



Epicardial and endocardial electrophysiological guided thoracoscopic surgery for atrial fibrillation: A multidisciplinary approach of atrial fibrillation ablation in challenging patients[☆]



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ABSTRACT

Introduction: Patients with atrial fibrillation (AF) with enlarged atria or previous pulmonary vein isolation (PVI) are challenging patients for catheter ablation. Thoracoscopic surgery is an effective treatment for these patients but comes at the cost of an increase in adverse events. Recently, electrophysiological (EP) guided approaches to thoracoscopic surgery have been described which consist of EP guidance by measurement of conduction block across ablation lines. In this study we describe the efficacy and safety of EP-guided thoracoscopic surgery for AF in patients with enlarged atria and/or prior failed catheter ablation.

Methods & results: A total of 72 patients were included. Two different approaches to EP-guided thoracoscopic surgery were implemented: epicardial or endocardial EP-guidance at the time of surgery. Residual intraoperative conduction requiring additional ablation was detected with epicardial or endocardial mapping techniques in 50% and 11%, respectively. Additional epicardial or endocardial ablation was performed until bidirectional block was confirmed. Follow-up consisted of an ECG and a 24 h Holter at 3, 6 and 12 months after the procedure. A total of 57 patients (79%) had freedom of AF and were off anti-arrhythmic drugs at one year follow-up (30 paroxysmal (83%), 27 persistent AF (75%)). Adverse events occurred in 13 patients (6 major). None of our patients died and all events were reversible.

Conclusion: EP-guidance of thoracoscopic surgery can be safely performed both epicardially and endocardially and is associated with a high rate of long-term maintenance of sinus rhythm in patients with enlarged atria and/or a previously failed ablation.

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1. Introduction

Atrial fibrillation (AF) is a growing problem in Western society and associated with a substantial healthcare expenditure [1]. Treatment of AF is difficult in patients who remain symptomatic despite anti-arrhythmic therapy, among others hampered by side effects of anti-arrhythmic drugs (AAD) and an incomplete pathophysiological understanding of the disease.

Catheter-based pulmonary vein antrum isolation (PVAI) [2] is most effective in patients with paroxysmal AF [3,4] and normally sized left

atria. In patients with more advanced disease multiple catheter ablation procedures or extensive ablation within the left atrium and of other triggers of AF may be needed to achieve an acceptable success rate [5]. Thoracoscopic pulmonary vein isolation (PVI) is an effective treatment for AF [6–8], but is more invasive than catheter ablation, and has a success rate of 69% in an unselected population [7]. Recently, a randomized multicenter study comparing catheter ablation and thoracoscopic surgery, showed superiority of the surgical approach (65.6% vs. 36.5% arrhythmia freedom at one year) in challenging patients with remodelled atria or prior failed ablation at the cost of an increase in adverse events [9].

Electrophysiological (EP) guided approaches applied during thoracoscopic PVI use catheter-derived EP endpoints to improve the outcome of surgery [10,11]. Electrophysiologists with experience in AF ablation can assess bidirectional conduction block across ablation lines with EP techniques (epicardially [10] or endocardially [11]). The collaboration between surgeon and EP in assessment of acute conduction block in one session possibly increases the single-procedure success

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rate of thoracoscopic surgery [12], without increasing of the adverse events. In this study we investigate the single procedure efficacy and safety of EP-guidance, using two different groups with either an epicardial or endocardial guidance of thoracoscopic surgery for AF in selected patients with remodelled atria or prior failed catheter ablation. This analysis was designed as an exploration of the value of EP-guidance during two different EP-guided thoracoscopic surgery approaches in challenging patients. In both approaches, an electrophysiologist contributes actively in the surgical procedure.

2. Methods

2.1. Patient population

Two centres participated in this study, the Academic Medical Center (AMC) in Amsterdam and the Maastricht University Medical Center (MUMC), Maastricht. Data were prospectively collected from consecutive patients with one year follow-up who underwent EP-guided thoracoscopic surgery for AF, all these patients had an indication for surgical ablation of AF according to the latest guidelines [5,13]. Inclusion of patients in this analysis was based on pre-procedural predictors of recurrence that identified patients that were considered less amenable to PVI and an earlier randomized study to warrant a historical comparison [9,14]. Inclusion criteria were; 1) a left atrial diameter of 40–44 mm and hypertension 2) left atrial diameter of ≥ 45 mm or 3) previous failed PVI. Patients with incomplete follow-up, defined as absence of 6 or 12 months outpatient follow-up, or without an adequate pre-procedural echocardiogram to assess left atrial diameter were excluded [9]. Definitions, clinical follow-up, classification of outcome and reporting of the results are according to the Heart Rhythm Society/European Heart Rhythm Association/European Cardiac Arrhythmia Society (HRS/EHRA/ECAS) consensus statement on catheter and surgical ablation [5].

2.2. Thoracoscopic surgery

Thoracoscopic surgery was employed in both centres, the different surgical procedures and mapping protocols have been described earlier in detail [10,11]. Surgery was performed under general anaesthesia on the beating heart. Ganglionic plexus (GP) were located anatomically and functional testing was performed with high frequency stimulation. GPs were subsequently ablated in the majority of patients until no vagal response could be elicited. Bilateral thoracoscopic PVI was performed with a radiofrequency bipolar clamp (AtriCure Isolator Transpolar Clamp, AtriCure Inc.). In patients with persistent AF or with induction of AF after the thoracoscopic PVI, additional left atrial lesions were created with a radiofrequency pen (AtriCure Isolator Bipolar Linear Pen and AtriCure Coolrail). In the epicardial EP-guided procedures these lines consisted of the Dallas lesion set [15], a superior and trigone line and an inferior line in the first 24 patients. In the endocardial EP-guided procedures a left box lesion set was created using a stepwise approach as described in Pison et al. [11], consisting of a superior line and inferior line, additionally right atrial lines were created (superior cava line, inferior cava line and intercaval lines) in patients with an enlarged right atrium and a left isthmus line in patients with a perimitral flutter. The left atrial appendage (LAA) was clipped using an endoscopic stapling device (Endo GIA stapler, Tyco Healthcare Group), according to surgeon preference.

2.3. Electrophysiological study

In the epicardial EP-guided approach PV entry and exit block was tested completely epicardially with custom-made electrodes and a diagnostic decapolar EP catheter (Radia XT, Bard) as described in De Groot et al. [16]. If no entry or exit block could be confirmed additional ablation with the bipolar clamp was applied until isolation was achieved. Additional ablation lines were tested epicardially and additional touch-up ablations were delivered epicardially with radiofrequency ablation pen (AtriCure Isolator Bipolar Linear Pen) until bidirectional block was achieved. All measurements were performed and analysed by an electrophysiologist using a dedicated EP-workstation (Bard Labssystem PRO 2.4A, Bard) [16]. For the endocardially EP-guided approach patients were heparinised after the thoracoscopic lesion set was applied and a His bundle and a coronary sinus catheter were introduced through a femoral venous approach. After transseptal puncture, PVs were mapped and isolation was assessed endocardially with a circular mapping catheter (Lasso, Biosense Webster). If PVs were not isolated, endocardial touch-up ablations were delivered with a 3.5-mm-tip catheter (ThermoCool, Biosense Webster). The epicardial lesions were subsequently tested endocardially for conduction block, with endocardial completion of the mitral isthmus line and touch-up of the epicardial lesion set in the absence of bidirectional conduction block. In patients with a history of typical cavotricuspid dependent atrial flutter an additional right atrial isthmus line was created endocardially. No ablation of complex fractionated atrial electrograms was performed.

2.4. Follow-up

After the procedure, patients were reinstated on their pre-procedural medication, including AAD. The first three months after the procedure were blanked for the determination of absence of AF. Patients were followed at the outpatient clinic with ECGs and a 24 h Holter at 3, 6 and 12 months after the procedure according to the HRS/EHRA/ECAS expert

consensus statement [5]. AADs were discontinued starting from the first outpatient visit, 3 months after the procedure.

2.5. Efficacy

The primary endpoint was freedom of AF, atrial flutter or atrial tachycardia lasting longer than 30 s on any ECG or Holter monitor after the blanking period without the use of AAD after 12 months [5]. A secondary outcome was defined as freedom from AF, atrial flutter or atrial tachycardia with/without the use of AAD after 12 months [5].

2.6. Safety

All adverse events during the peri-procedural period (within 30 days after the procedure) were monitored. Major adverse events were adverse events resulting in permanent injury or death, requiring intervention for treatment or extending hospital admission for more than 48 h [5]. All non-major adverse events were classified as other adverse events.

2.7. Statistical analysis

Data are presented as mean \pm standard deviation for normally distributed continuous variables or median and range for non-normal distribution. Categorical variables are presented in numbers with percentages. Differences were determined with an independent Student *T*-test for normally distributed data or a Mann–Whitney *U* test for not-normally distributed data. A Chi-square Test or Fisher's Exact Test was used for categorical variables. A univariate analysis was performed using binary logistic regression for failure of treatment at one year follow-up. Postoperative AF-free curves were calculated using the Kaplan–Meier method and compared with the log-rank test. Statistical analyses were carried out using SPSS, version 19.0. A *p*-value of <0.05 was considered significant.

3. Results

3.1. Patient characteristics

Hundred-and-two patients underwent EP-guided surgery for AF (Amsterdam *n* = 50, Maastricht *n* = 52) between 2008 and 2011. Seventy-seven met the inclusion criteria for this analysis and had a previous failed catheter ablation, an enlarged left atrium of ≥ 45 mm or hypertension and an enlarged left atrium 40–44 mm. Five patients were excluded due to insufficient follow up data (*n* = 3) or pre-procedural echocardiogram (*n* = 2) that precluded quantification of the left atrial diameter. In the remaining 72 patients, 31 (43%) had a previous catheter ablation, 48 (67%) had a left atrial diameter of ≥ 45 mm and 9 (13%) had a left atrial size of 40–44 mm with hypertension. Mean age was 59 ± 8.7 years (range 38–78) and 57 patients were male (79%). Thirty-six patients had paroxysmal AF (50%), 32 persistent AF (44%) and 4 longstanding persistent AF (6%). Eighteen patients (25%) had one previous PVAI, 13 (18%) had two or more previous PVAI. These procedures consisted either of a PVAI (*n* = 20) or PVAI with additional left atrial lesions (*n* = 11). The results of patients with persistent and longstanding persistent AF are combined and reported as persistent AF. Patient characteristics are shown in Table 1.

3.2. Electrophysiological guided procedure

A total of 36 procedures with an epicardial EP-guided approach (Amsterdam) and 36 with an endocardial EP-guided approach (Maastricht) were performed. In all but one procedure (with complete PV isolation after previous catheter ablation) PVI was performed. Of the 22 patients with quantitative information available on the number of ablation in the epicardial EP-guided approach 11 (50%) patients achieved PV isolation after 3–14 initial ablations (median 6.5). Additional epicardial ablation was performed, guided by the epicardial EP measurements, until bidirectional block was attained. Four patients (11%) in the endocardial EP-guided approach needed endocardial touch-up after a total of 6 epicardial ablations. In 48 patients (67%) additional atrial lesions were created; left atrial lesions in all, and additional right atrial lesions in 13 (18%). In the epicardial EP-guided approach epicardial EP measurements revealed residual conduction across at least one additional ablation line in all patients, and further epicardial ablation was performed until bidirectional block was attained. In the endocardial EP-guided approach the left atrial lines needed additional

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