Ablation of atrial fibrillation

de Maat, Gijs Eduard

Chapter 6

Surgical Minimally Invasive Pulmonary Vein Isolation for Lone Atrial Fibrillation: Mid-term Results of a Multi-Centre Study

G.E. De Maat*, A. Pozzoli*, M.F. Scholten, H.L. Hillege, I.C. Van Gelder, O.R. Alfieri, S. Benussi and M.A. Mariani

Innovations 2013; 8(6):410-5.

*Both authors contributed equally

ABSTRACT

Objective: Minimally invasive surgical pulmonary vein isolation (SMI-PVI) is an emerging therapy for the treatment of symptomatic drug refractory atrial fibrillation (AF). Nevertheless, the mid and long-term results of SMI-PVI remain unknown. The aim of this retrospective multi-center study is to report on mid-term efficacy and safety of SMI-PVI.

Methods: The study design was retrospective, multi-centric and observational. From July 2005 to November 2011, 86 patients with drug refractory paroxysmal or persistent AF underwent SMI-PVI in three centers. Patients were eligible for SMI-PVI when suffering from symptomatic, drug refractory AF or after failed transcatheter PVI. Success was defined as absence of AF on 24- or 96 hour Holter monitoring during follow-up, in the absence of anti-arrhythmic drugs (AADs).

Results: Mean age was 54 ± 11 years, 78% male. Median AF duration was 30 months (range, 2-203); paroxysmal AF was present in 86% of patients, persistent in 14%. Fifteen patients (17%) underwent previous transcatheter ablations. After a median follow-up of 24 months (range: 6-78), 72% of all patients were free from atrial arrhythmias without the use of AADs. With AADs this was 83%. Major perioperative adverse events occurred in 7 (8%) patients.

Conclusions: This retrospective multi-center study shows that SMI-PVI is effective at median 24 months follow-up for the treatment of mostly paroxysmal drug refractory AF. Perioperative adverse events do remain a point of caution.

INTRODUCTION

Atrial fibrillation (AF) is the most frequent cardiac rhythm disorder with an increasing prevalence and is responsible for substantial morbidity, mortality and use of healthcare resources[1]. Currently, the first choice for treating AF is pharmacological therapy with anti-arrhythmic drugs (AADs), which has shown to be effective in less than 40% of patients[2]. Unfortunately, AADs have considerable adverse effects[3]. Rhythm-control therapy for AF using transcatheter pulmonary vein isolation (PVI) has gained strong popularity in younger patients in recent years, especially those with paroxysmal AF[4, 5]. Success rates of transcatheter PVI vary widely, worsening with the progression of the disease to more persistent presentations. The technical difficulty of achieving transmural electrical isolation hampers the results of transcatheter PVI, especially long-term success and in one third of the patients more than one procedure is required to obtain stable sinus rhythm[6]. Minimally-invasve surgical PVI (SMI-PVI) was introduced in 2005 as an alternative to transcatheter PVI[7]. The SMI-PVI has the advantage of being less technically demanding than a conventional full Maze open-chest operation, delivering a continuous lesion with bipolar radiofrequency in the setting of epicardial, off pump ablation. Previous studies with SMI-PVI have described promising short-term follow-up success rates with freedom from AF without AADs in 64-73% of patients[8-11]. However, clinical outcome data beyond 1 year are largely unavailable. The aim of this paper is to report mid-term results of SMI-PVI, by analyzing both procedural efficacy and safety in patients with mostly paroxysmal AF.

METHODS

Patient Population

This observational, retrospective study examined a series of 86 consecutive patients treated with SMI-PVI between July 2005 and November 2011 in three centers. Inclusion criteria were symptomatic paroxysmal or persistent AF, without concomitant cardiac structural disease, refractory to class I and/or class III AADs or failed transcatheter PVI. Exclusion criteria for SMI-PVI were: left atrial size >55mm (parasternal echocardiographic view), prior heart or lung surgery, significant coronary disease or previous MI, left ventricle hypertrophy >12mm, previous hospitalization for heart failure, left ventricular dysfunction (ejection fraction <50%), moderate or severe mitral- or aortic valve disease, or lung disease (prior tuberculosis or COPD Gold class III-IV). Definitions of paroxysmal and persistent AF, success and failure of ablation, adverse events and follow-up monitoring were based on the Heart Rhythm Society Consensus Statement for the catheter and surgical ablation of AF[5].

Surgical Technique

When the technique was first introduced (2005), pulmonary veins (PVs) were targeted via bilateral video-assisted mini-thoracotomy. Since 2007, a switch was made to a totally thoracoscopic approach. All patients were operated in the supine decubitus position, with general anesthesia and double-lumen endotracheal intubation. After lung deflation, the pericardium was divided 2 cm anterior to the phrenic nerve from the superior vena cava to the inferior vena cava (IVC). Blunt dissection was used to access the oblique sinus between the right inferior pulmonary vein and the IVC, and both right pulmonary veins were surrounded with the help of an articulated lighted dissector (Lumitip, AtriCure, Inc, Cincinnati, Ohio). A rubber tube (Glidepath, AtriCure, Inc, Cincinnati, Ohio) was placed around the pulmonary veins. A 5-cm long bipolar radiofrequency clamp (Isolator, AtriCure, Inc, Cincinnati, Ohio) was advanced with the Glidepath attached to the tip of the lower jaw to guide it through the oblique sinus, until its tip could be visualized cephalic to the superior PV. Bipolar ablation was performed by closing the bipolar clamp along the left atrial cuff adjacent to the ostium of the PVs, taking care not to ablate the PVs themselves. This clamp produces a linear thermal lesion by radiofrequency energy. After ablation, the measurement of effective conduction block was performed by pacing within the PVs (exit block). After testing the conduction block, the lung was re-inflated. Then, from the left side, the left PVs and the left atrial appendage were addressed. The placement of thoracoscopic ports on the left side was similar to the right. After division of the ligament of Marshall, both left PVs were surrounded by a Glidepath with the aid of the articulated lighted dissector, as described for the right PVs. The ablation lesions were repeated at least 3 to 5 times on each side before testing of exit block. In the last 33 patients, ganglionic plexi were tested for inducibility by means of high rate pacing[12]. Whenever active ganglionic plexi were found these were additionally ablated using the monopolar Isolator Pen (Atricure). No additional linear ablations (ablation lines) were applied on the atria. All patients in AF were cardioverted to sinus rhythm for these measurements. Concerning left atrial appendage (LAA) management, the LAA was excised by stapling or excluded with the Atriclip™ device in all patients of the Center 1 series. The LAA was intentionally not addressed in the Center 3 and a subgroup of center 2 series.

Medication

During postoperative hospitalization, patients were treated with full-dose low-molecular-weight (LMW) heparin. Oral anti-coagulation (OAC) was restarted one month after surgery and LMW heparine was not stopped until INR >2.0 was reached. Anticoagulation treatment was determined based on the $CHADS_2VA_2Sc$ score for stroke[4, 13]. AADs were continued during the first three months, and when atrial arrhythmias occurred in this period, they were not treated with electrical cardioversion, as spontaneous conversion is known to occur frequently.

Follow-up

All patients visited the outpatient clinic and received standard care for patients treated for AF, and underwent 24h or 96h Holter Monitoring at 3, 6 and 12 months. Due to the observational nature of the study, no further specific investigation were requested for the patients. After the first year, follow-up was conducted annually or on indication, consisting of 24h-Holter monitoring and physical examination during outpatient visits. In case of early recurrence of atrial tachy-arrhythmias (before three month follow-up visit), patients underwent cardioversion.

Endpoints

The primary efficacy endpoint was defined as freedom from atrial arrhythmias, i.e. no evidence of AF, atrial flutter, or other atrial arrhythmias with a duration >30 seconds, as documented by Holter monitoring, or implantable cardioverter defibrillator/pacemaker interrogation, off class I or III AADs[5], in accordance with the definitions as described in the 2012 expert consensus statement on AF ablation[5].

Secondary efficacy endpoints were freedom from atrial arrhythmias with the use of AADs, freedom from atrial arrhythmias after SMI-PVI as first line invasive treatment (without previous transcatheter PVI) and freedom from atrial arrhythmias after SMI-PVI with additional ganglionic plexi ablation.

The safety endpoint was the occurrence of procedural and post-procedural adverse events. Adverse events were defined as an event that resulted in death or permanent injury, in temporarily injury that required intervention or specific treatment (eg. stroke, transient ischemic attack, major bleeding requiring surgery or blood transfusion or cardiac tamponade and/or perforation, significant/symptomatic PVs stenosis >70%, pericarditis and/or pericardial effusion, acute coronary syndrome, myocardial infarction, nervus phrenicus lesion, pneumothorax, wound infections, empyema, pneumonia, peri-procedural conversion to thoracotomy, and other non pre-defined events).

Data analysis

Baseline descriptive statistics are presented as mean ± standard deviation or median (range) for continuous variables, as appropriate, and counts with percentages for categorical variables. Differences between subgroups, in terms of patient characteristics at baseline, different follow-up times, and end of study were evaluated by the Student *t* test or the Mann-Whitney U test, depending on normality of the data. Chi-square or Fisher's exact test were used for comparison of categorical variables. Follow-up data were censored for patients who had a first recurrence of AF or had been followed through 1 February 2012. The observation time was calculated as the time from ablation until either the occurrence of AF or the moment of censoring. The statistical software package SPSS 20 was used for analysis.

RESULTS

Patient population

A total of 86 patients were treated with SMI-PVI in three centers, by two surgeons. The number of patients was 28, 25 and 33, respectively. Mean age was 54 ± 11, 67 (78%) patients were male. There were 74 (86%) patients with paroxysmal AF and 12 (14%) patients with persistent AF. AF was present for a median of 30 months (2-200) before the SMI-PVI procedure. Previous transcatheter PVI had been performed in 15 (17%) patients. Preoperatively, 4 (5%) patients had a pacemaker and 2 (2%) patients had an ICD. Patient baseline characteristics of the three groups are illustrated in detail in **Table 1**.

Table 1. Baseline characteristics

	SMI-PVI group (n = 86)	**Center 1 (n=28)**	**Center 2 (n=25)**	**Center 3 (n=33)**
Age, years	54 ± 11	56 ± 10	53 ± 12	51 ± 10
Male, n (%)	67 (78%)	24 (86%)	16 (64%)	27 (82%)
Type of AF				
Paroxysmal, n (%)	74 (86%)	24 (86%)	22 (88%)	28 (85%)
Persistent, n (%)	12 (14%)	4 (14%)	3 (12%)	5 (15%)
Median AF history, months [range]	30 [2-203]	36 [12-200]	17 [2-144]	41 [5-203]
Previous transcatheter PVI	15 (17%)	12 (80%)	3 (20%)	0 (0%)
EHRA-score				
II, n (%)	38 (44%)	10 (36%)	13 (52%)	15 (45%)
III, n (%)	48 (56%)	18 (64%)	12 (48%)	18 (55%)
NYHA-score				
II, n (%)	77 (90%)	27 (96%)	24 (96%)	26 (79%)
III, n (%)	9 (10%)	1 (4%)	1 (4%)	7 (21%)
Body Mass Index (kg/m^2)	27 ± 4	26 ± 3	28 ± 4	28 ± 3
Hypertension n, %	39 (35%)	12 (43%)	8 (32%)	10 (30%)
Echocardiographic findings				
Ejection Fraction	56 ± 6	59 ± 4	56 ± 8	55 ± 4
LA Parasternal Diameter (mm)	42 ± 6	43 ± 8	42 ± 6	42 ± 5

AADs= anti arrhythmic drugs TEE=Thrombo-embolic event LVEDD= Left Ventricular End Diastolic Diameter LVESD= Left Ventricular End Systolic Diameter ACE-I= Angiotensin Converting Enzyme inhibitor; ARB= angiotensin receptor blocker. LA = Left Atrium

Surgical Procedure

The procedure was performed successfully in all patients. More specifically, 13 (15%) of patients were treated via bilateral video-assisted mini-thoracotomy and 73 (85%) underwent a total thoracoscopic approach. No additional ablation lines were applied and additional

ablation of the ganglionic plexi was performed in 25 (29%) patients. Mean procedural time was 180±61 minutes. The left atrial appendage (LAA) was excised in 31 (36%) patients by stapling and was excluded in 10 (12%) patients using the Atriclip device (AtriCure, Inc, Cincinnati, Ohio). In 45 (52%) patients, the LAA was intentionally left unaddressed. Mean postoperative hospitalization was 7 ± 3 days.

Efficacy endpoints

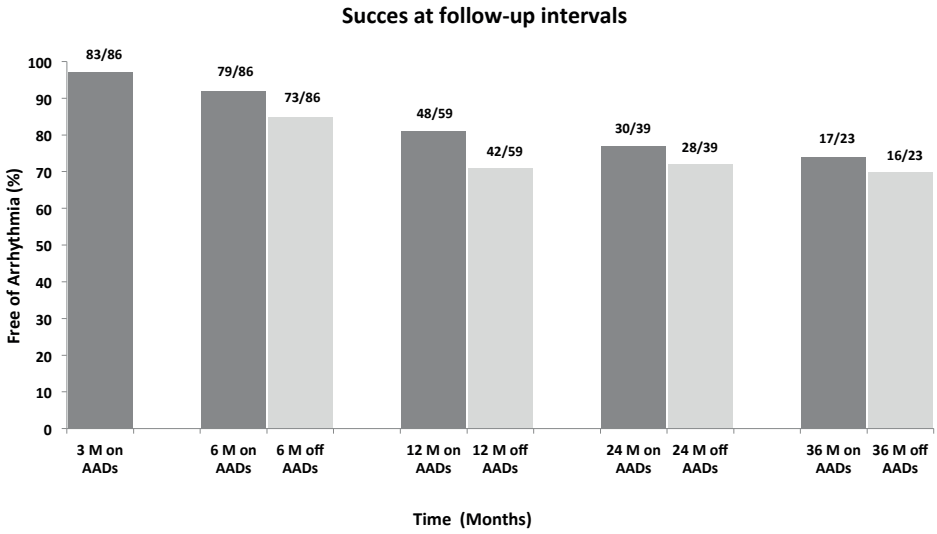
After a median follow-up of 24 months (6-78), 62 (72%) of all patients were free from atrial arrhythmias without the use of AADs. Success was higher when AADs were taken into account, with 71 (83%) patients free from atrial arrhythmias.

Over time, the percentage of patients free from atrial arrhythmias without AADs use was 71% at 12 months, 72% at 24 months and 69% at 36 months (**Figure 1**). With the use of AADs, freedom from atrial arrhythmias was 81%, 77% and 74% at 12, 24 and 36 months, respectively.

Among failures, which occurred mostly during the first year, 50% (12 out of 24 patients) received an additional transcatheter PVI. This resulted in a combined success of 80% freedom from arrhythmia at mid-term follow-up without AADs and 91% with AADs. In 2 patients a pacemaker was implanted due to sick sinus syndrome after SMI-PVI.

Overall freedom from OAC at mid-term follow-up was 72%, in the group with LAA exclusion this was 93%, in the group without LAA exclusion this was 53% (p>0.001).

Figure 1. Freedom from arrhythmia at mid-term follow-up



AADs= antiarrhythmic drugs M= months

Adverse events

Peri-procedural major adverse events occurred in 7 (8%) patients. During the procedure, 2 patients required conversion to sternotomy, 1 due to bleeding of the left atrial appendage and 1 due to laceration of the right pulmonary artery. One patient required unilateral (left side) conversion to mini-thoracotomy for left chest adhesions. During hospitalization, 2 patients had late tamponade (after 2 and 5 days) and 1 patient suffered from pericardial effusion. These patients required evacuation through VATS and recovered completely. In one case, pericardial effusion was not treated, and the patient recovered completely. One patient suffered from right sided homonymous anopsia, MRI showed signs of posterior cerebral ischeamia but was inconclusive, therefore there was a clinical diagnosis of stroke, confirmed by a neurologist. At one year follow-up the patient had recovered partially. No 30-days- or in-hospital mortality were recorded. As described, one patient suffered from a laceration of the right pulmonary artery and required conversion to sternotomy. Postoperatively, pulmonary artery angioplasty was performed by the interventional cardiologist. This patient died seven months after surgery due to a pulmonary embolism. Furthermore, minor adverse events occurred in 7 (8%) patients. We report 4 cases of pneumothorax, which were treated with chest drainage. Two transient phrenic nerve lesion were observed, at 3 months follow-up the patients had completely recovered. In one case pericardial effusion was not treated, and the patient recovered completely. All individual adverse events are listed in **Table 2**.

Table 2. Major and minor adverse events

Major adverse events	
Sternotomy or mini-thoracotomy due to	
a) auricular bleeding	1 patient
b) pulmonary artery laceration	1 patient
c) adhesions/adherences	1 patient
Late tamponade requiring VATS	2 patients
Pericardial effusion requiring VATS	1 patient
Stroke	1 patient
Total	**7 (8%)**
Minor adverse events	
Pneumothorax	4 patients
Transient unilateral paralysis diaphragm	2 patients
Pericardial effusion no treatment	1 patient
Total	**7 (8%)**

VATS=video assisted thoracoscopic surgery

Subgroup analysis

Of all patients, 71 (83%) underwent SMI-PVI as a first invasive treatment. In this sub-group, freedom from arrhythmia without AADs was obtained in 73%. These results do not differ significantly when compared to patients with previous transcatheter PVI (p=0.608).
When comparing results of SMI-PVI between paroxysmal- and persistent AF patients, the paroxysmal AF group shows 72% freedom from arrhythmia, compared to 70% in the persistent group (p=0.876).
In our study, additional ganglionic plexi ablation resulted in freedom from arrhythmia in 75% of patients; this was 72% in the group without additional GP ablation (p=0.810).
Comparing the patients with and without LAA exclusion, adverse events occurred in 20% and 13% respectively (p=0.438).

DISCUSSION

This study reports on a multi-center clinical experience with SMI-PVI, as a stand-alone procedure for the treatment of refractory AF. Our results show that SMI-PVI is effective for the treatment of mostly paroxysmal AF, and that benefits are maintained at mid-term follow-up. Perioperative adverse events do remain a point of caution.
In recent years, several publications have reported on short-term outcomes of SMI-PVI, showing promising results, with success rates without AADs ranging from 64%-73%[8-11]. However, almost no clinical results beyond 1 year are available. The recently published FAST-trial, which compared SMI-PVI to transcatheter PVI at 1 year follow-up, without AADs, documented a 66% freedom from arrhythmias after SMI-PVI against 37% after transcatheter PVI[8]. Compared to the FAST-trial, our data show a slightly higher success percentage with longer follow-up. This might be explained by the higher rate of persistent AF in the FAST-population (33%). Nevertheless, the population of the FAST trial differed from ours in that they enrolled patients less amenable to percutaneous treatment, with prior failed transcatheter PVI, left atrial diameter of 40 to 44 mm with hypertension or LA diameter > 44 mm.
Two recently published studies, reporting on outcome of SMI-PVI as stand-alone procedure, show 80% success at a mean of 17 months follow-up [14], and 90% success at a mean of 24 months[15]. Our study found slightly lower success rates compared to these reports, but in a larger patient population with prolonged follow-up and an extensive description of adverse events. Also, no additional ablation lines were applied in our series. The great majority of patients in this study underwent SMI-PVI as first line invasive treatment. In our sub-analysis, there was no significant difference compared to patients who underwent previous transcatheter PVI.

Surgical isolation of the pulmonary veins offers potential benefits; First, thanks to the use of bipolar radiofrequency with an automatic transmurality algorithm with impedance feedback, and systematical verification of exit block, SMI-PVI offers certainty regarding objective isolation of the PV's, via a total thoracoscopic approach. In around 90% of all cases, the trigger for paroxysmal AF originates from the PVs region[16]. Addressing the PVs is essential and in the majority of cases sufficient to control the arrhythmia. Lone SMI-PVI has proven to be a relatively safe and reproducible technique. However, using this lesion set, triggers in non-PV sites may lead to AF recurrence. In our study, SMI-PVI was performed without any additional linear ablations, although the literature reports a large variety of lesion sets [17-19].

Second, although not performed in all patients of our series, the surgical approach may offer the possibility to exclude the left atrial appendage in order to reduce the future risk of stroke[20]. These potential advantages notwithstanding, the LAA was not routinely addressed in patients treated at Center 3 and a subgroup of Center 2 in order to maintain left atrial contractility and prevent possible hydro-electrolytic unbalances[21]. This policy did not influence the primary endpoint or incidence of adverse events. Althoug, it resulted in a higher percentage of patients on OAC. When regarding future cardiac interventions, thoracoscopically entering the pericardium may leave some adhesions, but it does not exclude the possibility for later cardiac interventions through median sternotomy.

Finally, SMI-PVI via VATS offers the possibility to achieve autonomic nervous system denervation of the atria, as the ganglionic plexi are located on the epicardial surface of the atrial myocardium. Ganglionic plexi ablation remains controversial as the additional benefits compared to lone SMI-PVI have never been investigated in a randomized clinical trial[22]. Nonetheless, the combination of techniques has shown good clinical results [23].

Our study shows that, when both AADs and additional transcatheter PVI are considered, 91% of our population is free from atrial arrhythmia. In our experience, the feasibility and the encouraging results of repeated percutaneous ablation after failed SMI-PVI suggests the 2 procedures may perform well in a sequential multidisciplinary context.

Unfortunately, due to the invasive nature of the VATS approach, the higher efficacy of SMI-PVI was accompanied by a higher adverse event rate and longer hospitalization than for transcatheter PVI. In the presented patient group, fewer adverse events occurred than reported in other studies, though the reported incidence of adverse events remains high[8]. Most adverse events in the preliminary phase occurred in the very first patients, indicating lower complication rates as a surgeon's experience increases. No peri-operative mortality was registered. One peri-operative cerebrovascular accident with visual disorders and partial recovery was reported. In this 49 year old patient, the LAA was intentionally not excluded.

SMI-PVI is an effective treatment for mostly paroxysmal AF at mid-term follow-up. If combined with a progressive abatement of operative risk, mid-term results of SMI-PVI show

potential for a solid and durable first line non-pharmacological treatment for paroxysmal and persistent AF.

Study limitations

Although all patients in our study underwent the same SMI-PVI procedure, the population was heterogeneous when prior transcatheter ablation, additional GP ablation and LAA amputation are considered. The retrospective nature of this study means that no definite conclusions may be drawn regarding SMI-PVI efficacy. The extensive follow-up may counterbalance this. Furthermore, 24- and 96-hour Holter monitoring may underestimate the recurrence of AF. As observed in transcatheter PVI results, success is very likely to decrease over time. From this perspective, it will be interesting to report on long-term results (>36 months) when available.

CONCLUSIONS

This retrospective multi-center observational study shows that minimal invasive SMI-PVI was effective at median 24 months follow-up for the treatment of mostly paroxysmal drug refractory AF. Adverse events do remain a point of caution.

REFERENCES

[1] Miyasaka Y, Barnes ME, Gersh BJ, Cha SS, Bailey KR, Abhayaratna WP, Seward JB, Tsang TS. Secular trends in incidence of atrial fibrillation in olmsted county, minnesota, 1980 to 2000, and implications on the projections for future prevalence. *Circulation* 2006;114:119-25.

[2] Wilber DJ, Pappone C, Neuzil P, De Paola A, Marchlinski F, Natale A, Macle L, Daoud EG, Calkins H, Hall B, Reddy V, Augello G, Reynolds MR, Vinekar C, Liu CY, Berry SM, Berry DA, ThermoCool AF Trial Investigators. Comparison of antiarrhythmic drug therapy and radiofrequency catheter ablation in patients with paroxysmal atrial fibrillation: A randomized controlled trial. *JAMA* 2010;303:333-40.

[3] Van Gelder IC, Crijns HJ, Tieleman RG, Brugemann J, De Kam PJ, Gosselink AT, Verheugt FW, Lie KI. Chronic atrial fibrillation. success of serial cardioversion therapy and safety of oral anticoagulation. *Arch Intern Med* 1996;156:2585-92.

[4] European Heart Rhythm Association, European Association for Cardio-Thoracic Surgery, Camm AJ, Kirchhof P, Lip GY, Schotten U, Savelieva I, Ernst S, Van Gelder IC, Guidelines for the management of atrial fibrillation: The task force for the management of atrial fibrillation of the european society of cardiology (ESC). *Europace* 2010;12:1360-420.

[5] Calkins H, Kuck KH, Cappato R, Brugada J, Camm AJ, Chen SA, Crijns HJ et al. 2012 HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: Recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design: A report of the heart rhythm society (HRS) task force on catheter and surgical ablation of atrial fibrillation. *Europace* 2012;14:528-606.

[6] Weerasooriya R, Khairy P, Litalien J, Macle L, Hocini M, Sacher F, Lellouche N, Knecht S, Wright M, Nault I, Miyazaki S, Scavee C, Clementy J, Haissaguerre M, Jais P. Catheter ablation for atrial fibrillation: Are results maintained at 5 years of follow-up?. *J Am Coll Cardiol* 2011;57:160-6.

[7] Wolf RK, Schneeberger EW, Osterday R, Miller D, Merrill W, Flege JB,Jr, Gillinov AM. Video-assisted bilateral pulmonary vein isolation and left atrial appendage exclusion for atrial fibrillation. *J Thorac Cardiovasc Surg* 2005;130:797-802.

[8] Edgerton JR, Brinkman WT, Weaver T, Prince SL, Culica D, Herbert MA, Mack MJ. Pulmonary vein isolation and autonomic denervation for the management of paroxysmal atrial fibrillation by a minimally invasive surgical approach. *J Thorac Cardiovasc Surg* 2010;140:823-8.

[9] Han FT, Kasirajan V, Kowalski M, Kiser R, Wolfe L, Kalahasty G, Shepard RK, Wood MA, Ellenbogen KA. Results of a minimally invasive surgical pulmonary vein isolation and ganglionic plexi ablation for atrial fibrillation: Single-center experience with 12-month follow-up. *Circ Arrhythm Electrophysiol* 2009;2:370-7.

[10] Boersma LV, Castella M, van Boven W, Berruezo A, Yilmaz A, Nadal M, Sandoval E, Calvo N, Brugada J, Kelder J, Wijffels M, Mont L. Atrial fibrillation catheter ablation versus surgical ablation treatment (FAST): A 2-center randomized clinical trial. *Circulation* 2012;125:23-30.

[11] Santini M, Loiaconi V, Tocco MP, Mele F, Pandozi C. Feasibility and efficacy of minimally invasive stand-alone surgical ablation of atrial fibrillation. A single-center experience. *J Interv Card Electrophysiol* 2012.

[12] Mehall JR, Kohut RM,Jr, Schneeberger EW, Taketani T, Merrill WH, Wolf RK. Intraoperative epicardial electrophysiologic mapping and isolation of autonomic ganglionic plexi. *Ann Thorac Surg* 2007;83:538-41.

[13] Fuster V, Ryden LE, Cannom DS, Crijns HJ, Curtis AB, Ellenbogen KA, et al. ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation--executive summary. *J Am Coll Cardiol* 2006;48:854-906.

[14] Kasirajan V, Spradlin EA, Mormando TE, Medina AE, Ovadia P, Schwartzman DS, Gaines TE, Mumtaz MA, Downing SW, Ellenbogen KA. Minimally invasive surgery using bipolar radiofrequency energy is effective treatment for refractory atrial fibrillation. *Ann Thorac Surg* 2012;93:1456-61.

[15] Weimar T, Vosseler M, Czesla M, Boscheinen M, Hemmer WB, Doll KN. Approaching a paradigm shift: Endoscopic ablation of lone atrial fibrillation on the beating heart. *Ann Thorac Surg* 2012;94: 1886-92.

[16] Haissaguerre M, Jais P, Shah DC, Takahashi A, Hocini M, Quiniou G, Garrigue S, Le Mouroux A, Le Metayer P, Clementy J. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. *N Engl J Med* 1998;339:659-66.

[17] Klinkenberg TJ, Ahmed S, Ten Hagen A, Wiesfeld AC, Tan ES, Zijlstra F, Van Gelder IC. Feasibility and outcome of epicardial pulmonary vein isolation for lone atrial fibrillation using minimal invasive surgery and high intensity focused ultrasound. *Europace* 2009;11:1624-31.

[18] Krul SP, Driessen AH, van Boven WJ, Linnenbank AC, Geuzebroek GS, Jackman WM, Wilde AA, de Bakker JM, de Groot JR. 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. *Circ Arrhythm Electrophysiol* 2011;4: 262-70.

[19] Krul SP, Driessen AH, Zwinderman AH, van Boven WJ, Wilde AA, de Bakker JM, de Groot JR. Navigating the mini-maze: Systematic review of the first results and progress of minimally-invasive surgery in the treatment of atrial fibrillation. *Int J Cardiol* 2011.

[20] Cox JL, Ad N, Palazzo T. Impact of the maze procedure on the stroke rate in patients with atrial fibrillation. *J Thorac Cardiovasc Surg* 1999;118:833-40.

[21] Dunning J, Nagendran M, Alfieri OR, Elia S, Kappetein AP, Lockowandt U, Sarris GE, Kohl PH. Guideline for the surgical treatment of atrial fibrillation 2013;doi: 10.1093/ejcts/ezt413.

[22] Oh S, Zhang Y, Bibevski S, Marrouche NF, Natale A, Mazgalev TN. Vagal denervation and atrial fibrillation inducibility: Epicardial fat pad ablation does not have long-term effects. *Heart Rhythm* 2006; 3:701-8.

[23] Doll N, Pritzwald-Stegmann P, Czesla M, Kempfert J, Stenzel MA, Borger MA, Mohr FW. Ablation of ganglionic plexi during combined surgery for atrial fibrillation. *Ann Thorac Surg* 2008;86:1659-63.