Midterm outcomes of mini-invasive surgical and hybrid ablation of atrial fibrillation

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Background. We evaluated the feasibility and effectiveness of thoracoscopic and a staged surgical and transcatheter ablation technique to treat stand-alone atrial fibrillation (AF).

Methods. Between 2009 and 2016, a cohort of 65 patients underwent bilateral totally thoracoscopic ablation of symptomatic paroxysmal AF (n=30; 46%), persistent AF (n=18; 28%) or long-standing persistent AF (n=17; 26%) followed by catheter ablation in case of AF recurrence. Surgical box lesion procedure included bilateral pulmonary vein and left atrial posterior wall ablation using irrigated bipolar radiofrequency with documentation of conduction block.

Results. There were no intra- or peri-operative ablation-related complications. There was no operative mortality, no myocardial infarction, and no stroke. Skin-to-skin procedure time was 120.5 ± 22.0 min and the postoperative average length of stay was 8.1 ± 3.0 days. At discharge, 60 patients (92%) were in sinus rhythm. Median follow-up time was 866 days (IQR, 612–1185 days). One-year success rate after surgical procedure was 78% (off antiarrhythmic drugs). Eleven patients (17%) underwent catheter re-ablation. Sixty (92%) patients were free of atrial fibrillation after hybrid ablation (on demand) at 1 year follow up after the last ablation. The success at 24-months was achieved in 96% (paroxysmal) and 78% (persistent) patients. At the last follow-up control, 69% patients discontinued oral anticoagulant therapy.

Conclusions. Combination of mini-invasive surgical and endocardial treatment (two-stage hybrid procedure) is a safe and effective method for the treatment of isolated (lone) AF. This procedure provided good midterm outcomes.

Key words: atrial fibrillation, thoracoscopic ablation, hybrid ablation

INTRODUCTION

Atrial fibrillation (AF) is the most common chronic arrhythmia in the world, affecting 1% of the population, including nearly 5 million people in the European Union\textsuperscript{1,2}. The prevalence of AF is estimated to more than double in the next 50 years. AF is associated with increased mortality and increased risk of stroke, heart failure, and dementia\textsuperscript{3,4}. There are several approaches to the treatment of AF. Since pharmacological treatment with antiarrhythmic drugs (AADs) have limited efficacy in maintaining sinus rhythm and carry the risk of serious adverse effects, non-pharmacological treatment modalities have been introduced into routine practice\textsuperscript{5}.

Endocardial ablation of AF has emerged as an option for treating AF. The finding of focal AF with the foci in the pulmonary veins introduced by Haissaguerre et al., led to the introduction of focal pulmonary vein ablation into clinical practice\textsuperscript{6}. Later, a combination of pulmonary vein isolation and AF substrate modification has yielded promising results, mainly in patients with paroxysmal AF. However, the endocardial approach has variable results with a reported efficacy of 61 – 89% (ref.\textsuperscript{7,8}). Fiala et al. demonstrated a long-term efficacy of only between 20% to 30% after a single catheter procedure using an extensive ablation approach in long-standing persistent atrial fibrillation\textsuperscript{9}.

In addition to catheter ablation, there is rapid progress towards minimizing the invasiveness of surgical ablation of AF. The minimally invasive (thoracoscopic) surgical approach is a very promising method for the treatment of patients with “lone” AF, i.e. AF in the absence of underlying heart disease\textsuperscript{10}. Combination of surgical and catheter ablation in a hybrid approach seems to be a very attractive alternative for overcoming the limitations of the epi- and endocardial ablation approach alone.

The aim of this article was to report the midterm results of thoracoscopic radiofrequency ablation and effectiveness of the staged hybrid approach combining minimally invasive surgical ablation of AF (as a first step) with catheter ablation as a second step in case of AF recurrence.

MATERIALS AND METHODS

Patient population

The Ethics committee of our institute approved the study (reference number: 201708 S11P) and individual consents were obtained from the patients.
Patients requiring nonpharmacological treatment of AF and patients with a preference for minimally invasive surgery and/or earlier failure of catheter pulmonary vein isolation were eligible for the study. According to the guidelines, only patients who had failed to maintain sinus rhythm when using at least one AAD for symptomatic AF were included. The definition of paroxysmal AF, persistent AF and long-standing persistent AF (LSPAF), success and failure of ablation, and follow-up monitoring were based on the HRS/EHRA consensus statement for catheter and surgical ablation of AF (ref.7). Before surgery, all patients underwent clinical examination, 12-lead ECG, chest radiography and coronary angiography if aged 40 years or older. The possibility of underlying heart disease was excluded by transthoracic or esophageal echocardiography. No patients had undergone a previous cardiac operation.

Preoperative management

Oral anticoagulant therapy was discontinued 3 days before surgery and replaced by low-molecular-weight heparin when the international normalized ratio value was less than 2.0. AADs were continued during hospital admission. Before surgery transesophageal echocardiogram was performed to exclude thrombus in the left atrial appendage (LAA).

Surgical technique

The procedures were performed under general anesthesia with the trachea intubated using a double-lumen endotracheal tube for selective lung ventilation. The entire procedure was performed on the beating heart without the use of extracorporeal circulation.

The patient was placed in the supine position with both arms alongside the body and slightly below table level. A towel roll or inflatable pressure bag was placed under the right and left shoulder enabling rotation of the patient’s chest. The procedure started on the right side. After right lung deflation three ports were introduced into the pleural cavity at positions that correspond to a triangle. The port for the camera (11 mm) was introduced into the fifth intercostal space at the midaxillary line. The second port (5 mm, working port) was placed into the fourth intercostal space in the anterior-axillary line and the third port (11 mm working port) was placed into the sixth intercostal space in the anterior-axillary line. Lung collapse was facilitated by continuous carbon dioxide insufflation into the pleural cavity at 8 to 10 mm Hg. Visualization was accomplished with a 10.0 mm 0-degree endoscope. On the right side, the pericardium was widely opened at 1.5-2.0 cm anterior to the phrenic nerve. Pericardial retraction sutures were used to aid visualization. Blunt dissection was performed to open the oblique and transverse sinus. Flexible Gemini-s guides (Medtronic, Inc., Minneapolis, USA) were passed through the transverse and oblique sinus. Prior to ablation, electrical testing of the threshold for capture of the atria with pulmonary vein electrical stimulation was measured. Following this, the left side approach was established. Three ports were introduced into the left pleural cavity in a similar fashion to the right pleural cavity, except that the left ports were placed more posteriorly. The pericardium on the left side was opened just below the phrenic nerve. The flexible guides were retrieved out of the left thorax. The Gemini-s (Medtronic, Inc., Minneapolis, USA) was attached to the end of the guides outside the left chest. Using the guides the Gemini-s was inserted across the left pulmonary veins and the left atrium. The left part of the box lesion was performed. The clamp was closed proximal to the confluence of the pulmonary veins and the radiofrequency energy for ablation was applied. After the first ablation, the radiofrequency clamp was opened and placed approximately 3-5 mm away from the first ablation line. Four ablation lines were placed on each side. The aim was to create four parallel lines at the atrial cuff. The ligament of Marshall was dissected using scissors and coagulated.

The right pulmonary vein ablation lines were completed through the right-sided ports. At this time complete box lesion was obtained. Conduction block was then confirmed by pacing distally to the ablation line from inside the “box”. If conduction block was not achieved after the first radiofrequency application additional radiofrequency applications were given until pulmonary vein conduction block occurred. The pericardium was closed on the right side. Intercostal analgesic blockade was applied. A single chest drain was inserted through the scope site on each side of the chest and the wounds were closed and dressed in a standard manner. If the patient was in AF and did not convert to sinus rhythm during the ablation procedure, an attempt was made to restore sinus rhythm using external cardioversion.

Since December 2013, we have changed our protocol: we have added left atrial appendage occlusion by an epicardial clip (AtriCure Inc., West Chester, OH, USA), currently performed in 22 patients (n=34.4%).

Postoperative care and clinical follow-up

Postoperative management of pharmacologic therapy was conducted according to a standardized protocol. Until discharge, patients were monitored by telemetry and standard 12-lead ECG recordings. All patients were discharged on both antiarrhythmic and anticoagulant therapy. AADs were continued for at least 3 months after surgery and were then withdrawn in patients who maintained sinus rhythm. Electrical cardioversion was attempted for patients who remained in persistent AF at 1 month after the surgical procedure. Warfarin was administered one day following drain removal with a target international normalized ratio of 2-3. Anticoagulant therapy was withdrawn after 6 months if the Holter ECG monitoring showed a sinus rhythm, if patient had a low thromboembolic risk, and CHADS2 score was <2. Data were collected by prospective review of the patient’s hospital records. Regular follow-up visits were scheduled 3, 6 and 12 months after discharge and thereafter every 6 months. At each visit, the patients underwent physical examination, 12-lead ECG, transthoracic echocardiography and evaluation of 24-h Holter ECG monitoring or longer ECG monitoring. Patients with arrhythmia recurrence, regardless of the symptoms, were candidates for electri-
Transcatheter ablation was considered.

**Transcatheter procedure**

Staged transcatheter ablation procedure was performed only in patients showing AF recurrence after the 3 months blanking period following surgical ablation (“on demand catheter ablation”). Endocardial ablation procedures were performed using the Seldinger technique to introduce two transseptal sheaths via right femoral vein. Using the electro-anatomical navigation system (CARTO XP, CARTO 3 from March 2011, Biosense Webster Inc., Diamond Bar, CA), a virtual three-dimensional reconstruction of the anatomy, activation and voltage map of the left atrium was created. The posterior left atrium wall was mapped in details. If no potentials were recorded, a complete box-lesion was deemed present. Areas with persistent conductivity, referred to as gaps, were target for ablation. If atrial tachycardia persisted, detailed mapping of right and left atrium was constructed, and subsequently the source of the arrhythmia was ablated. Radiofrequency energy was applied using a 3.5-mm irrigated-tip catheter (Navistar Thermocool, Thermocool SF, Thermocool ST, Biosense Webster Inc.), flow 10-20 ml/min, energy was titrated up to 30 W (to 25 W on the posterior wall). Finally, the integrity of electrical isolation was confirmed with a circular catheter (Optima Plus, IBI, St. Jude Medical, Minetonka, MN). In patients with the history of typical right atrial flutter, we performed a cavo-tricuspid isthmus lesion line.

**End Points**

The primary end point was freedom from episodes of AF, atrial flutter, or atrial tachycardia without the use of AADs 12 months after surgical ablation. Patients who underwent catheter re-ablation were excluded as a failure. The secondary end point was freedom from episodes of AF, atrial flutter, or atrial tachycardia without the use of AADs after 12 months from the staged hybrid ablation (on demand ablation). Freedom from AF was defined as the absence of AF, atrial flutter, or atrial tachycardia episodes lasting > 30 s on any ECG record or 24-h Holter ECG monitoring or longer monitoring.

**Statistical analysis**

Continuous variables are expressed as means ± standard deviation for normative data, and as median (range, interquartile range [IQR]) for skewed data. Categorical data are given as absolute numbers and percentages. Arrhythmia-free survival was estimated using the Kaplan-Meier method.

**RESULTS**

**Patient characteristics**

Between 2009 and 2017, 65 patients with symptomatic lone AF that was resistant to anti-arrhythmic therapy underwent bilateral thoracoscopic radiofrequency ablation using the Gemini-S ablation system (Medtronic, Inc., Minneapolis, USA). There were 49 men (75.4%) and 16 women (24.6%) with a mean age of 58.2 ± 8.3 years. Thirty patients (46.2%) had paroxysmal AF, eighteen (27.7%) had persistent AF, and seventeen (26.1%) had LSPAF. The duration of AF was 52.7 ± 44.5 months (IQR, 18.5-79.0 months). Patient clinical characteristics are presented in Table I. Of the 65 patients, 7 patients (10.8%) had undergone prior catheter ablation. The left atrial dimension was 45.2 ± 5.4 mm. The duration of post-operative hospital stay was 8.1 ± 3.0 days. Our practice is to discharge patients with INR ratio of 2-3, and this strategy could have prolonged the length of hospital stay.

**Procedure details**

The mean procedure time was 120.5 ± 22.0 min. There were no operative complications and no need for conversion to sternotomy. The duration of stay in the intensive care unit was 24.9 ± 8.9 h.

**Follow-up**

At discharge, 60 (92%) patients were in sinus rhythm. After minimally invasive AF ablation and a blanking period of 3 months, 57 of 65 (88%) patients were in sinus rhythm according to at least 24-h Holter ECG monitoring or longer monitoring.

Follow-up data was collected for all 65 patients (100%). The median follow-up time was 866 days (IQR, 612-1185 days). All patients had a follow-up period of ≥1 year.

The primary end point (sinus rhythm at 1 year follow-up after surgical procedure) was reached in 51 of 65 (78%) patients (Fig. 1). These patients were free from AF, atrial flutter, and atrial tachycardia without the use of AADs after 12 months from the surgical procedure. Patients who underwent catheter re-ablation were also excluded as a failure. According the type of AF, one-year success rates were 86% (26/30) in paroxysmal AF and 71% (25/35)
in persistent AF patients (Fig. 2). In a subgroup of long-
standing persistent AF patients, the success rate was 47%
(8/17) at one year follow-up.
In eleven patients (17%), a follow-up catheter abla-
tion was performed because of paroxysmal AF or macro-
reentry atrial tachycardia in 10 patients and typical atrial
flutter in one patient. The box lesion was complete in 5 of
11 (45%) re-ablated patients. Linear ablation and substrate
ablation was performed in these patients. In patients with
incomplete box lesion, re-isolation of the box lesion was
performed (Fig. 3) and linear as well as substrate abla-
tion was added if necessary. In eight patients second re-
ablation was necessary. Nine of eleven patients (82%) who
underwent catheter re-ablation remained in sinus rhythm.
One patient with paroxysmal AF is waiting for the third re-
ablation. The main place of the gap in the box lesion was

Fig. 1. Kaplan–Meier curve representing freedom from arrhythmia after the thoraco-
sopic ablation for total patients.
AF- atrial fibrillation

Fig. 2. Kaplan–Meier curve representing freedom from arrhythmia after the thora-
coscopic ablation separately for paroxysmal and persistent atrial fibrillation patients.
AF- atrial fibrillation; Parox. – paroxysmal; Pers. – persistent
on the posterior left atrial wall at the connection of the left and right ablation lines. One patient underwent two unsuccessful re-ablations and was subsequently indicated for atrioventricular node ablation and cardiostimulator implantation.

At twelve months follow-up one patient has paroxysmal AF on AADs and one patient is waiting for re-ablation procedure. One patient with persistent AF refused re-ablation.

The freedom from episodes of AF without the use of AADs after 12 months from the staged hybrid ablation (the secondary end point) was reached in 92% patients (96% in paroxysmal AF and 86% in persistent AF patients) (Fig. 4). In patients with long-standing persistent AF the success was 71% (12/17). In the midterm follow-up of 24-months the success of hybrid ablation was achieved in 96% and 78% of paroxysmal and persistent AF patients, respectively. When repeat ablations were also included, arrhythmia control was achieved in 89% of persistent AF patients. In a subgroup of long-standing persistent patients 82% (14/17) were free of AF at 12 months follow-up after repeat ablations.

Oral anticoagulant therapy was discontinued in 45 (69%) patients at the time of follow-up control.

Seven patients (10.8%) had undergone prior catheter ablation. There were 4 paroxysmal and 3 persistent AF patients. In this sub-group of patients all were free of AF after the surgical ablation, with a mean follow-up period of 1204±97 days.

**Adverse events**

There were no hospitalization-related deaths. One patient (1.5%) experienced diaphragmatic dysfunction, which resolved 3 months after the surgical procedure. No patient experienced a postoperative myocardial infarction, transient ischemic attack, cerebrovascular accident, reoperation for bleeding, port site infection or required the implantation of a permanent pacemaker. No patient required blood transfusions. One patient (1.5%) had post-operative pleural effusion that was treated by uncomplicated thoracentesis.

**DISCUSSION**

The optimal therapy of paroxysmal AF and mainly persistent AF remains undecided. None of the currently available approaches provide complete abolition of the
arrhythmia. The aim of surgical treatment of AF is to restore sinus rhythm and normal systolic function of the left atrium. The Cox-Maze III operation, which was introduced into clinical practice in 1987, is still considered the gold standard for the surgical treatment of AF. Cox et al. has reported success rates of more than 95% in patients undergoing the Cox-Maze III procedure\textsuperscript{41}. However, the complexity and mortality associated with the cut-and-sew maze procedure has limited its acceptance among cardiac surgeons. In a special subgroup of patients with AF and without heart disease, referred to as lone AF patients, the minimally invasive technique has been used since 2005, when Wolf et al. reported the first successful minimally invasive ablation of AF (ref.\textsuperscript{12}).

In the surgeries reported here, we used saline-irrigated bipolar radiofrequency device. The bipolar application of radiofrequency energy achieves better transmurality of the ablation lines than the unipolar application\textsuperscript{13-15}. An additional benefit of bipolar ablation is that current density is confined to the tissue between the two electrodes on the jaws. Additionally, bipolar RF devices have the capability of providing immediate feedback on the transmurality. The thoracoscopic approach avoids the need for a sternotomy or rib-spreading thoracotomy. The epicardial approach enables this procedure to be performed on a beating heart, avoiding the need for cardiopulmonary bypass and its associated complications.

There is increasing concern about the inefficacy of simply pulmonary vein isolation for the treatment of persistent AF and LSPAF. From the literature the more extensively performed left atrial ablation the more is the probability to restore and to maintain sinus rhythm in patients undergoing surgical ablation\textsuperscript{16}. The box lesion approach used in this study results in wide isolation of the pulmonary veins and the posterior part of the left atrium. Lee et al. stated that the left atrial posterior wall is one of the most important sources of AF in dilated atria\textsuperscript{17}. In a study conducted by Minakata et al., the use of a box lesion and coronary sinus ablation were independent predictors of the maintenance of sinus rhythm at 6 months after ablation (\(P=0.011\)) and in a study performed by Damiano et al. the failure to isolate the posterior left atrial wall was a predictor of recurrence of AF (\(P=0.022\)) (ref.\textsuperscript{18,19}).

In accordance with other studies, we found that the proportion of patients free from AF without AADs at 12 months post-surgery was higher among paroxysmal AF patients (86\%) than in persistent AF (71\%) patients (in LSPAF 47\%). Van Laar et al. published their experience with surgical and endocardial ablation carried out in two sequential steps for the treatment of persistent AF and LSPAF, and reported a success rate of 86.7\% after a mean follow-up of 20.7 ± 4.5 months\textsuperscript{24}. Bulava et al. published similar results when applying the two-stage hybrid approach for the management of patients with chronic AF, reporting a success rate as high 77\% at 12-month follow-up and without the need of AADs. However good control of arrhythmia (with reintroduction of AADs) was reached in 86\% of patients at 12-month follow-up and when repeat ablations were also included the success arrhythmia control was achieved in 97\% of patients. The success rate of 95.5\% (off AADs) was also seen in midterm follow-up of 18-24 months\textsuperscript{25}. Wojtaszczyk et al. recently reported 84.1\% of patients in sinus rhythm one year after the pericardioscopic hybrid approach\textsuperscript{26}. Our study demonstrates the trend in current treatments for atrial fibrillation, mainly persistent and long-standing persistent AF, which needs the close cooperation between cardiac surgeons and invasive cardiologists in the hybrid approach, whether single-session or sequential.

The efficacy of isolate epicardial thoracoscopic ablation versus endocardial catheter ablation using radiofrequency energy remains unclear. Phan et al. reported the first meta-analysis of comparative studies investigating minimally invasive thoracoscopic ablation versus catheter
ablation. Surgical approach was demonstrated to be superior to catheter at 6-month (81.0 vs 64.3%, \( P<0.03 \)) and 12-month (78.4 vs 53%, \( P<0.0001 \)) follow-up for freedom from AF and off-AADs. Repeat ablations were more frequent in catheter group (4.7 vs 24.4%, \( P<0.0001 \)) (ref.27).

Recently, Kim et al. in their meta-analysis reported a higher proportion of patients free of AF and off-AAD at 12 months of follow-up in thoracoscopic group than after catheter ablation, both in the randomized control trials (\( P<0.001 \), relative risk \( 1.77 \)) and in the retrospective cohort studies (\( p<0.01 \), relative risk. 1.68). Based on this data, thoracoscopic ablation was found to be more effective than catheter ablation. However, thoracoscopic approach had a higher rate of intermediate post-procedure complications than catheter ablation. In randomized control trial, severe adverse events were significantly more frequent (\( P=0.007 \), relative risk, 7.23). The long-term efficacy of thoracoscopic approach, and superiority over catheter ablation remains to be determined29.

Budera et al. published a paper that summarized the complications of thoracoscopic ablation from studies that were published in the last 7 years. The average incidence of serious complications was as high as 4.8%. This was mainly due to conversion to the sternotomy (1.28%) and phrenic nerve palsy (0.75%) in the early period of thoracoscopic surgery29. However, Bulava et al. reported 13% of major complications during the surgical part of hybrid procedure29. Van Laar et al. in review study reported the incidence of major complications of 3% and no operative mortality. It is likely, that as the learning curve is reversed, complication rates will decrease29.

CONCLUSION

This study has some limitations. These results may not be generalized as they were observed in a single surgeon experience. The small patient population and the short follow-up do not allow us to draw definite conclusions. Larger series with long-term follow-up are needed. Another limitation of this study is that 46% patients from the study group had paroxysmal AF and only 54% patients had persistent AF. For this reason, we have reported results for patients with paroxysmal AF and persistent AF. Another limitation of this study is that left atrial appendage was occluded in only 34.4% of patients. Finally, longer ECG monitoring and longer follow-up are needed especially in the light of ablation results that show a steep failure rate after the first year of follow-up.

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