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REVIEW

Catheter ablation of atrial fibrillation: current status, techniques, outcomes, and challenges

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Abstract

Atrial fibrillation (AF) is the most common human arrhythmia. Interventional treatment with catheter ablation is an established technique that is increasingly applied and has become one of the main treatment modalities in patients with AF. Ablation results in significant improvement of symptoms and the quality of life. There is as yet no clear evidence of any impact of the procedure on hard clinical endpoints, except in patients with heart failure, who seem to benefit significantly from ablation. The cornerstone of the procedure is the achievement of pulmonary vein isolation. Radiofrequency energy is the main applied energy source, but cryoballoon ablation has emerged as a safe and effective alternative to radiofrequency ablation. Additional ablation strategies and novel technical features have been proposed but without unequivocal proof of clinical benefit. The most promising of these seems to be substrate mapping of the left atrium with substrate modification in areas with low voltage as an adjunct to pulmonary vein isolation. Complication rates remain considerable despite accumulated experience and can be partly reduced by application of preventive measures.

Key words: atrial fibrillation, catheter ablation, complications

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INTRODUCTION

Atrial fibrillation (AF) is the most common human arrhythmia, causing significant morbidity and mortality, and its prevalence is expected to increase substantially due to the growing age of the population and the increase in the prevalence of risk factors predisposing to AF [1]. Interventional treatment with catheter ablation has emerged in the last two decades as a novel interventional technique for treatment of AF, with success rates that are substantially better than those of medical treatment, with regard to successful maintenance of sinus rhythm. Therefore, it is not surprising that the number of AF ablations performed throughout Europe has increased significantly; the method has become one of the pillars in the management of patients with AF and is recommended in the guidelines of the European Society of Cardiology for several clinical settings [2–4]. Despite this great success, significant uncertainties regarding AF ablation remain, and important challenges still lie ahead.

CHOICE OF THE APPROPRIATE TECHNIQUE FOR AF ABLATION AND ITS OUTCOME

Following the seminal recognition of the importance of ectopic beats originating from the pulmonary veins (PVs) for the initiation of AF [5], AF ablation techniques are mainly focused on electrical isolation of the PVs from the surrounding atrial myocardium. Indeed, achievement of complete electrical pulmonary vein isolation (PVI) is the cornerstone of successful AF ablation [6]. However, the choice of the appropriate ablation technique, in particular considering the underlying substrate of the individual patient, remains an issue.

Currently, the majority of AF ablation procedures are performed with the use of a radiofrequency (RF) energy source [6]. However, recent findings challenge the dominant role of RF ablation. In particular, cryoablation has emerged as a solid alternative that can be applied safely and with similar success rates compared with RF ablation, particularly in patients with paroxysmal AF, as recently demonstrated in the FIRE AND ICE

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trial [7]. The efficacy and safety of cryoballoon ablation in paroxysmal AF, including more challenging or specific clinical settings such as elderly patients, patients with heart failure, or patients undergoing first-line ablation, have been confirmed in several other studies [8–10]. Cryoablation may have the additional advantage of shorter procedure times [11, 12] and appears to be less operator-dependent and more reproducible compared with RF ablation [13]. This is an important aspect because success rates of RF ablation for AF are reported to be operator-dependent [14]. Further studies have demonstrated that the satisfactory results of cryoballoon ablation are independent of PV anatomy, which means that the technique can be applied in the presence of different anatomical variants of PV with similar results [15]. Complication rates of cryoablation are comparable with those of RF ablation procedures but with a different complication spectrum, as will be described in the following sections. Overall, cryoablation has emerged as a solid alternative to RF ablation for the treatment of paroxysmal AF and is expected to gain further significance in the future [16].

A whole variety of other circular multi-electrode systems have been proposed with the aim of easy, practical, and reliable achievement of PVI [17–22]. Despite promising initial results, these devices have not managed to become an established tool for AF ablation, partly because severe complications have been reported after the use of one of them [23].

Overall, the success rate of catheter ablation for AF, defined as maintenance of sinus rhythm and freedom from AF recurrences without antiarrhythmic drugs, is 60% to 65% at one year [6]. In longer follow-up, this rate is reduced [24] and has been reported to be as low as 40% at five years after a single procedure [25]. Apart from the maintenance of sinus rhythm, the procedure has a significant effect on symptoms, quality of life and functional capacity that are substantially improved after ablation [26–28]. Reassuringly, no significant differences in the outcome of the procedure have been reported across different geographies [29].

In patients with persistent AF, the outcome of AF ablation is poorer than in patients with paroxysmal AF [6], probably due to the underlying substrate, which is in many cases more complex and potentially reduces the success rates of techniques focusing solely on PVI. Thus, in a recent meta-analysis of studies on AF ablation in patients with persistent and long-standing persistent AF, efficacy of a single ablation procedure was reported to be as low as 43% [30]. To increase the success rates of ablation in these patients, several techniques have been proposed, such as targeting of complex fractionated electrograms, linear ablation in the left atrium, rotor mapping, and ablation or substrate modification [31]. However, the additive value of most of these strategies is either absent or not clear yet. In the STAR AF II trial, the placement of linear lesions and the ablation of complex fractionated electrograms did not result in better outcome compared with PVI alone in patients with persistent AF [32], and these results have been corroborated by subsequent publications [33, 34]. Rotor mapping and ablation is a safe technique [35], but evidence regarding the associated benefits is also contradictory [36, 37]. Substrate-based ablation with targeted ablation of low-voltage areas in the left atrium by placement of strategic lesions in addition to PVI seems to be promising, resulting in higher success rates compared with conventional strategies, as recently shown in a randomised comparison of these two approaches [38, 39]. Examples of assessment of the left atrial substrate and of a substrate-based ablation are shown in Figures 1 and 2.

Interestingly, cryoballoon ablation may also play a significant role in persistent AF, with several studies reporting favourable outcome and similar success rates to RF ablation [40–42]. Additional ablation lesions such as roof lesions or empirical left atrial appendage isolation that can be placed with the cryoballoon during the ablation procedure have been proposed in order to increase the success rate [43, 44]. However, the need for and the additive value of such techniques remain to be confirmed in larger studies, and persistent AF is reported as a significant factor associated with recurrences in the context of cryoablation [45].

Adenosine administration for demonstration of non-PV triggers and for unmasking dormant PV conduction has been proposed as a strategy to increase the success rate of the procedure [46]. This was confirmed in a recent meta-analysis indicating a potential benefit of adenosine administration for detection of dormant conduction [47]. Nevertheless, adenosine testing cannot be used as a substitute for the waiting period following successful PVI [48] but rather as an adjunct.

Technical developments constantly provide additional options for safe and successful performance of the procedure. The advent of three-dimensional mapping systems has completely transformed the clinical routine of electrophysiology. Particularly in the field of AF, these mapping systems have made the wide application of AF ablation possible [49]. Subsequent technical features such as measurement of the ablation catheter contact force and calculation of the force-time integral have recently been proposed as additional tools for the achievement of durable PVI [50–54]. Although some reports indicate a reduction of fluoroscopy time and radiation dose with the use of these features, their additive value [55], and in particular the additive benefit compared with conventional ablation techniques, still needs to be determined. Nevertheless, the complication rate does not seem to be positively affected [55]. High-density mapping of the left atrium has also recently been introduced [56–58] and has been reported to improve results of the procedure. The additive value of this novel mapping technology remains to be confirmed in larger studies.

SAFETY OF AF ABLATION

Given the elective character of the procedure, procedural safety as reflected by the associated complications is of para-

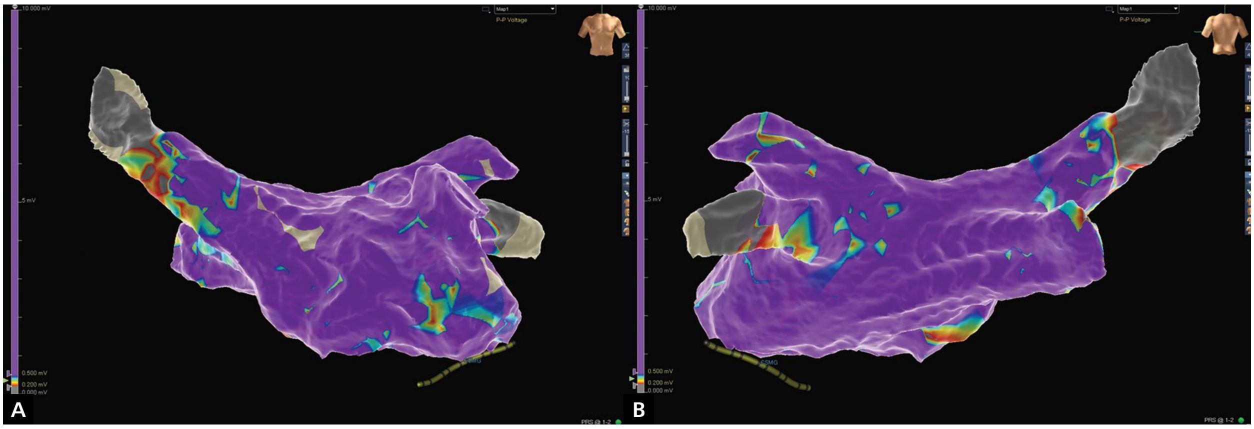

Figure 1. Voltage mapping of the left atrium during an ablation procedure for atrial fibrillation. Depicted are anteroposterior (**A**) and posteroanterior (**B**) views of the three-dimensional reconstruction of the left atrium. The purple colour indicates normal voltage in the left atrium with a threshold of 0.5 mV

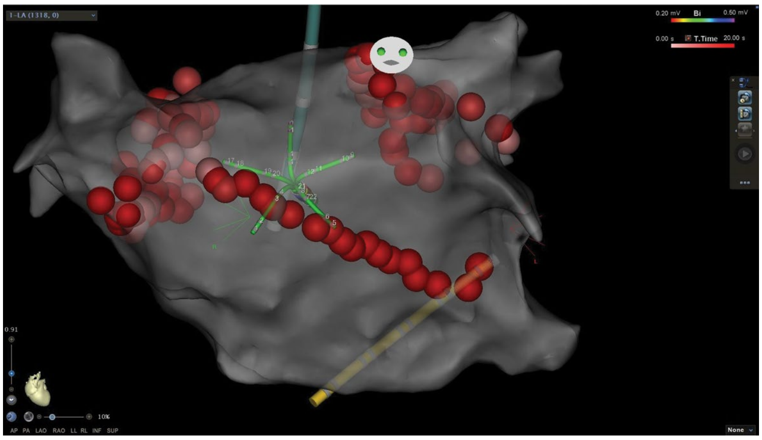

Figure 2. Substrate modification in an atrial fibrillation ablation procedure. Depicted is the three-dimensional reconstruction of the left atrium. The red dots show the ablation lesions. Circumferential ablation lesions are placed around the left and the right pulmonary veins. Additionally, a linear lesion is placed across the septum due to abnormal voltage in this area

mount importance. Complication rates of AF ablation seem to be influenced by patient characteristics. With a growing number of comorbidities, the complication risk increases [59–61]. Although temporal trends show a decrease in the complication rates over the last 15 years [59], they remain considerable, even in high-volume centres [62]. The most frequent, immediately threatening complication is cardiac tamponade, which occurs in approximately 0.9% to 1.3% of cases [6, 63]. The majority of cases with tamponade can be successfully managed with pericardiocentesis, but in a small minority, emergent surgical treatment may become necessary [64].

The second most important complication in terms of severity and risk of permanent sequelae consists of thromboembolic events that may lead to stroke or transient ischaemic attacks in approximately 0.4% of cases [6, 65]. These are observed predominantly directly after the procedure or within the first 24 h, and fortunately in most cases they have a relatively benign course [65].

A rare but very important complication, because of the life-threatening character and the poor outcome, is atrial-oesophageal fistula caused by thermal injury of the oesophagus due to the anatomic vicinity of the oesophagus to the posterior left atrial wall. This complication occurs with a time delay of one to four weeks after the procedure in approximately 1‰ of the cases [66], although earlier manifestations are possible [6]. Several techniques are applied to prevent the development of this catastrophic complication [67]. The preventive action that is most frequently applied in clinical practice is measurement of the intraluminal oesophageal temperature [68]. In the event of temperature rise, energy application is terminated in order to prevent oesophageal injury. The findings regarding the impact of these preventive measures on the outcome of the procedure are contradictory. Although some studies report that preventive premature termination of RF energy during PVI does not affect adversely the long-term outcome of the procedure [69, 70], other studies report an association of segments with PV reconnections in patients undergoing redo procedures and elevated oesophageal temperature during the index procedure [71]. It is important to know that the risk of atrial-oesophageal fistula still exists and that the above-mentioned preventive actions have limitations because the measured temperature does not necessarily reflect the true maximal temperature of the oesophagus [72], and more importantly, several cases have been reported to occur despite oesophageal temperature monitoring [66].

Cryoballoon ablation shows some differences from RF ablation with regard to complications. In particular, phrenic nerve palsy, caused by the vicinity of the phrenic nerve to the ablation field, is a major complication after cryoballoon ablation [41, 73–75]. Different measures for prevention of this complication are applied in clinical practice [76]. Among them, the most easily applied is palpation of diaphragmatic contraction at the time of pacing of the phrenic nerve during the procedure.

CRITICAL APPRAISAL OF THE PROCEDURE

Despite all successes of AF ablation in terms of effective maintenance of sinus rhythm and symptom relief, a major determinant of the value of the procedure in the overall context of management of AF patients will be the direct comparison with conservative treatment in terms of important clinical outcomes, such as mortality and hospitalisations. The publication of the results of the CABANA trial, the only large randomised comparison between catheter ablation and drug treatment with hard clinical endpoints, will be crucial for this assessment. Presentation of the main results of the trial showed no significant difference between ablation and drug treatment in the composite clinical primary endpoint in the intention-to-treat analysis [77]. The full results, once available, will provide further insight into the lessons that need to be learned from this very important trial.

A specific patient population that may derive significant benefit from the procedure in terms of hard clinical endpoints is the group of patients with heart failure. Previous studies have demonstrated a significant improvement of left ventricular function following catheter ablation for AF in patients with reduced left ventricular systolic function [78–80]. Recently, the CASTLE-AF trial showed a marked reduction of the primary endpoint that was a composite of death from any cause or hospitalisation for worsening heart failure in patients with AF and a reduced left ventricular ejection fraction of ≤ 35% [81] randomised to catheter ablation, compared with conservative treatment. Recurrences of the arrhythmia after the procedure seem to strongly predict major adverse outcomes during follow-up [82].

CONCLUSIONS

Atrial fibrillation ablation has developed into a main treatment modality for patients with AF, resulting in significant improvement of symptoms and the quality of life. Until now, there has been no evidence of any impact of the procedure on hard clinical endpoints, except in patients with heart failure. PVI is the cornerstone of the procedure, most widely achieved by RF ablation, whereas cryoballoon ablation has emerged as a safe and effective alternative to RF. Additional ablation strategies have been proposed, especially for persistent AF, but an unequivocal positive impact on the success rate of these procedures compared with PVI only remains to be demonstrated. Similarly, there are a variety of novel technical developments, but their additive value remains to be proven. Complication rates remain considerable even in high-volume centres, despite accumulated experience; preventive measures during the procedure may reduce the occurrence of some threatening adverse events.

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