

Total thoracoscopic ablation in patients with atrial fibrillation and left ventricular dysfunction



Hye Ree Kim, MD,^a Dong-Seop Jeong, MD, PhD,^b Hee-Jin Kwon, MD,^a Seung-Jung Park, MD, PhD,^a Kyoung-Min Park, MD, PhD,^a June Soo Kim, MD, PhD,^a and Young Keun On, MD, PhD^a

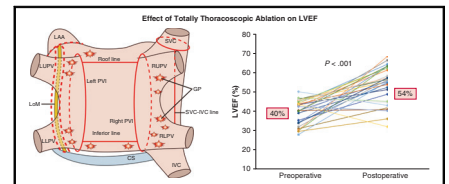
ABSTRACT

Objective: To evaluate the effectiveness and safety of totally thoracoscopic ablation (TTA) in patients with left ventricular (LV) dysfunction for treatment of atrial fibrillation (AF) refractory to antiarrhythmic drug (AAD) therapy.

Methods: Between January 2012 and December 2018, 31 patients underwent TTA with drug-refractory AF and preoperative left ventricular ejection fraction (LVEF) <50% were included. Of the 31 patients, 8 received additional catheter ablation with an electrophysiologic study within 3 months after TTA. The rhythm outcome was obtained by 12-lead electrocardiography or 24-hour Holter monitoring.

Results: The patient cohort had a mean age of 54.9 ± 9.0 years and consisted of 51.6% with persistent AF ($n = 16$), 45.2% with long-standing persistent AF ($n = 14$), and 3.2% with paroxysmal AF ($n = 1$). No patients died during the follow-up period. Compared with baseline, mean postoperative LVEF at 3 months (interquartile range [IQR], 2-6 months) increased significantly (from $39.7 \pm 6.1\%$ to $53.6 \pm 9.3\%$; $P < .001$). At 25 months (IQR, 14-45 months), LVEF was sustained or further improved (from $39.7 \pm 6.1\%$ to $58.1 \pm 7.5\%$; $P < .001$). The rate of sinus rhythm state was 93.5% (29 of 31), and freedom from arrhythmias off AADs after the final procedure was 61.3% (19 of 31) at a median follow-up of 32 months (IQR, 24-54 months).

Conclusions: TTA is a safe and effective procedure that improves LV function and restores sinus rhythm in AF patients with LV dysfunction. (JTCVS Techniques 2021;8:60-6)



Improvement of left ventricular ejection fraction following totally thoracoscopic ablation.

CENTRAL MESSAGE

Minimally invasive surgical ablation through a thoracoscopic approach is safe and effective in improving left ventricular function and restoring sinus rhythm.

PERSPECTIVE

Totally thoracoscopic ablation (TTA) can be considered as an alternative to catheter ablation to improve outcomes in patients with left ventricular (LV) dysfunction for atrial fibrillation (AF) refractory to antiarrhythmic drugs. We evaluated the safety and effectiveness of TTA in patients with AF and LV dysfunction.

See Commentaries on pages 67 and 69.

▶ Video clip is available online.

From the ^aDivision of Cardiology, Department of Internal Medicine, Heart, Vascular and Stroke Institute and ^bDepartment of Thoracic and Cardiovascular Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea.

Drs Kim and Jeong contributed equally to this work and should be considered co-first authors.

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Address for reprints: Young Keun On, MD, PhD, Division of Cardiology, Department of Internal Medicine, Samsung Medical Center, Heart, Vascular, and Stroke Institute, Sungkyunkwan University School of Medicine, 81 Irwin-ro, Gangnam-gu, Seoul 06351, Republic of Korea (E-mail: yk.on@samsung.com).

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Atrial fibrillation (AF) and heart failure (HF) share multiple risk factors and pathophysiology.¹⁻³ In a global AF registry, the rates of HF were 33% in paroxysmal AF, 44% in persistent AF, and 56% in permanent AF,¹ and the rates of both HF and coexisting AF continue to increase. Regardless of which comes first, patients with concomitant HF and AF have been associated with synergistically worse symptoms and poorer outcomes.^{3,4} Finding effective rhythm control therapies for these patients is important given that the maintenance of sinus rhythm has been associated with decreased mortality and HF hospitalization.⁵

Totally thoracoscopic ablation (TTA) for patients with drug-refractory or failed prior catheter ablation AF with class 2A indication has evolved rapidly.⁶⁻⁹ A randomized clinical trial showed that thoracoscopic surgical ablation was superior to catheter ablation in achieving freedom from AF.¹⁰ However, the adverse events associated with

Abbreviations and Acronyms

AAD	= antiarrhythmic drug
AF	= atrial fibrillation
ECG	= electrocardiography
GP	= ganglionated plexus
HF	= heart failure
IQR	= interquartile range
LA	= left atrium/atrial
LV	= left ventricle/ventricular
LVEF	= left ventricular ejection fraction
PV	= pulmonary vein
TTA	= totally thoracoscopic ablation

surgical ablation seem to be more frequent than those associated with catheter ablation.^{11,12}

To date, there have been few reports investigating the effectiveness and safety of TTA in AF patients with left ventricular (LV) dysfunction.⁹ In the present study, we evaluated sinus rhythm maintenance, changes in echocardiographic parameters, and complications in patients with LV dysfunction undergoing TTA for treatment of drug-refractory AF.

METHODS

Study Population

This registry study enrolled 31 consecutive patients who underwent TTA with drug-refractory AF and impaired LV systolic function (LV ejection fraction [LVEF] <50%) at our medical center between January 2012 and December 2018. All patients had a recent (<6 months) assessment of LVEF with a transthoracic echocardiogram before surgery. Before an indication for TTA, failure of antiarrhythmic drugs (AADs) in controlling the symptoms of AF or maintaining sinus rhythm had to be documented. Definitions of paroxysmal, persistent, and long-standing persistent AF were based on the Heart Rhythm Society, European Heart Rhythm Association, and European Cardiac Arrhythmia Society consensus statement.⁸ The center's Institutional Review Board approved the study protocol and publication of data (2020-09-034-001; September 10, 2020), and patients provided informed written consent for the publication of their study data.

Surgical Procedure

At our institution, "totally thoracoscopic" is defined as a video-assisted thoracoscopic surgical technique without the aid of cardiopulmonary bypass or the Da Vinci robotic system. This technique is performed via 3 holes (two 5-mm ports and one 10-mm port) bilaterally. Starting on the right side, a 5-mm port is introduced into the fourth intercostal space at the mid-axillary line. Carbon dioxide insufflation is used to expand the operative field and depress the diaphragm. The remaining 2 ports are placed in the third intercostal space at the anterior axillary line and in the sixth intercostal space at the mid-axillary line. After pericardial tenting, a lighted dissector (Lumitip Dissector, AtriCure, Cincinnati, Ohio) is used to pass a rubber band under the pulmonary vein (PV) antrum through the oblique sinus. Then a clamp (Isolator Transpolar Clamp; AtriCure) is connected to the rubber band and positioned around the PV antrum.

PV antrum isolation is performed by 6 applications of bipolar radiofrequency energy to the clamps around the PV antrum. To prevent macro-reentry, additional superior and inferior ablation lines connecting

both PV isolation lines are created epicardially using a linear pen device (AtriCure). Confirmation of ablation lines is performed via pacing testing using the AtriCure Colltip pen. This procedure is repeated on the left side.

Ganglionated plexuses (GPs) are subsequently ablated in the epicardial fat pad anterior side of the right superior and inferior PVs, the inferior side of the right inferior PV, and the left atrial (LA) posterior wall. On the left side, GPs in the fat pads on the LA roof, medial to the left superior PV and inferior side of the inferior PV, are also identified and ablated. High-frequency stimulation is used at ablation, and its response is defined as a $\geq 50\%$ increase in the R-R interval. Using a bipolar ablation pen (Isolator Transpolar pen; AtriCure), high-frequency stimulation is delivered (cycle length, 60 ms; 16 Hz; pulse width, 1.0 ms) in output increments from 1 to 25 mA. When high-frequency stimulation does not evoke a vagal response, ablation is performed on the basis of anatomic landmarks. Additional GP ablation is performed when necessary.

After PV and GP ablation, the ligament of Marshall is dissected and ablated. Once all ablation is completed and the conduction block is confirmed, the LA appendage is removed using an Echelon Flex 60 articulating endoscopic linear stapler (Ethicon Endo-Surgery, Cincinnati, Ohio) (Figure 1 and Video 1).

Electrophysiologic Study Procedure

An electrophysiologic study was performed within 3 months after TTA in 8 patients who were documented with typical atrial flutter before or during admission for TTA. For each patient, a duo-decapolar catheter was placed into the right atrium and coronary sinus, and a quadripolar catheter was placed into the right ventricle apex. After positioning the catheters, access to the LA was achieved through a standard transseptal puncture using the Brockenbrough technique. Lasso catheters were inserted into the PVs, and their potentials were checked. Three-dimensional reconstructions of the LA and PVs were created using the CARTO 3 system (Biosense Webster, Diamond Bar, Calif). Image integration with computed tomography scans was performed.

Postoperative Care and Follow-up

Following TTA, all patients were monitored for the first 24 hours in the intensive care unit. After pericardial effusion was excluded by transthoracic echocardiography, heparin infusion was started 4 hours after surgery and titrated according to the activated partial thromboplastin time (target between 60 and 80 seconds). The day after the procedure, oral anticoagulation (warfarin or non-vitamin K antagonist oral anticoagulant) was started. In the absence of contraindication, AADs were continued after surgery.

An early event was defined as an event that occurred within the first 30 postoperative days, and all later events were defined as late events. Early events included stroke, sinus node dysfunction, bleeding, and other major adverse events associated with TTA. In cases of persistent postoperative AF during admission, at least one attempt was made to restore sinus rhythm via electrical cardioversion.

All patients were followed up at 2 weeks, 3 months, 6 months, and every 6 months thereafter. At each visit, 12-lead electrocardiography (ECG) or 24-hour Holter monitoring was performed to evaluate rhythm and atrial activity. Recurrence was defined as symptomatic or asymptomatic episodes of AF lasting longer than 30 seconds and identified on 12-lead ECG or 24-hour Holter monitoring after a blanking period of 3 months. When the rhythm was stable and restoration of both atrial activities was confirmed, AADs were discontinued at 3 months or up to 6 months. Sinus rhythm off AADs was defined as freedom from AF with discontinuation of AADs for at least 12 months. LVEF was assessed by transthoracic echocardiography.

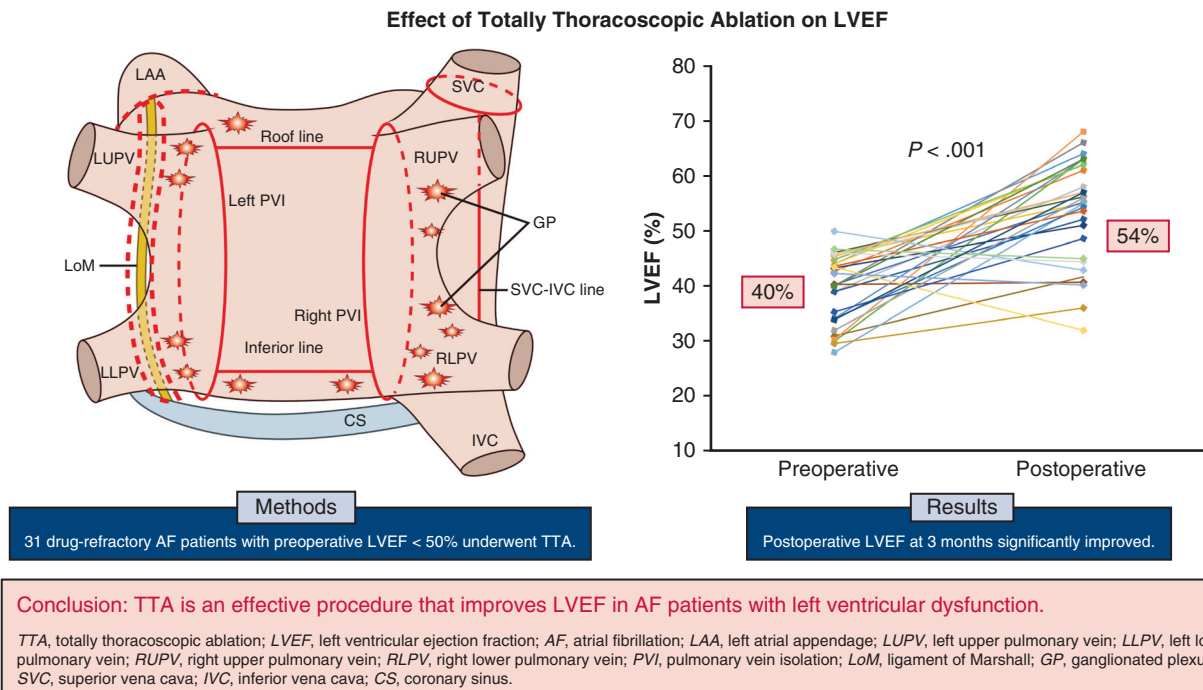
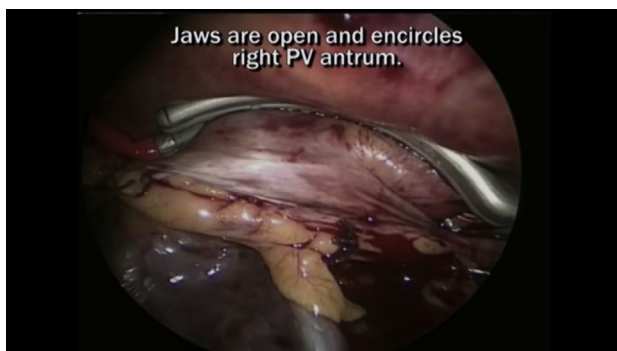


FIGURE 1. *Left*, schematic illustration of surgical ablation lesion. *Right*, improvement of left ventricular function in patients with left ventricular ejection fraction (LVEF) <50% at a median of 3 months following totally thoroscopic ablation. The mean LVEF improved from $39.7 \pm 6.1\%$ to $53.6 \pm 9.3\%$ ($P < .001$). LAA, Left atrial appendage, SVC, superior vena cava; LUPV, left upper pulmonary vein; RUPV, right upper pulmonary vein; PVI, pulmonary vein isolation; GP, ganglionated plexus; LoM, ligament of Marshall; IVC, inferior vena cava; LLPV, left lower pulmonary vein; RLPV, right lower pulmonary vein; CS, coronary sinus; AF, atrial fibrillation; TTA, totally thoroscopic ablation.

Statistical Analysis

All statistical analyses were performed using SPSS version 25.0 (IBM, Armonk, NY). Baseline data are presented as frequency or mean \pm standard deviation. The duration of follow-up is presented as median and interquartile range (IQR). Continuous variables were compared using Student's *t* test, and categorical variables were compared using the χ^2 test. All tests were 2-sided, and a *P* value < .05 was considered statistically significant.



VIDEO 1. Minimally invasive surgical atrial fibrillation ablation through a thoroscopic approach. Video available at: [https://www.jtcvs.org/article/S2666-2507\(21\)00298-4/fulltext](https://www.jtcvs.org/article/S2666-2507(21)00298-4/fulltext).

RESULTS

Patient-Related Characteristics

Between July 20, 2012, and 28 December 2018, 31 patients (90.3% male; mean age, 54.9 ± 9.0 years) with impaired LV systolic function (mean LVEF at baseline, $39.6 \pm 6.1\%$) underwent TTA. The baseline characteristics of these patients are summarized in Table 1. The cohort consisted of 16 patients with persistent AF (51.6%), 14 patients with long-standing persistent AF (45.2%), and 1 patient with paroxysmal AF.

Bilateral PV epicardial isolation was performed in all patients. The LA appendage was resected in all but 1 patient (96.8%). The reason for not excluding the LA appendage was that the LA was small with severe LV systolic dysfunction (LVEF, 28%). Eight patients who had documented typical atrial flutter before or during admission for TTA underwent additional radiofrequency catheter ablation on cavotricuspid isthmus. PV potential was checked, and PV isolation was confirmed in all 8 patients. Thoroscopic and postoperative electrophysiologic procedural data are shown in Table 2.

Echocardiographic Outcomes

All patients in this analysis had at least 2 recorded echocardiograms. Compared with baseline, LVEF was

TABLE 1. Baseline patient characteristics (N = 31)

Characteristic	Value
Age, y, mean \pm SD; range	54.9 \pm 9.0; 37-75
Male sex, n (%)	28 (90.3)
BMI, kg/m ² , mean \pm SD; range	27.4 \pm 2.9; 22.2-33.1
Hypertension, n (%)	17 (54.8)
Diabetes mellitus, n (%)	3 (9.7)
Prior stroke, n (%)	5 (16.1)
Prior PCI, n (%)	2 (6.5)
Chronic kidney disease, n (%)	1 (3.2)
Thyroid disease, n (%)	2 (6.5)
Duration of AF, mo, mean \pm SD; range	55.5 \pm 55.5; 3-242
Type of AF, n (%)	
Paroxysmal	1 (3.2)
Persistent	16 (51.6)
Long-standing persistent	14 (45.2)
CHA ₂ DS ₂ -VASc score, mean \pm SD; range	2.2 \pm 1.3; 1-6
Prior catheter ablation, n (%)	7 (22.6)
Echocardiographic findings, mean \pm SD; range	
LA volume index, mL/m ²	50.5 \pm 17.1; 29.7-92.6
LA diameter, mm	45.2 \pm 7.4; 34.0-64.6
LVEF, %	39.6 \pm 6.1; 28.0-49.9
Follow up duration, mo, median (IQR); range	32 (24-54); 6-96

SD, Standard deviation; BMI, body mass index; PCI, percutaneous coronary intervention; AF, atrial fibrillation; CHA₂DS₂-VASc, congestive heart failure, hypertension, age, diabetes, prior stroke or transient ischemic attack or thromboembolism, vascular disease, and female sex; LA, left atrium; LVEF, left ventricular ejection fraction; IQR, interquartile range.

significantly increased at 3 months (IQR, 2-6 months) postoperatively (from 39.7 \pm 6.1% to 53.6 \pm 9.3%; $P < .001$) (Figure 1). Eight patients who underwent additional catheter ablation underwent follow-up echocardiography before the procedure.

At the last follow-up echocardiogram (at a median of 25 months; IQR, 14-45 months), LVEF was sustained or further improved (from 39.7 \pm 6.1% to 58.1 \pm 7.5%; $P < .001$). Two patients did not show an improvement in LVEF; one of these patients had an implanted permanent pacemaker due to sick sinus syndrome with a long duration of AF prior to TTA, and the other patient had an LA volume index of 89.3 mL/m², the most dilated LA in this series. In addition, a relative decrease in LA volume index, with no statistically significant difference, was observed during the last follow-up period (from 50.5 \pm 17.1 to 46.2 \pm 15.1; $P = .060$) (Table 3).

TABLE 2. Procedure characteristics (N = 31)

Characteristic	Value, n (%)
Thoracoscopic procedures	31 (100)
PV isolation	31 (100)
GP ablation	29 (93.5)
Roof line ablation	27 (87.1)
Inferior line ablation	29 (93.5)
Division of ligament of Marshall	28 (90.3)
LA appendage removed	30 (96.8)
SVC circular ablation	12 (38.7)
SVC-IVC linear ablation	2 (6.5)
Intraoperative sinus conversion	28 (90.3)
Spontaneous	14 (50.0)
Cardioversion	14 (50.0)
Postoperative EPS	8 (25.8)
Roof line ablation	1 (12.5)
CTI ablation	8 (100)
Mitral isthmus ablation	2 (25.0)
Septal ablation	1 (12.5)

PV, Pulmonary vein; GP, ganglionated plexus; LA, left atrium; SVC, superior vena cava; IVC, inferior vena cava; EPS, electrophysiologic study; CTI, cavotricuspid isthmus.

Rhythm Outcomes

At a median follow-up of 32 months (IQR, 24-57 months), the freedom from atrial arrhythmia was 61.3% (19 of 31 patients) (Figure 2). AF never recurred in these 19 patients after TTA. With or without additional intervention including catheter ablation or AADs, 93.5% (29 of 31) of the patients had a sinus rhythm state on ECG or 24-hour Holter monitoring at the last follow-up.

Complications

No patient died during the procedure or throughout follow-up. No conversions to sternotomy were required. Reoperation was performed in 1 patient because of hemothorax. One patient experienced a minor stroke postoperatively after discontinuation of heparin before starting oral anticoagulation. Sinus node dysfunction was observed in 2 patients, both of whom spontaneously recovered to normal sinus rhythm. Two cases of pulmonary complication were observed, including asthma attack and pulmonary edema. All patients recovered without sequelae. One patient received a permanent pacemaker implantation during follow-up; however, this was not directly related to the thoracoscopic procedure (Table 4).

DISCUSSION

We present our single-center experience with the potential long-term clinical advantages of minimally invasive thoracoscopic ablation in patients with AF, especially in a subgroup of high-risk patients with LV dysfunction. Our main findings can be summarized as follows: (1) LVEF was significantly increased between baseline and

TABLE 3. Outcomes of echocardiographic parameters at baseline and follow-up

Parameter	Preoperative	Postoperative	P value	Last follow-up	P value*
Follow-up, mo, median (IQR)		4.8 (2-6)		31.3 (16-45)	
LVEF, %, mean ± SD	39.7 ± 6.1	53.6 ± 9.3	<.001	58.1 ± 7.5	<.001
LA diameter, mm, mean ± SD	45.2 ± 7.4	46.1 ± 5.2	.285	45.4 ± 5.0	.871
LAVI, mL/m ² , mean ± SD	50.5 ± 17.1	48.0 ± 7.1	.341	46.1 ± 15.2	.060

IQR, Interquartile rang; LVEF, left ventricular ejection fraction; SD, standard deviation; LA, left atrium; LAVI, left atrial volume index. *Reference; preoperative value.

postoperative/long term follow-up; (2) the arrhythmia-free off-AAD success rate with a single procedure of TTA was 61.3% at a median follow-up of 32 months; and (3) the rate of early surgical-related complications was 16%, with no deaths.

There have been few studies reporting the outcomes of minimally invasive surgical ablation using a thoracoscopic approach for patients with LV dysfunction and lone AF.⁹ Several retrospective studies of the Cox-Maze procedure have shown improved LV function after surgical AF ablation in patients with impaired LV function. Stulak and colleagues¹³ from the Mayo Clinic reported improved LVEF

immediately after the Cox-Maze III procedure and was sustained at last follow-up (median, 48 months) in 23 patients with persistent AF and LV dysfunction. Ad and colleagues¹⁴ from the Inova Heart Center reported a significant improvement in LVEF, from 30 ± 5.0% to 45 ± 13.0%, at a mean of 1.5 ± 11.3 months in 44 patients following the Cox-Maze III/IV procedure. Adademir and colleagues¹⁵ demonstrated the efficacy of the stand-alone Cox-Maze IV procedure in patients with AF and LV dysfunction. We would like to show the efficacy of the thoracoscopic epicardial ablation technique in this population of AF with LV dysfunction.

Enrollment, Follow-up and Rhythm outcomes following TTA

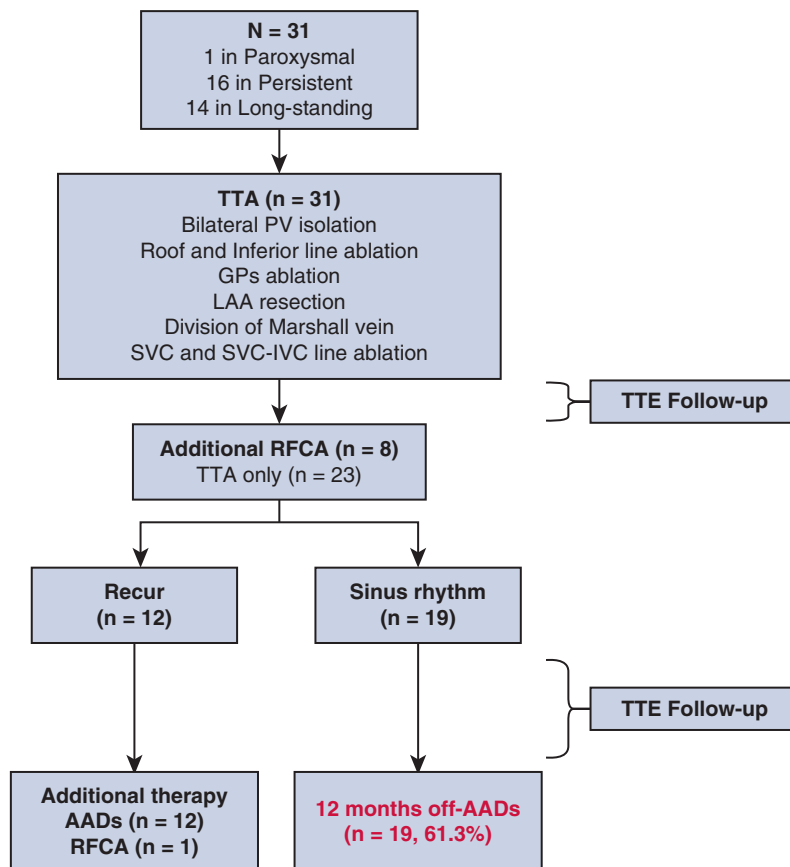


FIGURE 2. Flow diagram of enrollment, follow-up, and rhythm outcomes at a median 32 months following totally thoracoscopic ablation. TTA, Totally thoracoscopic ablation; PV, pulmonary vein; GP, ganglionated plexus; LAA, left atrial appendage; SVC, superior vena cava; IVC, inferior vena cava; TTE, transthoracic echocardiography; RFCA, radiofrequency catheter ablation; AAD, anti-arrhythmic drug.

TABLE 4. Postprocedural complications (N = 31)

Complication	Value, n (%)
Mortality	0 (0)
Early events	
Conversion to surgical procedure	0 (0)
Hemothorax requiring reoperation	1 (3.2)
Neurologic complication (minor stroke)	1 (3.2)
Sinus node dysfunction	2 (6.5)
Pericardial effusion	0 (0)
Pulmonary complications	2 (6.5)
Late events	
Pulmonary vein to esophageal fistula	0 (0)
Neurologic complication	0 (0)
Pacemaker implantation	1 (3.2)
Bleeding from anticoagulation	0 (0)

In AF patients with LV dysfunction, restoration of sinus rhythm has several advantages. First, recovery of atrial contraction can result in increased LV filling and cardiac output.¹⁶ Second, regularity of ventricular response is also associated with increased cardiac output regardless of heart rate.¹⁷ A previous study demonstrated that irregular ventricular pacing resulted in a 12% decrease in cardiac output compared with regular ventricular pacing.¹⁷ Sairaku and colleagues¹⁸ showed that rate control alone during AF without sinus conversion may result in incomplete cure of tachycardia-induced cardiomyopathy. Especially in patients with a high probability of recurrence because of abnormal substrates, a reduction in AF burden and restoration of sinus rhythm may contribute to improvement of LV dysfunction and maintenance of cardiac function.¹⁴ Following recovery of LV function, patients require regular follow-up and monitoring of their individual substrates related to AF recurrence.

In 1 patient, we did not resect the LA appendage because the LA was small with severe LV dysfunction. The LA appendage has several important mechanical functions as a reservoir and due to its intrinsic contractile property. In an in vivo study, LA appendage removal result in decreased LA compliance—associated reservoir function, with subsequent decreased LV filling and diminished cardiac output.¹⁹ Phan and colleagues²⁰ reported significant increases in LA filling pressure and LA size among nonvalvular AF patients after LA appendage closure. Remnant LA appendage could have a positive effect on LV function. Further investigation of the potential effects of LA appendage removal on heart function is needed, especially in patients with AF and LV dysfunction.

Our data show a 16% rate of complications without sequelae, pacemaker requirement, or death. The Atrial Fibrillation Catheter Ablation versus Surgical Ablation Treatment (FAST) Study,¹⁰ a prospective randomized trial including 120 patients with drug-refractory AF or failed

prior catheter ablation, reported a higher success rate but also a higher complication rate after TTA compared with catheter ablation. Surgical ablation is more invasive and carries a higher complication rate than catheter ablation.^{8,11}

In a recent randomized trial of catheter ablation versus thoracoscopic surgical ablation in long-standing persistent AF (CASA-AF), thoracoscopic surgical ablation had a 15% rate of serious complications within 30 days, including 1 death.²¹ A systemic safety analysis of TTA found a 30-day postoperative complication rate of 11.8%.⁹ Surgical ablation is part of a growing trend toward less invasive and thoracoscopic approaches, during which complications related to surgery can be expected to decrease.

A 61.3% arrhythmia-free success rate with a single procedure at a median of 2.6-year follow-up in patients with left ventricular dysfunction is comparable to the results reported after TTA. Previous studies focusing on long-term outcomes after TTA, including hybrid ablation, have reported success rates ranging from 38% to 83% for up to 5 years, depending on the AF subtype (paroxysmal or persistent), duration of follow-up, and use of AADs.²²⁻²⁵ An observational study found a 60% overall freedom from AF at a mean follow-up of 4.0 ± 0.6 years in a population with normal LV function.²⁶

A single procedure alone cannot perfectly treat AF.²⁷ A major advantage of TTA is the achievement and maintenance of PV isolation. However, TTA has difficulty accessing cavotricuspid isthmus, septal line, and mitral isthmus lesions.²⁸ In previous studies, one cause of AF recurrence after catheter ablation has been faulty reconnection and gaps of PV isolation.^{29,30} Therefore, confirmation of PV isolation and additional ablation by electrophysiologic study after surgical ablation is expected to improve outcomes with minimal adverse effects, especially in long-standing persistent AF.

Our study has several limitations. The first is the small number of patients at a single center, which could result in bias and incomplete data, impairing the generalizability of our results. Second, 12-lead ECG and 24-hour Holter monitoring are less effective in detecting asymptomatic atrial arrhythmia compared with implantable loop recording systems, and thus the rate of arrhythmia recurrence may have been underestimated. Third, in patients with AF at baseline and with a successful ablation procedure, echocardiographic measurements were obtained during AF at baseline and sinus rhythm at follow-up, possibly introducing noise in the estimation of actual changes.

To summarize, TTA was effective in restoring LV function and sinus rhythm in our cohort of AF patients with LV dysfunction. The complications related to TTA were reversible and not expected to adversely affect prognosis. Where suitably trained thoracoscopic surgeons are available, TTA should be considered as an alternative or adjunct

to catheter ablation to improve outcomes related to recurrent AF in patients with LV dysfunction.

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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