Clinical results in a single tertiary care center

Catheter ablation for atrial fibrillation in a real-world setting

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Summary

Introduction: Several prospective multi-center randomized trials have established the efficacy of catheter ablation in patients with atrial fibrillation (AF). The aim of this study was to assess the mid-term results after AF ablation in a real-world cohort in a single tertiary care center in Switzerland.
Methods: This prospective registry comprised all patients with paroxysmal or persistent AF undergoing a catheter ablation procedure at the University Heart Center Zurich between June 2009 and April 2013 with a clinical follow-up including symptom assessment and long-term ECG monitoring for at least 24 hours.
Results: A total of 275 consecutive ablation procedures were performed in 201 patients (mean age 62 ± 9 years, 75% men). Patients had paroxysmal AF in 62% and persistent in 38%. Left ventricular ejection fraction as assessed by transthoracic echocardiogram was 58 ± 8%, the diameter of the left atrium averaged 44 ± 7 mm. Hypertension was present in 49%, coronary artery disease in 13% of patients. Pericardial tamponade occurred in 3% of the procedures. No other major complication requiring interventions or cardiac surgery was observed. After a follow-up period of 19.1 ± 11.8 months, 84% of the patients had a significant (>90%) reduction of their arrhythmia burden. Freedom from AF was observed in 73% of all patients.
Conclusion: In our cohort sinus rhythm was maintained in the majority of patients who underwent catheter ablation for paroxysmal or persistent AF after a mid-term follow-up with a very low periprocedural complication rate.

Key words: Atrial fibrillation; catheter ablation; outcome

Introduction

Atrial fibrillation (AF) is the most common rhythm disorder affecting about 5 million people in Europe with an important impact on morbidity and mortality [1]. Catheter ablation has become a well-established and widely performed treatment option for many patients with AF, especially after failed antiarrhythmic drug therapy. Several prospective multi-center randomized trials have shown the superiority of catheter ablation over antiarrhythmic drug therapy in patients with AF [2–4]. Although randomized clinical trials are the gold standard for evidence-based medicine, the patient population enrolled and randomized in such trials may not truly represent real-life patients. Thus, it was the aim of the present study to assess the mid- to long-term outcome of all consecutively enrolled patients with AF treated by catheter ablation in a real-world setting of a single tertiary care center in Switzerland.

Methods

All patients with symptomatic AF undergoing catheter ablation procedure at the University Heart Center Zurich between June 2009 and April 2013 were consecutively enrolled in our prospective registry. According to the guidelines of the ESC *(European Society of Cardiology)*, which were updated two times during the study period, the indication for catheter ablation evolved significantly. Before 2010 catheter ablation was an option only for patients with symptomatic AF after failure of one or more antiarrhythmic drug therapies, after 2012 ablation therapy became an accepted first-line treatment in selected patients with paroxysmal AF and structurally normal hearts. All patients gave informed consent prior to the procedure. Findings obtained at the follow-up visits were collected, which included symptom assessment and ECG monitoring for at least 24 hours after 3, 6, 12 and 24 months or until the time of the last follow-up. In 94% of all patients Holter ECGs were available for analysis during follow-up. In the remaining 6% of patients arrhythmia burden was assessed by ECG recordings and symptoms.
Clinical results were described and categorized into 3 groups. First patient group had lack of any remaining arrhythmia symptoms and absence of AF lasting >30 seconds on Holter ECG recordings. Second group had a significant reduction in arrhythmia burden defined as significant reduction of arrhythmia symptoms and >90% reduction in arrhythmia duration during Holter ECG recordings. Third group consisted of the remaining patients. Patients were categorized in these 3 groups independently of the use of antiarrhythmic drugs.

Catheter ablation technique used in all patients included wide-area circumferential point-by-point radiofrequency (RF) ablations around the ipsilateral pulmonary veins ostia with the procedural endpoint of electrical isolation of each pulmonary vein from the left atrium confirmed by a circular 20-polar mapping catheter placed within the pulmonary vein (fig. 1). Additional linear lesions (roof line, mitral isthmus line) or substrate modification (ablation of complex atrial fractionated electrograms in the left atrium) for persistent AF were performed at the discretion of the operator. In most cases RF energy was delivered for lesion creation, in few cases alternative energy sources such as cryoenergy (n = 6) or laser light (n = 2) were used [5, 8–10, 67]. In 30 (11%) out of 267 RF ablation procedures a novel ablation catheter was used, which is capable to measure tissue contact force and to determine orientation of the catheter tip in real-time. The catheters were manipulated and steered manually in all patients, except for 2 patients, in whom remote robotic navigation by Amigo system (Catheter Robotics, Budd Lake, NJ, USA) was applied [11].

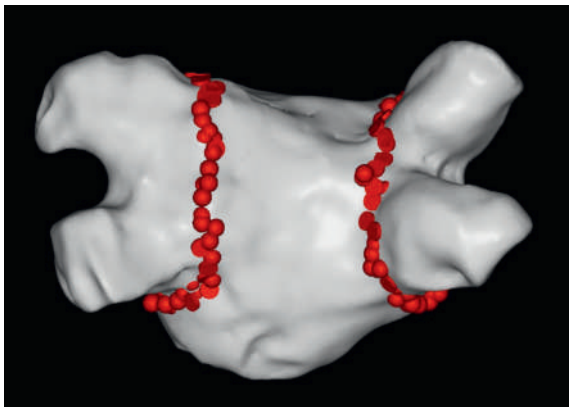

Figure 1: Three-dimensional electroanatomical map of the left atrium and the pulmonary vein ostia in a posterior projection with circumferential ablation lesions (red points) around ipsilateral pulmonary veins. From: Haegeli LM, Calkins H. Catheter ablation of atrial fibrillation: An update. Eur Heart J. 2014;35:2454–9, reprinted with permission.

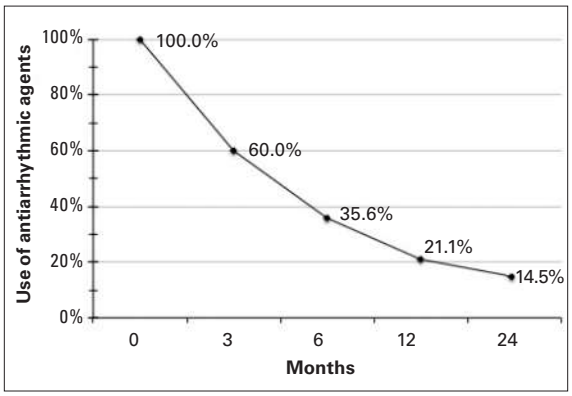

Figure 2: After catheter ablation, the use of antiarrhythmic drugs decreased continuously with only 15% still taking antiarrhythmic agents after 24 months.

All patients underwent cardiac imaging either by magnetic resonance (MR) or computerized tomography (CT) of the pulmonary vein anatomy prior to the procedure to identify anatomical variants (i.e., common left ostium of upper and lower pulmonary vein or third right-sided pulmonary vein). For mapping and ablation in the left atrium, a three-dimensional electroanatomical mapping system CARTO XP or CARTO 3 system (Biosense Webster, Diamond Bar, CA, USA) was used, which also allowed for the integration of preacquired MR or CT images [12].

Results

Patient characteristics: A total of 275 consecutive ablation procedures were performed in 201 patients. 137 patients (68%) underwent a single ablation procedure and 64 patients (32%) repeated procedures. In 55 patients one, and in only 9 patients two redo procedures were performed. The mean number of ablation procedures per patient was 1.37. The mean age of the patients was 62 ± 9 years, 150 were men (75%) and 51 women (25%). At the time of the procedure, patients had paroxysmal AF in 62% and persistent AF in 38% (table 1). 7 patients had long-standing (>1 year) persistent AF. The mean time between detection of AF and ablation procedure was 6.1 ± 4.5 years. Most patients had a structurally normal heart with preserved systolic left ventricular function on echocardiography (EF 58.8 ± 7.9%) and mildly enlarged atria (44 ± 7 mm). However, 23 patients had an impaired systolic left ventricular function on echocardiography (EF <50%). The mean EF was 42.4 ± 6.7% in this subgroup of patients. 35 patients (13%) had coronary artery disease and 10 patients (4%) a history of clinical manifest heart failure. 139 patients were taking oral anticoagulation (phenprocoumon) at the time of referral to ablation. None of the patients enrolled during the period of the study were taking any of the novel oral anticoagulants. 61% of all patients were taking specific antiarrhythmic drugs at the time of ablation procedure. Amiodarone was the most frequently used antiarrhythmic agent at the time of ablation procedure (table 1).

Procedural complications: Pericardial tamponade occurred in 8 patients (3%). All patients with pericardial tamponade could be successfully treated by percutaneous puncture and drainage without the need for surgical intervention. Furthermore, hemodynamically stable pericardial effusion, not requiring drainage, was

Table 1

Demographics		
Number of ablations	275	
Number of patients	201	
Ablations per patient	1.37	
Age (years)	62±9.09	
Male (%)	75	
Left ventricular ejection fraction (EF)	58±8.06	
Left atrium diameter (mm)	44±6.84	
Comorbidities		
Hypertension	134	49%
Coronary artery disease	35	13%
Diabetes mellitus	23	8%
TIA/CVA	28	10%
Heart failure	10	4%
Type of AF		
Paroxysmal AF	125	62%
Persistent AF	76	38%
CHA_2DS_2-VASc-Score		
Patients with 0 points	70	25%
Patients with 1 point	63	23%
Patients with 2 points	60	22%
Patients with 3 points	46	17%
Patients with 4 points	25	9%
Patients with 5 points	10	4%
Patients with 6 points	1	0.4%
Antiarrhythmic drugs before ablation		
No antiarrhythmic drugs	107	39%
With antiarrhythmic drugs	168	61%
Amiodarone	67	24%
Dronedarone	48	17%
Sotalol	3	1%
Flecainide	34	12%
Propafenone	14	5%
Digoxin	9	3%

Table 2

2-Year Results of Patients with Paroxysmal and Persistent AF		
Paroxysmal AF before ablation	125	
2-year follow-up available	54	100%
SR	38	70.4%
Paroxysmal AF	15	27.8%
Persistent AF	1	1.8%
Permanent AF	0	0%
Persistent AF before ablation	76	
2-year follow-up available	22	100%
SR	14	63.6%
Paroxysmal AF	5	22.7%
Persistent AF	2	9.1%
Permanent AF	1	4.6%

seen in 2 patients (0.7%) and an aneurysma spurium of the femoral artery in 7 patients (2.5%). No other major complication requiring interventions or surgery was observed. Furthermore, no post-procedural complications (i.e., transient ischemic attack, stroke or pulmonary vein stenosis) were documented.

Long-term results: After a mean follow-up of 19.1 ± 11.8 months, 84% of patients had a significant (>90%) reduction of their arrhythmia burden. Freedom from any AF and atrial arrhythmias were observed in 73% of all patients. We performed a subgroup analysis differentiating patients with paroxysmal from persistent AF and included only those who had a follow-up of 24 months or more. 70% of patients with paroxysmal AF were free from any AF and atrial arrhythmias 24 months after ablation procedure compared to 64% of patients with persistent AF (table 2).

At the time of procedure, 39% of patients were off specific antiarrhythmic agents. These patients discontinued already drug regimen due to failure or were referred for first-line ablation procedure. The remaining 61% of patients, who were on antiarrhythmic drug therapy, were advised to continue with the pre-procedural antiarrhythmic drug regimen for at least 3 months after the procedure in order to prevent episodes of AF during the blanking period. If patients were in SR thereafter, antiarrhythmic agents were discontinued. After ablation the use of antiarrhythmic drugs decreased continuously with only 40 patients (15%) still taking antiarrhythmic agents after 24 months (fig. 2). Among them, only 14 patients (5.3%) are still having AF documented.

64 patients underwent a redo ablation for arrhythmia recurrence. In the vast majority of the patients reconnection of one or more pulmonary veins was the cause of recurrent AF. In these cases re-isolation of the pulmonary veins was performed. In only 8 patients we identified non-pulmonary vein foci or left atrial flutter circuits, which were mostly highly symptomatic and the initiating cause of AF recurrence.

Discussion

Our study shows that 73% of patients who underwent catheter ablation for paroxysmal or persistent AF in a real-world setting were completely free of any AF or atrial arrhythmias nearly two years after the procedure. Moreover, an additional 11% of patients experienced a significant (>90%) reduction of the arrhythmia burden. Major complications occurred in 3% of patients, however, there were no residual sequelae. The subgroup analysis of patients who completed the full post-procedural follow-up of at least 24 months de-

monstrated a success rate of 70% for patients with paroxysmal AF and 64% for patients with persistent AF.

Selection of patient (i.e., paroxysmal versus persistent AF), technique of ablation and differences of reporting protocols determine the ablation results. In general, ablation results are attenuated, if Holter recordings are intensified in duration and frequency, as more episodes of silent AF are detected. Therefore, definitions for success are heterogeneous. For the purpose of clinical trial an international expert consensus document on AF ablation proposes that success is best described as freedom from any asymptomatic and symptomatic atrial arrhythmia lasting [3] 30 seconds at one year after AF ablation [2]. However, from a clinical perspective, a significant reduction of symptomatic episodes of AF may be considered as a successful endpoint. Further, a post-procedural blanking period lasting at least 3 months is recommended, in which episodes of atrial fibrillation or flutter are due to transient inflammation from the ablation lesions and are not representing failure of the ablation.

63 AF ablation trials were included in a meta-analysis which demonstrated success rate after one or more ablation procedures and *off* antiarrhythmic drug therapy of 71%, and if still *on* antiarrhythmic drugs of 77% [13]. In comparison, successful rhythm control by antiarrhythmic drugs alone was modest with a rate of 52%. More than 12 prospective, randomized studies showed superiority of catheter ablation over drug therapy alone for sinus rhythm maintenance in AF patients [14–20]. However, most of these trials enrolled predominantly patients with paroxysmal AF and having failed a first attempt with antiarrhythmic drugs. A meta-analysis of 4 of these trials demonstrated that 76% of patients were in sinus rhythm after ablation versus 19% of patients who were randomized to drug treatment [21]. The MANTRA-PAF (Medical Antiarrhythmic Treatment or Radiofrequency Ablation in Paroxysmal Atrial Fibrillation) trial compared the results of 294 patients randomized either to first-line catheter ablation or to antiarrhythmic drug therapy. After 2 years significantly more patients in the interventional arm were free from any AF (85 vs 71%) and symptomatic AF (93 vs 84%) [19]. Quality of life was also significantly improved in the interventional arm. In the RAAFT-2 (Radiofrequency Ablation vs Antiarrhythmic Drugs as First-Line Treatment of Paroxysmal Atrial Fibrillation) trial the incidence of AF was significantly decreased after ablation compared to pharmacological treatment after 2 years among 127 treatment-naïve patients with paroxysmal AF [20, 2, 22]. Recently, a large observational trial demonstrated long-term freedom from atrial arrhythmia in 47% of patients 4.8 years after last ablation procedure [23]. Our results compare well with these randomized trials, with 73% of patients being free from AF and 84% having a significant reduction of arrhythmia burden – especially as 38% of our enrolled patients had already persistent AF, a patient population which is less well represented in the large randomized ablation trials.

Catheter ablation of AF is a challenging and complex intervention, which is associated with a risk of complications. In 2005, an international survey reported a 6% incidence of major complications (tamponade, stroke, pulmonary vein stenosis or death) [24]. An update of this survey was recently published and reported a complication rate which has decreased to 4.5% [25]. Another survey of AF ablation with data derived from 162 centers provided detailed information on 32 intra- or postprocedural deaths out of 32 569 patients (0.1%) [26]. Cause of death was tamponade in 8 patients (25% of deaths), cerebrovascular embolism in 5 (16%), atrio-esophageal fistula in 5 (16%), and pneumonia in 2 (6%). In a recent systematic review analyzing data from 192 studies the periprocedural complication rate was 2.9%, while the rate of tamponade was only 0.9%. However, in the majority of these trials major complications were not defined prospectively. Furthermore, the patients age in this recent review was 57 years and therefore lower compared to our elderly patient population with an age of 62 years [27]. In our study no other major complications (i.e., stroke or other thromboembolic events) were recorded and the overall complication rate was lower than in the most recent survey from Cappato et al. [25]. Technological advancements and improvements of technique will further increase the safety of the procedure.

Catheter ablation is superior to pharmacological treatment in patients with paroxysmal AF and structurally normal hearts as demonstrated in multiple randomized trials. However, many important questions remain open. We need more data about the impact of AF ablation on survival and stroke beyond rhythm and symptom control. AF patients have an increased risk of stroke as well as an increased mortality, it is unclear whether successful rhythm control by ablation procedure results in reduction of stroke and mortality. According to the HRS consensus document the patient's CHA_2DS_2-VASc score (congestive heart failure, hypertension, age ≥75 (doubled), diabetes, stroke (doubled), vascular disease, age 65–75, and sex category (female)), rather than the presence of AF, determine the need for long-term anticoagulation after ablation [2]. The EAST study (Early Treatment of Atrial Fibrillation for Stroke Prevention Trial) is currently enrolling patient with recent onset of AF and aims to assess the impact of early

rhythm control on both stroke and mortality [28–30]. Similarly at our center, patients qualifying for anticoagulation according to the CHA_2DS_2-VASc score continue to receive anticoagulation therapy independent of the success of the ablation procedure [31–33].

In accordance to the recommendations of the ESC *(European Society of Cardiology)*, we perform catheter ablation in symptomatic patients with paroxysmal AF having failed with one antiarrhythmic drug (class I indication with a level of evidence A) [2–4]. First-line catheter ablation therapy is considered as reasonable in selected patients with paroxysmal AF and absence of structural heart disease (class IIa indication with a level of evidence B). The same level of indication is valid for patients with persistent AF and failure of drug treatment. Currently, the primary goal of AF ablation is control of symptoms and improvement of quality of life [28–30].

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Limitations

This retrospective single-center cohort study has the limitation of pooling patients with paroxysmal as well as persistent AF and does not aim to provide success rates for specific patient groups.

Conclusions

Catheter ablation is an effective and established therapy for patients with symptomatic AF. Our study demonstrates that sinus rhythm was maintained in most patients undergoing catheter ablation for paroxysmal or persistent AF after a mid-term follow-up with a low periprocedural complication rate. These results from a real-world setting compare well to those from several prospective randomized trials.

Disclosure statement
LM Haegeli has received consulting fees from Daiichi Sankyo; Lecture/consulting fees from Sanofi-Aventis, Medtronic, Biosense Webster, Sorin, Boehringer-Ingelheim, Novartis. AM Saguner has received conference support from Biosense Webster, Biotronik, Boston Scientific. J Steffel has received consultant and/or speaker fees from Amgen, AstraZeneca, Bayer HealthCare, Biotronik, Biosense Webster, Boehringer-Ingelheim, Boston Scientific, Bristol-Myers Squibb, Daiichi Sankyo, Cook Medical, Medtronic, Novartis, Pfizer, Roche, Sanofi-Aventis, Sorin and St. Jude Medical, and is co-director of CorXL LLC. He also reports grant support through his institution from Bayer HealthCare, Daiichi Sankyo, and St. Jude Medical. TF Lüscher has received educational and research grants to the institution from Bayer HealthCare, Boehringer-Ingelheim, Biotronik, Daiichi Sankyo, Medtronic and St. Jude Medical as well as honoraria from Boehringer-Ingelheim, Daiichi Sankyo.

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The full list of references is included in the online version of the article at www.cardiovascmed.ch.

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