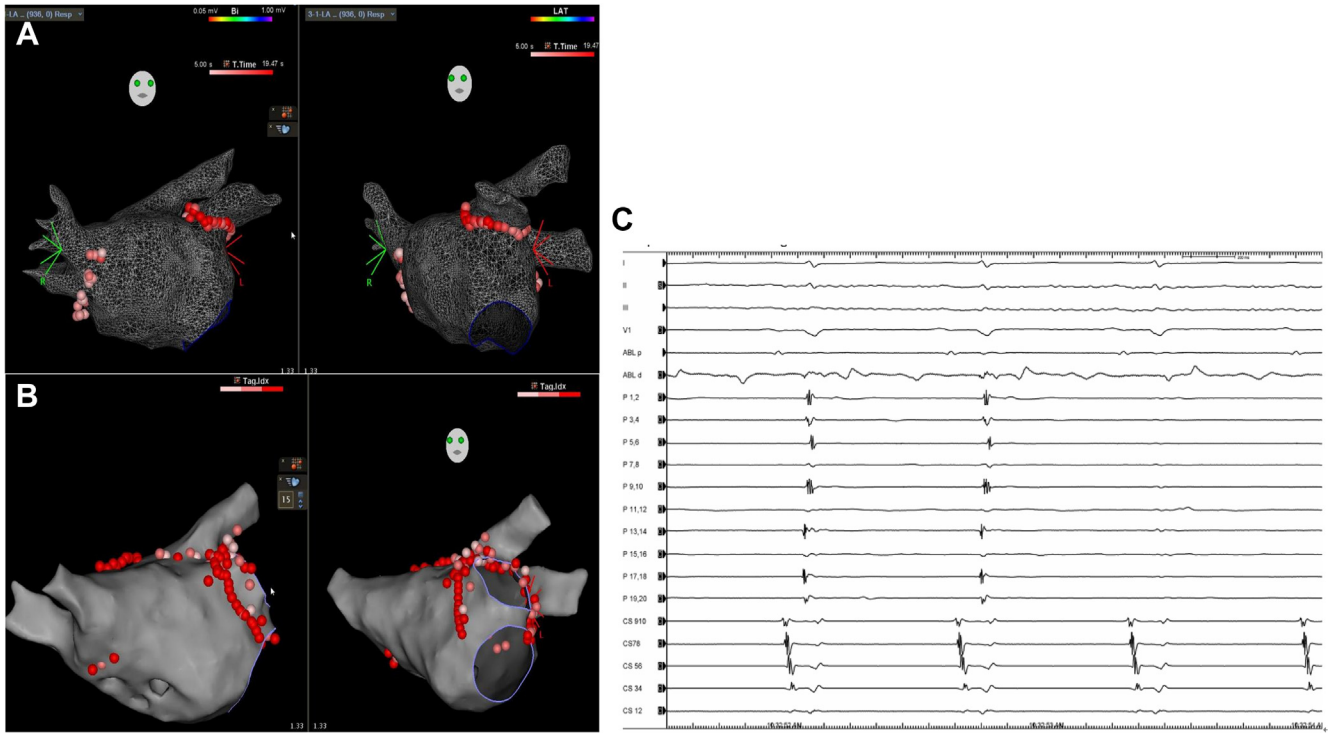

Figure 2 **A:** and **B:** Two techniques of EILAA, **C:** The electrocardiogram showed the electrical isolation of the LAA. EILAA = electrical isolation of left atrial appendage; LAA = left atrial appendage.

index procedure. Patients initially visited outpatient clinics at 1, 3, and 6 months and every 3 or 6 months thereafter. At least 24-hour Holter monitoring was performed at 3, 6, and 12 months after the index procedure and at any time if the patient complained of palpitations. Postprocedural transthoracic echocardiography and transesophageal echocardiography (TEE) were performed at the physician's discretion.

Statistical analysis

Continuous variables were reported as mean ± SD and were compared using the *t* test or Wilcoxon rank sum test (for non-normally distributed data). Categorical variables were reported as number (percentage) and were compared using the χ^2 test or Fisher exact test, as appropriate. Time to recurrence was plotted using the Kaplan-Meier product limit method and compared using the log-rank test. All *P* values were 2-sided, with those less than .05 considered statistically significant. All statistical analyses were performed using the R statistical package, version 4.2.3 (http://www.r-project.org).

Results

Baseline characteristics and data analysis

Among 41 patients with AF in whom EILAA was achieved, complete EILAA was not achieved in 2 patients. Three patients achieved EILAA inadvertently. Twenty-three patients were male (56.1%) with a mean age of 66.4 ± 8.5 years. Eight patients had previously undergone open heart surgery (19.5%), including valve replacement and repair, septal myectomy, and Maze operation. Among patients who underwent heart surgery, 5 underwent the Maze operation. Among all patients, 37 (90.2%) had persistent AF, of whom 35 (85.4%) had long-standing persistent AF. The median duration of AF was 5.0 years (interquartile range 4.0–10.0 years), and 65.8% of patients underwent a previous procedure, either surgical or catheter ablation, for AF. The mean left ventricular ejection fraction was 53.1% ± 10.2%; the mean left atrial (LA) dimension was 50.6 ± 8.7 mm; and the mean LA volume index was 65.0 ± 25.9 mL/m^2. The mean CHA_2DS_2-VASc score was 2.8 ± 1.6, and 34 patients (82.9%) had a score of 2 or higher. The baseline characteristics of the patients are presented in Table 1.

Procedural characteristics

Among 41 patients with AF in whom EILAA was included, complete EILAA was not achieved in 2 patients. EILAA occurred inadvertently in 3 patients. The total procedure time was 215.1 ± 92.3 minutes, and the total fluoroscopy time was 9.3 ± 17.5 minutes. The acute success rate was 95.1%. Linear ablation was performed in 32 patients (80%), and only 8 patients (20.0%) achieved EILAA through ostial ablation. During the ablation procedure for EILAA, 1 patient had cardiac tamponade, which was drained with pericardiocentesis without sequelae. The procedural characteristics of the patients are presented in Table 2.

Outcomes

The median follow-up duration was 12.2 months (interquartile range 8.0–18.3 months) (Table 3). Early recurrence

Table 1 Baseline characteristics of the study population (N = 41)

Characteristic	Value
Age (y)	66.4 ± 8.5
Male	23 (56.1)
Body mass index (kg/m^2)	27.4 ± 9.3
Comorbidities	
Hypertension	19 (46.3)
Diabetes mellitus	7 (17.1)
Prior stroke	5 (12.2)
Congestive heart failure	22 (53.7)
Coronary artery disease	3 (7.3)
Prior open heart surgery	8 (19.5)
AF duration (y)	5.0 (4.0–10.0)
Paroxysmal AF	4 (9.8)
Persistent AF	37 (90.2)
Long-standing persistent AF	35 (85.4)
CHA_2DS_2-VASc score	
0	2 (4.9)
1	5 (12.2)
≥2	34 (82.9)
CHA_2DS_2VASc score	2.8 ± 1.6
Oral anticoagulation	41 (100)
Warfarin	14 (34.1)
DOACs	27 (65.9)
Previous procedure, either surgical or catheter ablation, for AF	25 (65.8)
Echocardiographic parameters	
LVEDD (mm)	51.0 ± 5.8
LVEF (%)	53.1 ± 10.2
LA dimension (mm)	50.6 ± 8.7
LA volume index (mL/m^2)	65.0 ± 25.9

Values are presented as mean ± SD, median (interquartile range), or n (%).

AF = atrial fibrillation; DOAC = direct oral anticoagulant; LA = left atrium; LVEDD = left ventricular end diastolic dimension; LVEF = left ventricular ejection fraction.

Table 2 Procedural characteristics of the study population (N = 41)

Characteristic	Value
Total procedure time (min)	215.1 ± 92.3
Ablation time (min)	43.8 ± 36.8
Fluoroscopy time (min)	9.3 ± 17.5
Fluoroscopy dose (mGy·m^2)	234.3 ± 205.0
Lesion of EILAA	
Ostial ablation	8 (20.0)
Linear ablation	32 (80.0)
Lesion of ablation	
Pulmonary vein isolation	41 (100)
Other non-PV ablation	
Cavotricuspid isthmus ablation	33 (80.5)
LA roofline ablation	31 (75.6)
Mitral isthmus ablation	32 (78.0)
Left atrial anterior line ablation	20 (48.8)
Left atrial posterior line ablation	26 (63.4)
Isolation of superior vena cava	29 (70.7)
Intercaval linear ablation	24 (58.5)
Failure of EILAA	2 (4.9)
Procedure-related complications	
Cardiac tamponade	1 (2.4)

EILAA = electrical isolation of the left atrial appendage; PV = pulmonary vein; other abbreviations as in Table 1.

Table 3 Outcomes of EILAA

Outcome	Value
Follow-up duration (mo)	12.2 (8.0–18.3)
Early recurrence during the blanking period	18 (43.9)
Late recurrence	21 (51.2)
1-y recurrence rate (%)	42
Final maintenance of sinus rhythm during follow-up	36 (87.7)
Stroke	3 (7.3)
Stroke under appropriate OAC therapy	1 (2.6%)
Thrombus of the LAA under appropriate OAC therapy	1

Values are presented as mean ± SD, median (interquartile range), or n (%).

LAA = left atrial appendage; OAC = oral anticoagulation; other abbreviations as in Table 1.

during the blanking period within 90 days of the procedure was observed in 18 patients (43.9%). Late recurrence after the blanking period occurred in 21 patients (51.2%), with AF being the most common type of recurrence, accounting for 71% of cases. The 1-year recurrence rate of atrial arrhythmia after EILAA was 42%. Final maintenance of sinus rhythm, either under antiarrhythmic drugs or through redo ablation, was achieved in 36 patients (87.8%) during follow-up (Figure 3). Among the 3 patients who had a stroke, 2 cases occurred during transient discontinuation of OAC therapy. Of these, one patient was on warfarin and had a stroke when the international normalized ratio was not within the target range while the other patient was on a direct OAC but had a stroke during a period of therapy interruption. Consequently, only 1 stroke occurred during appropriate OAC therapy. This patient suffered a minor stroke involving an infarction in the middle cerebral artery territory and subsequently underwent LAA occlusion. No deaths occurred during follow-up. In all 41 patients, postprocedure follow-up was conducted. LAA occlusion was provided in 2 patients after EILAA.

Follow-up echocardiography

Considering the role of modulating the LA pressure-volume relationship of the LAA, we analyzed changes in the early diastolic filling velocity/early diastolic velocity of the mitral annulus (E/E') ratio before and after EILAA. The mean pre-EILAA E/E' ratio was 14.89 and the post-EILAA E/E' ratio was 17.17, with a mean difference in the E/E' ratio of 2.9 (P = .41). The mean pre-EILAA peak tricuspid regurgitation velocity was 2.64 and the post-EILAA peak tricuspid regurgitation velocity was 2.72, with a mean difference of 0.08 (P = .25). Among the 41 patients, postprocedure follow-up TEE was performed in 4 patients. Spontaneous echo contrast without a definite thrombus in the LAA was observed in 3 patients, whereas in 1 patient, a thrombus attached to the LAA ostium and ridge was identified without the recurrence of AF while the patient was undergoing appropriate OAC therapy (Figure 4).

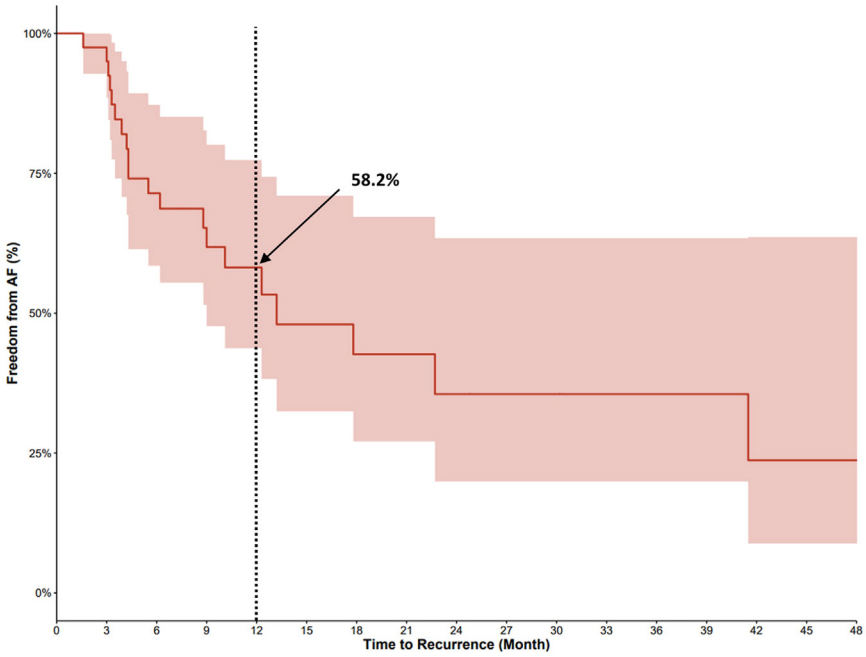

Figure 3 Kaplan-Meier survival curve for freedom from AF recurrences. AF = atrial fibrillation.

Durability of EILAA

Among patients with recurrence after EILAA, 8 underwent redo ablation because of the recurrence of atrial tachyarrhythmia. Durable isolation of the LAA was confirmed in all patients except for 1. In 1 of 8 patients, reconnection was observed, and after additional ablation along the ridge, successful reisolation was achieved.

Discussion

In this retrospective analysis using a single-center prospective registry data in an East Asian population, the major findings were as follows: (1) The patients who underwent EILAA predominantly had advanced AF characterized by long-standing persistent AF, a large LA dimension, and a history of undergoing more than 1 surgical or catheter ablation for AF. (2) Despite the majority of patients having advanced AF, EILAA proved to be an effective ablation strategy, as evidenced by the favorable outcome. (3) All patients underwent lifelong anticoagulation, which resulted in a low rate of stroke or systemic embolism with appropriate OAC therapy, even with extended follow-up.

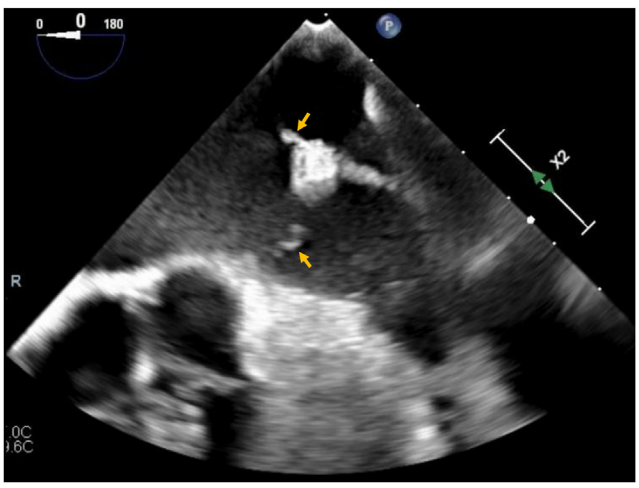

Figure 4 Index patients with thrombus on ostium of LAA under OAC. LAA = left atrial appendage; OAC = Oral anticoagulants.

The significance of the LAA for trigger and reentrant drivers that participate in the maintenance of AF and atrial tachyarrhythmia has been reported.[15,16] The previous studies showed approximately 20%–30% of firing from the LAA in patients with AF during the procedure. Furthermore, in 8% of patients without a PV trigger, the LAA was identified as the sole source of arrhythmia in both paroxysmal and nonparoxysmal AF cases.[15] Ablation targeting the LAA, particularly focusing on areas with long-fractionated or mid-diastolic electrograms in the LAA, has been shown to be highly effective in improving rhythm outcomes.[8–12,15,17] In these studies, despite the majority being patients with long-standing persistent AF, a 1-year recurrence rate of approximately 45% was observed. A meta-analysis drawing from 9 qualified studies further revealed that the overall atrial arrhythmia rate was 31% over a mean follow-up period of 40.5 months. Notably, even when procedures performed empirically, without specific consideration for LAA triggers, were analyzed, the recurrence presented a promising rate of 36%.[11] Most previous research on ELAAI has been based on prospective or retrospective observational studies. However, Di Biase et al[9] conducted a randomized controlled trial, dividing approximately 80 patients with long-standing persistent AF

into 2 groups: one undergoing Maze-like extensive ablation alone and the other undergoing both Maze-like extensive ablation and ELAAI. Their study demonstrated a 1-year recurrence rate of 44% and showed a significant reduction in the risk of additional rhythm outcomes, with an adjusted hazard ratio of 2.22 (95% confidence interval 1.29–3.81; $P = .004$). Similarly, in the present study, even though it was not a comparative analysis with a control group, patients with long-standing AF comprised 85% of the population. Given their advanced disease status, a 1-year recurrence rate of 42% was observed, demonstrating substantial efficacy. Furthermore, the maintenance of final sinus rhythm was achieved in 87.7% of cases through redo procedures and the administration of antiarrhythmic drugs. This rate, particularly given the context of advanced disease status, suggests a significant improvement in rhythm outcomes. Moreover, the success rate of ELAAI in procedures was approximately 95%, with remarkably favorable durable isolation of ELAAI being confirmed in redo cases. Considering the same embryological origin between the LAA and the left atrium and the likelihood that LAA tissue properties might trigger AF in a way comparable to the PVs, the importance of targeting the LAA for electrical separation to improve the success rate of the ablation treatment warrants strong emphasis.[18]

Stroke and systemic thromboembolism after ELAAI remain significant concerns. However, previous studies have reported conflicting outcomes regarding thromboembolic risk. In meta-analyses, the incidence of stroke/transient ischemic attack after ELAAI varied widely, ranging from 0% to 15% across studies, with cerebral thromboembolic event rates showing no significant difference between the experimental and control groups at 40-month follow-up.[11] Although some studies have reported an increased risk ratio compared with control groups,[10,19,20] others found the event rate to be lower than or comparable to that in controls.[8,9,15,21,22] Yorgun et al[12] demonstrated that 7.2% of patients had ischemic stroke/transient ischemic attack, with the median time to cerebrovascular event occurrence being 24 months after the index procedure, indicating a relatively long-term risk. They found a lower LAA emptying velocity in patients with thromboembolism than in their counterparts on TEE, and all patients with ischemic stroke had a CHA_2DS_2-VASc score of $\geq$2. However, all ischemic stroke events were attributed to the interruption of anticoagulation therapy. Even though previous studies demonstrated an increased risk of thromboembolism, they showed that under appropriate OAC therapy, the stroke risk was similar to that of the non-ELAAI group, with no significant differences.[19,20] Similarly, in the present study, stroke or transient ischemic attack occurred in 3 patients (7.3%), with only 1 having a stroke under appropriate OAC therapy, and this patient had a CHA_2DS_2-VASc score of $\geq$2.

When considering rhythm outcomes and thromboembolism risk, creating ostial lesions rather than extensive linear ablation demonstrated better outcomes in terms of efficacy and safety.[11] A recent report emphasized the necessity of lifelong continuation of OAC and early LAA closure to prevent thromboembolic events.[8,23,24] Considering a larger area of isolation with linear ablation procedures, it is plausible that ostial ablation would reduce thromboembolic risk associated with ELAA. In this study, 2 patients underwent percutaneous LAA closure during the follow-up period.

Given the function of the LAA as a volume reservoir for the left atrium, there were additional concerns regarding the potential failure to modulate LA pressure-volume overload after ELAAI. Park et al[10] found that the postprocedural E/E' ratio in the ELAAI group was significantly higher than its baseline value (increasing from 13.1 $\pm$ 2.8 to 14.1 $\pm$ 2.8; $P = .008$). However, comparisons of E/E' ratios at baseline and follow-up between the ELAAI group and the without LAA isolation showed no significant differences. In the present study, we found no significant differences in E/E' ratios between baseline and follow-up measurements.

Our study has several limitations. First, despite including the highest proportion of patients with long-standing persistent AF and an extensively long duration of AF, this was a retrospective analysis, which limits the effect of various confounders. Second, the control group that who did not undergo LAA isolation; therefore, there was no comparison of efficacy and safety outcomes of EILAA with those without EILAA. However, considering the generally reported recurrence rate and stroke incidence in patients with long-standing AF after catheter ablation, the outcomes after EILAA appear favorable. Third, we were unable to perform TEE in every patient during follow-up, which might limit our ability to demonstrate the exact physiological effects of EILAA. Furthermore, recovery of connection after EILAA is a common phenomenon, which might create a hurdle to attributing the clinical benefit solely to the EILAA procedure itself. Moreover, we could not confirm durable EILAA for all study patients and only 2 patients underwent LAA occlusion because the reimbursement system in Korea does not cover LAA occlusion in patients who underwent EILAA. Considering thromboembolic risk associated with transient interruption of OAC therapy, LAA occlusion should be covered in all patients who underwent EILAA in the Korean national reimbursement system. Finally, given the small sample size, it was difficult to generalize the findings, and there is a potential to overestimate or underestimate the effect of EILAA.

Conclusion

EILAA is an effective ablation strategy in patients with super-long-standing persistent AF who were unresponsive to either catheter or surgical ablation or at a high risk of recurrence with a high CHA_2DS_2-VASc score. Lifelong anticoagulation is mandatory for patients undergoing EILAA, and early closure of the LAA should be considered.

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Patient Consent: All patients provided their written informed consent before inclusion in the Asan Medical Center-atrial fibrillation ablation registry.

Ethics Statement: This study adhered to the ethical principles outlined in the Declaration of Helsinki and was approved by the Institutional Review Board of Asan Medical Center.

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