Autonomic and surgical substrate modulation of atrial fibrillation

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Chapter 7

Thoracoscopic video-assisted pulmonary vein antrum isolation, ganglionated plexus ablation, and periprocedural confirmation of ablation lesions: First results of a hybrid surgical-electrophysiological approach for atrial fibrillation

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ABSTRACT

Introduction
Thoracoscopic pulmonary vein isolation (PVI) and ganglion plexus ablation is a novel approach in the treatment of atrial fibrillation (AF). We hypothesize that meticulous electrophysiological confirmation of PVI results in fewer recurrences of AF during follow-up.

Methods
Surgery was performed through 3 ports bilaterally. Ganglion plexus were localized and subsequently ablated. PVI was performed and entry and exit block was confirmed. Additional left atrial ablation lines were created and conduction block verified in patients with nonparoxysmal AF. The left atrial appendage was removed. Freedom of AF was assessed by ECGs and Holter monitoring every 3 months or during symptoms of arrhythmia. Antiarrhythmic drugs were discontinued after 3 months and oral anticoagulants were discontinued according to the guidelines.

Results
Thirty-one patients were treated (16 paroxysmal AF, 13 persistent AF, 2 long-standing persistent AF). Thirteen patients with nonparoxysmal received additional left atrial ablation lines. After 1 year, 19 of 22 patients (86%) had no recurrences of AF, atrial flutter, or atrial tachycardia and were not using antiarrhythmic drugs (11/12 paroxysmal, 7/9 persistent, and 1/1 long-standing persistent). Three patients had a sternotomy because of uncontrolled bleeding during thoracoscopic surgery. Four adverse events were 1 hemothorax, 1 pneumothorax, and 2 pneumonia. No thromboembolic complications or mortality occurred.

Conclusions
Thoracoscopic surgery with PVI and ganglion plexus ablation for AF is a safe and successful procedure with a single procedure success rate of 86% at 1 year. Electrophysiological guided thoracic PVI and additional left atrial ablation line creation presumably contributes in achieving a high success rate in the surgical treatment of AF.
INTRODUCTION

Atrial fibrillation (AF) is the most common chronic arrhythmia in the world and has a major health burden to Western society. The lifetime risk of AF for subjects 55 years old is 23.8% in men and 22.2% in women. AF is associated with an increased risk of stroke, heart failure, and dementia. Pulmonary vein isolation (PVI) by catheter ablation is a widely accepted intervention of medically refractory AF in patients with no or minimal heart disease. The success percentages of catheter PVI vary greatly by center and the specific technique used, with a single procedure success rate of 57% to 77%. Risks of this procedure include thromboembolic complications, tamponade, and esophagus ulcers. In addition to catheter ablation, surgical techniques, particularly by Cox-Maze III procedure, have been effective in the treatment of AF. These are invasive and technically difficult procedures requiring a median sternotomy. A minimal invasive procedure aims at combining the success rate of surgical treatment with a minimal invasive approach. Since 2005, multiple studies have been published using minimal invasive surgery with slight variations in operating technique, energy source used, and a success rate varying between 62% to 91%. We use a hybrid approach with extensive periprocedural electrophysiological testing during thoracoscopic pulmonary vein antrum isolation, left atrial ablation lines, and ganglion plexus (GP) ablation. We hypothesize that meticulous electrophysiological confirmation of ablation lines results in fewer recurrences during follow-up.

METHODS

Patient population

Patients with an indication for nonpharmacologic treatment of AF were eligible, as well as patients with a preference for minimal invasive surgery and/or an earlier failed catheter PVI attempt. This indication consisted of (1) ≥1 antiarrhythmic drugs (AAD) in standard dosage that failed or were not tolerated and (2) documentation of AF available within the 12 months before the procedure. Age of the patients was between 43 and 77 years. Patients who received an earlier catheter PVI ablation and PVI-naive patients were eligible for this procedure. Definitions of paroxysmal, persistent AF and long-standing persistent AF, success and failure of ablation, major adverse events, and follow-up monitoring were based on the HRS/EHRA consensus statement for catheter and surgical ablation of AF. All patients underwent 12-lead ECG, chest radiography, 24-hour Holter, transthoracic echocardiogram, and laboratory tests before surgery. MRI, exercise test, and pulmonary function test were performed on indication in the first 20 patients but were routinely performed in the last 10.
Preoperative care

Patients were admitted the day before surgery. Oral anticoagulation was discontinued 3 to 4 days before surgery. AAD were continued during hospital admission. Directly before surgery, a transesophageal echocardiogram was made to exclude thrombus in the left atrial appendage (LAA).

Surgical technique

Surgery was performed under general anesthesia. A double-lumen endotracheal tube for selective lung ventilation was placed. Surgery was started on the patient’s right side with 10-mm ports; 2 ports in the fourth and sixth intercostal space midaxillary line, and 1 port in the third or fourth intercostal space anterior axillary line. GPs were localized as described previously with high frequency stimulation (18 V, 1-ms pulse width, 1000 Hz) on the anterior right GP and inferior right GP. High-frequency pacing was delivered through an Atricure Cooltip (Atricure Inc, Cincinnati, OH) ablation pen positioned on the fat pad containing the GP and connected to an external pacemaker device, Oscor Pace 203H DDD External Dual-Chamber Pacemaker (Oscor Inc, Palm Harbor, FL). Localization of GPs was confirmed when high frequency pacing induced AV block or increased the R-R interval >50%. GPs were subsequently ablated with bipolar radiofrequency energy through the AtriCure Cooltip pen. A lighted dissector (AtriCure Lumitip Dissector) was used to pass a rubber banding under the pulmonary venous (PV) antrum after blunt dissection of the Waterstone groove. An AtriCure Isolator Transpolar Clamp was then connected to the rubber banding and positioned gently around the PV antrum. PV antrum isolation was achieved by application of bipolar radiofrequency energy to the clamps around the PV antrum. After confirmation of PVI (see below), the procedure was repeated on the left side of the thorax. The ligament of Marshall was dissected and ablated in all patients. In patients with persistent AF and long-standing persistent AF (LSPAF), additional left atrial lines (ALAL) were created. The ALAL consisted of a superior line (SL) and in selected patients an additional inferior line (IL). The SL connects the ablation lines encircling the right and left PVs, preventing reentry around both PV isolation (PVI) scars. In addition, an ablation line between the SL and the left fibrous trigone was made (the trigone line, TL). This ablation line prevents macro reentry around the connected PV antrum ablation lines similar to a mitral isthmus line as commonly used in catheter ablation for AF. After the ablation procedure and confirmation of conduction block, the LAA was removed with an endoscopic stapling device (Endo Gia stapler, Tyco Healthcare Group, North Haven, CT). On completion of the procedure, single chest drains were inserted; one in each side of the chest.
Electrophysiological testing

Before PVI, local electrograms were recorded from the PVs with a custom-made multi-electrode (6 gold-plated electrodes positioned in a circle around a central electrode; interelectrode distance, 1 mm). As a reference for atrial activity, we positioned a standard decapolar electrophysiology catheter (C. R. Bard Inc, Murray Hill, NJ) behind the atrium. We recorded electrograms, as described elsewhere, at 7 predefined locations: superior side of the superior vein, anterior side of the superior vein, inferior side of the superior vein, the confluence where both veins join, superior side of the inferior vein, anterior side of the inferior vein, and inferior side of the inferior veins. After ablation with the bipolar clamp, PVI was confirmed by placing the recording electrode on the same locations, on the PV side of the ablation scar. Electrograms were interpreted using a mobile electrophysiological work station (Bard Labsystem PRO 2.4A, C. R. Bard Inc). The PV antrum was considered isolated if either no potentials (bipolar recording) were recorded distal from the scar or if potentials were recorded of a slow automatic rhythm, dissociated from the atrial depolarizations (Figure 1). Far-field signals were identified by similar timing and morphology of the electrogram when positioning the recording electrode at varying Figure 1. PV recordings before and after PVI during sinus rhythm. Shown are leads I and II of the surface ECG and epicardial electrograms of the reference catheter and the custom-made electrode (right inferior pulmonary vein, RIPV). The reference catheter is positioned from the right side behind the atrium. The distal electrodes record from the left side of the atrium. Before ablation, there is activation of the antrum of the RIPV. After

![Figure 1](image-url)
ablation, the recordings on the RIPV show no potentials conducted to the RIPV distance from the scar. If potentials persisted, indicating that the PVs had not been isolated, the clamp was repositioned and further radiofrequency current was applied until PVI was confirmed. If an IL was made, the electric isolation of the box created by the SL and IL was tested by demonstration of entry block (absence of electrograms either during sinus rhythm or during AF) and exit block (pacing from within the box without capturing the atrium). In patients in AF during this testing of exit block, an attempt to electric cardioversion was undertaken. In patients who remained in AF after electric cardioversion, no further attempts were undertaken to prove exit block. In patients in whom atrial morphology restricted the creation of ALAL, the IL was not made because this line is not necessary to prevent reentry around the PVs. Conduction block across the TL was tested by recording the activation sequence across the ablation line. The atrium was paced proximal from the one side of the line. The custom-made multi-electrode was positioned at several positions distal to the TL, closer to and more distant from the line. An activation sequence where activation under the multi-electrode propagated toward the ablation line (ie, activation came around both PVI circles toward the TL) confirmed conduction block across the line. In contrast, an impulse propagating away from the TL, hence coming from the side where the atrium was paced from, proved persistent conduction (Figure 2).

**Perioperative and postoperative care**

After the procedure, patients were transferred to the recovery room and subsequently to the ward of the cardiothoracic surgery department on the same day. Chest drains were removed the day after surgery, and chest radiographs were routinely performed before and after removal. Anticoagulation with coumarin derivatives was reinstituted in all patients after the procedure, before chest drain removal. Unfractionated heparin was started as soon as bleeding risk allowed and continued until the patient’s international normalized ratio was >2.0. Oral anticoagulants were continued for at least 3 months after the procedure and AAD were continued. Episodes of AF lasting >24 hours were treated with an electric cardioversion (ECV). Patients were discharged depending on the rapidity of clinical recovery.

**Follow-up**

Patients were seen at the surgical outpatient clinic 10 days after the procedure for wound inspection and removal of sutures. The first 3 months after the procedure were used as a blanking period for the determination of absence of AF. If AF recurred, within the 3 months, patients received ECV and the same antiarrhythmic treatment as before the surgery. Rate control was instituted to prevent mean ventricular rates <90/min if applicable. Patients were followed up every 3 months with a 24-hour Holter and an ECG.
Figure 2. – Electrophysiological confirmation of ALAL. Schematic view of the posterior LA during confirmation of conduction block of the TL (B and C) and the SL (D through F). A, Schematic representation of the posterior LA with the ALAL. B and C, Confirmation of conduction block of the TL. Shown are leads I and II of the surface ECG with corresponding epicardial electrogram from the multielectrode. B, Multi-electrode is positioned far to the left from the TL (I); atrial conduction time from the stimulus (S) to the multielectrode is 200 ms. C, Multi-electrode is positioned on the scar of the TL (II). There is a double potential on C, the right of the scar, that is activated after 45 ms and the other side of the scar after 214 ms. The activation sequence confirms conduction block across the TL. D through F, Confirmation of conduction block of the SL. Shown are leads I and II of the surface ECG with corresponding epicardial electrogram from the multi-electrode. D, Multi-electrode is positioned far from the SL; atrial conduction time from the stimulus (S) to the multi-electrode is 60 ms (I). E, Multi-electrode is positioned closer to the SL; conduction time is increased to 100 ms (II). F, Final recording directly under the SL shows a conduction time of 154 ms (III). These sequential measurements determine the direction of atrial activation, which, in this figure, confirms isolation of the SL.

ALAL: additional left atrial lines, IL: inferior line, LA: left atrium, LPV: left pulmonary veins, RPV: right pulmonary veins, LPVI: left pulmonary vein isolation line, RPVI: right pulmonary veins isolation line, S: stimulus, SL: superior line, TL: trigone line.
until 2 years after the procedure. An MRI was made after 6 months for the detection of PV stenosis. Antiarrhythmic medication was discontinued starting from the first outpatient visit, 3 months after the procedure. After 6 months, oral anticoagulants were discontinued in patients with a CHADS2 score $>1$ if, after discontinuation of antiarrhythmic medication, there was absence of documentation of AF on either Holter or ECG or complaints suggestive of AF. In patients with higher CHADS2 scores, the anticoagulant regimen was adjusted according to the guidelines.4

**End points**
The primary end point was freedom from episodes of AF, atrial flutter, or atrial tachycardia without the use of AAD after 12 months. The secondary end point was freedom from episodes of AF, atrial flutter, or atrial tachycardia without the use of antiarrhythmic therapy after minimally invasive AF ablation and a after the blanking period of 3 months. Freedom from AF was defined as the absence of episodes of AF, atrial flutter, or atrial tachycardia lasting $>30$ seconds on any ECG or 24-hour Holter monitoring.10

**Statistical analysis**
Data are presented as mean±SD (range) or median (interquartile range, IQR) for continuous variables and numbers with percentages for categorical variables. Postoperative AF-free curves were calculated using the Kaplan–Meier method. Statistical analyses were carried out using GraphPad Prism, version 5.0.

**RESULTS**

**Patient characteristics**
Thirty-one patients underwent the procedure between November 2008 and June 2010. The mean age of patients was 57±7 years (range, 43 to 77 years), with 25 of 31 (81%) patients being male. Sixteen patients had paroxysmal AF, 13 patients had persistent AF, and 2 patients had LSPAF. Patient characteristics are shown in Table 1.

**Procedure and admission details**
Median procedure time was 191 minutes (IQR, 53; range, 136 to 355) in patients in whom no ALAL were made, compared with 217 minutes (IQR, 110; range, 166 to 540) in procedures with ALAL (median time of all procedures, 205 minutes; IQR, 78). No vagal response could be evoked using high-frequency stimulation after GP ablation in all patients. One patient refused GP ablation and thus GP ablation was not performed in this patient. PVs were successfully isolated in all patients. In 12 patients, the number of radiofrequency
**Table 1.** – Patient characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Minimal Invasive Surgery (n=31)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>57 (43-77)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>25 (81%)</td>
</tr>
<tr>
<td>Body mass index, mean ± SD, kg/m²</td>
<td>29 ± 4</td>
</tr>
<tr>
<td>Systolic blood pressure, mean ± SD, mmHg</td>
<td>133 ± 16</td>
</tr>
<tr>
<td>Diastolic blood pressure, mean ± SD, mmHg</td>
<td>79 ± 7</td>
</tr>
<tr>
<td>Type of AF</td>
<td></td>
</tr>
<tr>
<td>Paroxysmal, n (%)</td>
<td>16 (52%)</td>
</tr>
<tr>
<td>Persistent, n (%)</td>
<td>13 (42%)</td>
</tr>
<tr>
<td>Long standing Persistent, n (%)</td>
<td>2 (6%)</td>
</tr>
<tr>
<td>Total duration of AF, median, range, years</td>
<td>8 (1-25)</td>
</tr>
<tr>
<td>Previous AAD use, n (%)</td>
<td>31 (100%)</td>
</tr>
<tr>
<td>Number of previous AAD</td>
<td>4 (1-6)</td>
</tr>
<tr>
<td>Previous catheter PVI, n (%)</td>
<td>14 (45%)</td>
</tr>
<tr>
<td>Paroxysmal, n (%)</td>
<td>7 (23%)</td>
</tr>
<tr>
<td>Persistent, n (%)</td>
<td>7 (23%)</td>
</tr>
<tr>
<td>Long standing Persistent, n (%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Previous atrial flutter ablation, n (%)</td>
<td>4 (13%)</td>
</tr>
<tr>
<td>CHADS²-score, mean ± SD</td>
<td>0.5 ± 0.6</td>
</tr>
<tr>
<td>Congestive heart failure, n (%)</td>
<td>1 (3%)</td>
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<tr>
<td>Hypertension, n (%)</td>
<td>10 (32%)</td>
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<tr>
<td>Age &gt;75, n (%)</td>
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<tr>
<td>Diabetes, n (%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Stroke, n (%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>TIA, n (%)</td>
<td>2 (6%)</td>
</tr>
<tr>
<td>Thromboembolic event, n (%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Other cardiovascular disease, n (%)</td>
<td>3 (10%)</td>
</tr>
<tr>
<td>Myocarditis, n (%)</td>
<td>2 (6%)</td>
</tr>
<tr>
<td>Brugada syndrome, n (%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Medication at inclusion</td>
<td></td>
</tr>
<tr>
<td>ASA, n (%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Oral anticoagulation, n (%)</td>
<td>30 (97%)</td>
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<td>Statins, n (%)</td>
<td>9 (29%)</td>
</tr>
<tr>
<td>ACE-I/ARB, n (%)</td>
<td>14 (45%)</td>
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<tr>
<td>Beta-blocker, n (%)</td>
<td>13 (42%)</td>
</tr>
<tr>
<td>Amiodarone, n (%)</td>
<td>7 (23%)</td>
</tr>
<tr>
<td>Diltiazem, Verapamil, n (%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Digoxin, n (%)</td>
<td>3 (10%)</td>
</tr>
<tr>
<td>Dysonapramide, n (%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Flecainide, n (%)</td>
<td>8 (26%)</td>
</tr>
<tr>
<td>Sotalol, n (%)</td>
<td>8 (26%)</td>
</tr>
<tr>
<td>Echocardiographic finding*</td>
<td></td>
</tr>
<tr>
<td>Left atrial size, parasternal, long axis, mean ± SD, mm</td>
<td>47 ± 7</td>
</tr>
<tr>
<td>LAA thrombus, n (%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

*Echo available in n=30 patients.

applications was counted. Isolation of the right and left PV required additional radiofre-
quency applications in 4 of 12 and 7 of 12, respectively (up to 4 times). The total number
of radiofrequency applications ranged from 3 to 14. Thirteen patients with persistent AF
and LSPAF received ALAL. In 2 patients with persistent AF, no additional ablation lines
were made because of anatomic restrictions in one, and the inadvertent presumption
of paroxysmal AF in another patient. In 29 of 31 (94%) patients, the LAA could success-
fully be stapled and removed; in 2 patients, the LAA could not be removed because of
bleeding during the procedure. Median hospital stay was 6 days (IQR, 3; range, 4 to 12).
Average chest drain duration was 2 days (IQR, 0; range, 1 to 6). Procedure and admission
details are shown in Table 2.

Table 2. – Procedure and admission details

<table>
<thead>
<tr>
<th>Minimal Invasive Surgery (n=31)</th>
</tr>
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<tbody>
<tr>
<td>Procedure Time, median, range, min</td>
</tr>
<tr>
<td>GP ablation, n (%)</td>
</tr>
<tr>
<td>Additional left atrial ablation lines, n (%)</td>
</tr>
<tr>
<td>Superior line, n (%)</td>
</tr>
<tr>
<td>Trigone line, n (%)</td>
</tr>
<tr>
<td>Inferior line, n (%)</td>
</tr>
<tr>
<td>LAA removed, n (%)</td>
</tr>
<tr>
<td>Conversion to sternotomy, n (%)</td>
</tr>
<tr>
<td>Mortality, n (%)</td>
</tr>
<tr>
<td>Duration of pleural drainage, median, range, days</td>
</tr>
<tr>
<td>AF on discharge, n (%)</td>
</tr>
<tr>
<td>ECV during hospital stay, n (%)</td>
</tr>
<tr>
<td>Duration of hospital stay, median, range, days</td>
</tr>
<tr>
<td>Discharge with AAD, n (%)</td>
</tr>
</tbody>
</table>

GP: ganglionic plexus, LAA: left atrial appendage, AF: atrial fibrillation, ECV: electrical cardioversion,
AAD: anti-arrhythmic drugs

Follow-up
Median follow-up was 375 days (IQR, 285; range, 104 to 730). Twenty-two patients
(71%) had a follow-up of 1 year or more. During the first 3 months after the procedure,
blanked for the analysis of recurrence of AF, 9 (30%) patients received an ECV and 3
(10%) patients received 2 or more ECV. ECV was performed in 4 (13%) patients after the
first follow-up visit. One patient (No. 5) was categorized as late responder after receiv-
ing an ECV 115 days after the procedure. He remained in sinus rhythm since. Figure 3
illustrates the freedom from AF in a Kaplan–Meier plot. Figure 4 shows the duration of
follow-up and recurrences of AF in individual patients.
Figure 3. – Kaplan–Meier curve representing the percentage estimates of patients with freedom from AF, atrial flutter, and atrial tachycardia up to 2 years after surgery. The number of patient free from recurrence, total patients, and total patients specified by type of AF are shown at the bottom of the figure.
AF: atrial fibrillation.

Figure 4. – Individual patient timeline: Individual patient follow-up including ECVs and blanking period. In this figure, individual follow-up and all recurrences of AF (light gray) are plotted. Bars indicate the total numbers of days since the procedure. Patients with recurrences of AF, atrial flutter, or atrial tachycardia are indicated with an “F.” ECVs are marked with a star (✱) on the individual patient bars. Patients with persistent AF have a box (□) around their number, and patients with long-standing persistent AF have a circle (○) around their number.
AF: atrial fibrillation, ECV: electrical cardioversion.
**End points**

A total of 19 of 22 patients (86%) reached the primary end point (11/12 paroxysmal AF, 7/9 persistent AF, and 1/1 LSP AF). These patients were free from AF, atrial flutter, or atrial tachycardia without the use of AAD at 1 year of the procedure. Table 3 elaborates on the 3 patients who did not meet the primary end point. The secondary end point was reached by 26 of 31 (84%) patients (14/16 paroxysmal AF, 10/13 persistent AF, and 2/2 LSP AF). Of these patients, 16 of 31 (52%) patients discontinued oral anticoagulants. Patients without oral anticoagulants were followed for a median of 636 days (IQR, 180; range, 305 to 730), compared with 325 days (IQR, 90; range, 180 to 469) of follow-up for patients with oral anticoagulants (excluding failed patients). Note that most patients still taking anticoagulants were the patients with the shorter follow-up. In the 5 patients who did not reach the secondary end point, 4 had recurrences and 1 patient required AAD at individual follow-up (Table 3).

<table>
<thead>
<tr>
<th>Table 3. – Patients not reaching endpoints</th>
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<tbody>
<tr>
<td>Patient number</td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td>Patients who did not reach primary endpoint (n=3)</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>4</td>
</tr>
<tr>
<td>21</td>
</tr>
<tr>
<td>Patients who did not reach secondary endpoint (n=2)</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>29</td>
</tr>
</tbody>
</table>

*AF: atrial fibrillation, AAD: anti-arrhythmic drugs, AT: atrial tachycardia, ALAL: additional left atrial lines, SR: sinus rhythm*

**Adverse events**

During the procedures, 3 patients had a sternotomy because of bleeding that could not be controlled with thoracoscopic surgery (2 left atrial bleedings and 1 bleeding from the aorta). We suspect that the sternotomies might have been related to the learning curve of the procedure because this occurred in patients 3, 7, and 19. One patient had a hemothorax resulting from bleeding from the entrance of one of the thoracoscopic
ports. There were 3 minor events; during admission, 1 patient had a pneumothorax after removal of the chest drains. Two patients had a pneumonia successfully treated with antibiotic therapy. The MRIs made after 6-month follow-up showed no signs of PV stenosis in any patient. No thromboembolic complications or deaths occurred.

**DISCUSSION**

In this report, we describe our first experiences with a hybrid approach of thoracoscopic PVI and GP ablation and LAA exclusion for AF. The percentage of patients free from AF and not using AAD after 1 year was 86%. Even with the small number of patients that we report here, these results make this technique a promising approach to the treatment of AF. In our view, the collaboration between surgeon and cardiologist is beneficial to the outcome of the procedure. Potentially, the high single procedure success rate described in this report may be a cost-effective treatment for AF. However, further studies are needed to elucidate this issue.

**Electrophysiological measurements of PVI and ALAL**

There are various reports on minimally invasive or thoracoscopic ablation of the PVs.\(^8\)\(^,\)\(^14\)\(^,\)\(^15\) Our approach differs from those reports because we made the electrophysiological confirmation of the ablation the mainstay of the treatment. Frequently, the surgeon had to repeat the ablations because initial ablation did not result in conduction block. We cannot exclude that the increased number of radiofrequency applications rather than the electrophysiological evaluation is responsible for the success of the procedure. However, this matter can only be solved by demonstrating isolation or conduction block. Because of the anatomic aspect of the PVs and the shape of the bipolar radiofrequency clamp, certain areas are more likely to show conduction of atrial activity. These areas comprise the confluence where the PVs join and the superior side of the superior and inferior side of the inferior PVs. In addition to this, the success of radiofrequency application might further be increased by dissection of the epicardial fat surrounding the PV antrum.

It is thought that only PVI is not enough to maintain sinus rhythm in patients with persistent or long-standing persistent AF.\(^6\) There are few data that show which surgical lesions are easy reproducible, safe, and actually benefit the patient and prevent reentry tachycardias or modify the AF substrate.\(^12\)\(^,\)\(^16\)\(^,\)\(^17\) We use a series of left atrial lines adapted from Edgerton et al.\(^16\) We chose an epicardial approach for confirmation of the ablation lines. Potentially, complications related to additional left atrial catheter–based ablation such as stroke (related to transseptal puncture) and bleeding as a result of full heparinization can be prevented. We think that conduction block, preferably bidirectional conduction block, must be proven. The nature of the procedure, that is, the fact
that half of the procedure is carried out from the right side with the right lung collapsed and the other half from the left side with the left lung collapsed, makes a rigid protocol necessary. That is, the right side of the SL and the TL must be completed and confirmed before the additional lines from the left side can be made. Therefore, we accept proof of unidirectional block. Of course we realize that this potentially leaves an arrhythmogenic substrate, but from our follow-up data thus far, this does not seem to play a major role. Speculations on efficacy of PVI and ALAL in LSPAF would be premature because there were only 2 patients with LSPAF. These patients did not deviate from the rest of the cohort during follow-up.

**GP ablation**

With epicardial ablation during thoracoscopic surgery, the fat pads in which the GPs reside can be selectively targeted. There are both experimental and clinical data showing that autonomic modulation or partial innervation contributes to the success of treating AF. Indeed, a vagal response occurring during catheter ablation of AF was associated with a higher success rate of the procedure. Additionally, the targeted approach of complex fractionated atrial electrograms, a marker of GP activity, has yielded success as a standalone intervention. However, complex fractionated atrial electrograms are a result of multiple causes and do not always correspond that well with the location of the GPs.

By ablation of the GPs in addition to PVI, we thus target multiple arrhythmogenic causes of AF. It is unclear how much the GPs affect the PVs once there is a solid PVI. In animal models in which only GPs were ablated, return of GP activity was observed 4 weeks after the procedure. However, ablation of the GPs presumably destroys not only the nerve endings but also the cell bodies. This might potentially prevent the complete recovery and function of the GPs. One might speculate that the favorable results on medium term (≥1 year) that we present here are at least in part due to this lack of reinnervation, but without data supporting this hypothesis, this remains a speculation. One might also speculate that even if the effect of GP ablation is temporary, the absence of GP activity during the first few weeks after the procedure affects electrophysiological remodeling and thereby adds to freedom from AF.

**Limitations**

It cannot be excluded that event monitoring more extensive than serial 24-hour Holter electrograms or the implantation of loop monitor would capture episodes of AF not documented with our procedure. In a small, nonrandomized, observational study setting, it is hard to justify an invasive rhythm monitoring device. We are confident however, that most asymptomatic episodes come to our attention with our current follow-up protocol.

We report in this article the first patients who underwent this procedure in our institution. The procedure protocol was refined over time. Extensive measurement, GP ablation,
and PVI ablation remained unchanged, but the types of lines made in the ALAL varied over the course of time. Because the treatment of AF comprises an elective procedure for a nonlethal condition, we let surgical considerations on safety of the patient always prevail over electrophysiological completeness.

Because 45% of the patients reported here underwent a previous catheter ablation for AF, it cannot be excluded that this favorably influenced our results. However, all patients had documented recurrences of AF before being enrolled in this study. Moreover, the PVs were not isolated in any of these patients (data not shown). Therefore, we cannot conclude that previous ablation affected the outcome of the current study.

CONCLUSIONS

A minimal invasive surgical approach with thoracoscopic video-assisted surgery with PVI and GP ablation for AF is a safe and successful procedure with a single-procedure success rate of 86% at 1 year without the use of AAD. Electrophysiological guided thorough PVI and ALAL creation presumably contribute in achieving a high success rate in the surgical epicardial approach in treatment of AF. Removal of the LAA is an additional advantage compared with the endocardial approach of AF treatment. The contribution of the ALAL and GP ablation in this procedure and their effect on success rate must be evaluated in further studies.

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REFERENCES


