Catheter ablation of atrial fibrillation – Current status and future directions

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Abstract

Atrial fibrillation (AF) is the most common arrhythmia experienced in clinical practice (approx. 1% predominance in adult population). To obtain sinus rhythm antiarrhythmic medications such as amiodarone have evolved as the most effective available and hence frequently used therapy. In contrast, its long-term efficacy turned out to be rather moderate and could cause serious side effects. Thus, catheter ablation seems to be a reasonable alternative in particular for patients with drug-refractory AF. However, the development in ablation strategies remains to be complex with often lengthy procedures. This study investigates whether a novel multielectrode catheter, delivering duty-cycled bipolar/unipolar RF energy, is feasible and safe. Therefore, 67 consecutive patients with paroxysmal/persistent AF have been analysed. PV isolation with the PVAC catheter was feasible and safe with shorter fluoroscopy/procedural results and good clinical efficacy at 6 months (stable sinus rhythm in 87%).

Abbreviations

AF	Atrial Fibrillation
AT	Atrial Tachycardia
CFAE	Complex Fractionated Electrograms
CS	Coronary Sinus
CT	Computed Tomography
ECG	Electrocardiogram
PV	Pulmonary Vein
PVAC	Pulmonary Vein Ablation Catheter
PVI	Pulmonary Vein Isolation
RV	Right Ventricle
RF	Radiofrequency
RR	Risk Reduction
RRR	Relative Risk Reduction

Introduction

In clinical practice atrial fibrillation (AF) can be considered as the most frequent type of arrhythmia. Approximately 1 % of all adults predominantly suffer from atrial fibrillation (1, 2).

According to cutting-edge guidelines antiarrhythmic drug therapy should be the first step regarding medical care for patients with either paroxysmal or persistent atrial fibrillation. Only about 50% of the recurrences at 1 year can be prevented by antiarrhythmic therapy (other than amiodarone). On the contrary amiodarone is seen as the most effective antiarrhythmic therapy in preventing recurrences. The efficacy is about 65% of treated patients with a one year recurrence rate of 35% (3, 4). Moreover, one-third of patients treated with amiodarone are most likely to stop their medications due to adverse effects. Consequently, it is indispensable to look for more effective therapies in order to prevent and treat atrial fibrillation such as catheter ablation.

The steady increase in ablation procedures on AF can be noticed around the world – success rates vary from 50% to 80%. This particular type of therapy has been accepted in such a fast way that the American

Heart Association / American College of Cardiology / European Society of Cardiology (AHA / ACC / ESC) has come up with guidelines on atrial fibrillation ablation considering it *as a second-line therapy in patients with AF who have failed or are intolerant to antiarrhythmic therapy.*

Randomized trials comparing radiofrequency ablation with antiarrhythmic medications in patients with atrial fibrillation

Until now there are six randomized and controlled studies (5-10) comparing radiofrequency ablation with antiarrhythmic medications in patients with atrial fibrillation. There was only one trial randomizing patients as first-line therapy. Patients verifying with either paroxysmal or persistent atrial fibrillation were involved in five of the studies (5, 7-10). Oral et al. enrolled patients with persistent AF (>6 months of AF) who showed recurrent AF within a week of a successful cardioversion or even had failed cardioversion. Patient that were included in two of the studies had been tested on two common antiarrhythmic medications (e. g. amiodarone). Three trials referred to the predominance of structural heart disease. According to these studies around two-third of patients suffered from structural heart disease, in particular hypertensive heart disease.

Ablation technique

In combination with linear ablation and ablation of complex fractionated electrograms (CFAE) in the left and right atria five of the six trials used a hybrid radiofrequency ablation approach. For each case pulmonary vein isolation (PVI) was included. The majority of these trials were carried out at high-volume centers, with expert operators performing the ablation (6-10). RF energy was used as the energy source within all the studies. All studies made use of nonfluoroscopic mapping guidance (e. g. CARTO™, Biosense-Webster, CA, USA). To determine successful ablation all studies were working with electrophysiological endpoints (demonstration of PVI). Further endpoints such as the completion of lesion set and presence of bidirectional block across the mitral isthmus or roof-lines were used by trials that worked with linear lesions (6-8, 10). A second ablation procedure during the blanking period was possible within four studies, varying from 2 to 3 months. Remarkable intersection from the antiarrhythmic drugs (AAD) group to the RF ablation arm could be found amongst three of the studies (6, 9,10). The reason why almost every trial used AAD between the first 2 or 3 months of post-radiofrequency ablation can be put down to the fact that this regimen would prevent episodes of AF. Therefore the left atrium was able to remodel in the mean time. Within this 3-month period the studies did not take recurrences at an early stage into account. The antiarrhytmic medication group had a combination of drugs such as sotalol, amiodarone, and class I agents to the patients who were taking part in this group.

Outcomes

In most cases, atrial fibrillation was observed with the help of ambulatory electrocardiogram (ECG) event monitors and transtelephonic monitors. The monitoring process of patients was performed at fixed intervals, and symptomatic episodes were documented where applicable. Success was seen in the maintenance of sinus rhythm with or without antiarrhythmic medications (RF ablation arm) after one year. The primary outcome among all studies was atrial fibrillation recurrences at one year. AF episodes between 30 seconds and 3 minutes were temporary and therefore not seen as recurrences (6-10). In comparison with the control group (antiarrhythmic medications) the treatment group (catheter-based ablation of AF) demonstrated a significantly lower rate of recurrent AF at one year according to a pooled analysis (see Figure 1) (11).

Within the medically treated group pooled risk of recurrent AF at one year was 73% and 24% in the RF group. The P value < 0.001 indicates that overall test results were highly significant.

New technologies – Pulmonary vein isolation by duty-cycled bipolar and unipolar radiofrequency energy with a multielectrode ablation catheter

Progress in the development of new ablation catheters has been made slightly. Catheter ablation in the traditional way is operated in a single-tip, point-by-point ablation process. Therefore highly qualified operator skills are necessary to get along with this technique and long lasting procedures that often take up to 4 hours. Furthermore, it is difficult to design contiguous transmural lesions with a single-point catheter. This is

Study name	Risk ratio	Lower limit	Upper limit	Z-Value	p-Value
	Statistics for each study				
Thai Study	0.333	0.112	0.995	-1.970	0.049
Natale et al.	0.204	0.078	0.531	-3.259	0.001
APAF Study	0.187	0.113	0.307	-6.606	0.000
CACAF Study	0.483	0.366	0.638	-5.142	0.000
Morady et al.	0.618	0.387	0.987	-2.016	0.044
	0.348	0.212	0.572	-4.173	0.000

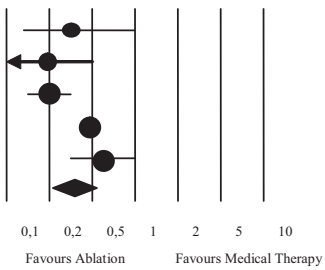

Figure 1. Forest plot from meta-analysis of randomized trials comparing catheter ablation with antiarrhythmic medications in patients with AF. Final analysis including data from five published trials.
RF = radiofrequency; AF = atrial fibrillation;RR = relative risk.

one reason for the necessity of specialized RF ablation catheters specifically designed for AF ablation.

Methods

Patients and procedure

Our study consisted of 67 consecutive patients with paroxysmal or persistent AF seen between October 2008 and August 2009. All patients had documented symptomatic AF refractory to one or more antiarrhythmic drugs within the past 6 months. Preprocedural screening consisted of transthoracic echocardiography and cardiac CT to exclude contraindications for ablation and definition of the PV anatomy. 3 patients had coronary heart disease, left atrial appendage thrombus, atrial enlargement greater than 53 mm, or mitral insufficiency higher than grade 2. The international normalized ratio of patients was ≤ 1.5 on the day of the procedure. Mapping with the pulmonary vein ablation catheter (PVAC; Ablation Frontiers, Inc., Carlsbad, CA, USA) was performed with an electrophysiologic recording system (Sensis XP, Siemens Healthcare, Erlangen, Germany and Labsystem, C.R. Bard, inc, Lowell, MA, USA) using filter settings of 30 to 500 kHz. No additional nonfluoroscopic guiding or steering systems were used. A 6Fr sheath was introduced through the right femoral vein under local anesthesia. A quadripolar catheter was introduced in the right ventricle (RV) for pacing purposes. Another 6Fr sheath was introduced through the left cubital vein under local anesthesia. A decapolar catheter was introduced in the coronary sinus (CS). A standard transseptal puncture was performed using a needle with a 12Fr nonsteerable sheath (Ablation Frontiers, Inc., Carlsbad, CA, USA). This sheath has a 9.5Fr or larger inner lumen diameter to accommodate the PVAC. A single heparin bolus of 5,000 international units was administered with additonal heparin bolus according to ACT. Postprocedural management included 6 hours of bedrest with a compression bandage and a hospitalization until next morning. Antiarrhythmic drugs were continued for the first 3 months, with all patients taking oral anticoagulants. After 3 months, anticoagulation was continued as guided by the CHADS2 score.

Catheter

The PVAC is a 9Fr, over-the-wire, circular, decapolar mapping and ablation catheter with a 25-mm-diameter array at the distal tip (Figure 2). The two control knobs of the handle make it possible that the bidirectional deflection of the shaft as well as the extension of the distal tip are able to form a spiral configuration (see Figure 3). Five bipolar recordings performed mapping through adjacent electrode pairs. By engaging the array against anatomic structures and rotating the catheter shaft the electrode array's diameter can be altered effectively. With the help of a 0.032-inch guidewire catheter placement and stability around the PVs is guaranteed. Meanwhile the guidewire is carefully selected and placed into position of different side-branches to modify the tissue. Thus, the electrode interfaces around the PV circumference.

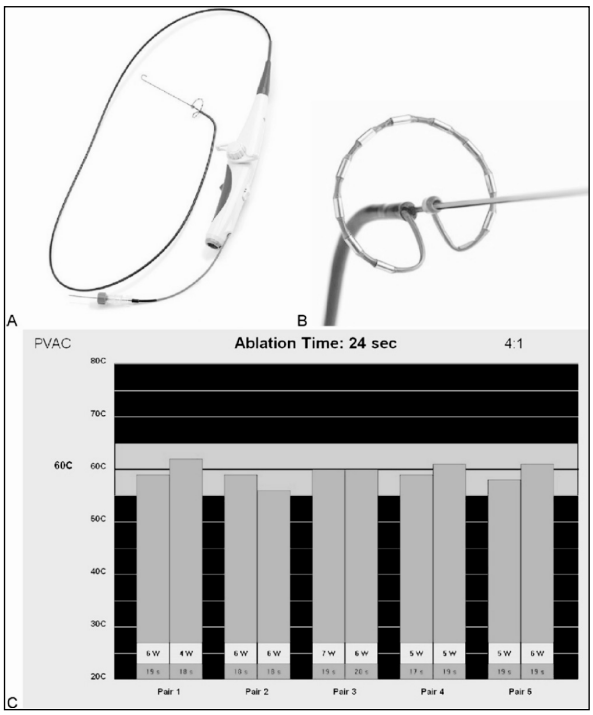

Figure 2. ***A:*** *Pulmonary vein ablation catheter (PVAC) loaded with a 0.032-inch guidewire and dual-control knobs on catheter handle.* ***B:*** *Distal array portion of the PVAC showing ten 3-mm electrodes with 3-mm spacing.* ***C:*** *Example of generator display during ablation with PVAC, with temperature and power for each electrode and number of seconds each electrode was within target temperature during the ablation.*

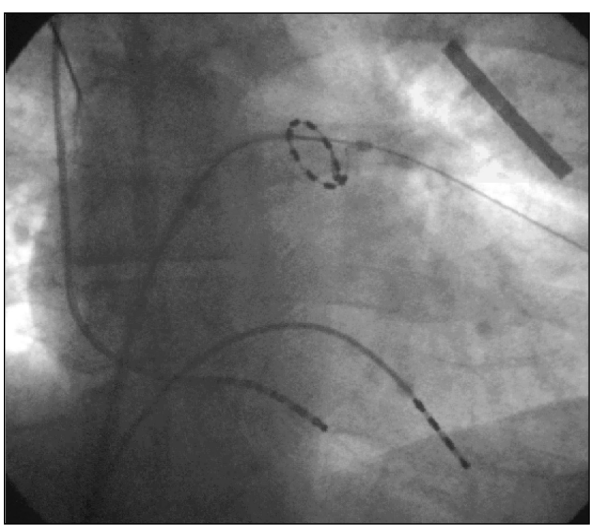

Figure 3. Fluoroscopic view of the pulmonary vein ablation catheter (PVAC) with electrode array extended in the left inferior pulmonary vein.

Generator

By the use of the GENius multichannel (Ablation Frontiers, Inc.) it is possible to deliver up to 12 electrodes independently with energy. In addition to that the energy can be transferred either unipolar or bipolar with a fixed duty-cycle.

A specific software algorithm controls the temperature of energy delivery throughout individual electrodes during RF application. This software algorithm modulates power in order to reach the user-defined target temperature, avoids overshoot and at the same time it limits power to a maximum of 8 W per electrode when using the PVAC in power settings like 4:1 or 10 W. The 4:1 ratio of bipolar/unipolar energy is the most common used power setting for PVAC in the PV antrum to accomplish transmurality in the PV antrum and lower damage beyond the atrial wall.

Ablation protocol

A 0.032-inch guidewire inside the PV was used to position the PVAC in the left atrium. Furthermore, the PVAC was advanced until it was wedged within the antrum proximal to the ostium. The ideal position was found on the basis of electrograms and was seeking to discover and ablate local potentials on every electrode that could be found for each application. Changes of the PVAC's position have been made in order to reach a optimal tissue apposition. These changes were possible due to rotation of the array, manipulation of the steerable sheath, furthermore due to changes of the PVAC shaft, counterclockwise opening or clockwise closing of the PVAC electrode array or extention of the spiral array tip into the PV. The delivery of energy was guaranteed throughout selected electrode pairs with local potentials and adjacent electrode pairs. Thus, bipolar energy was able to currently flow to the target electrode from both sides. In general, every application took around 60 seconds. Therefore, the target temperature of 60 °C was reached while using the generator which in turn was set up to adjust power for every single electrode in the selected pairs. The approach was done for all PVs over and over again, until all local potentials were abolished.

Follow-up

Check-ups with patients took part in our outpatient clinic at 3 and 6 months after the procedure. After following a blanking period of 3 months antiarrhythmic medications (drugs) were discontinued. In case of palpitations or any other symptoms that may have occurred after 3 months, patients were asked to consult a physician or to visit the hospital for ECG, Holter or event monitoring. Six months after the procedure patients undertook a four-day Holter monitoring off antiarrhythmic drugs. A definition of "being free from AF" was seen in the non-appearance of AF/flutter for at least 30 seconds. In addition to that, possible adverse events such as cerebrovascular accident, tamponade, hematoma, phrenic nerve lesions, or gastrointestinal and pulmonary events were documented.

Results

The characteristics of the patient group are given in Table 1. Among the 67 patients undergoing the ablation procedure, 23 were female. Mean patient age was 58 ± 10 years (range 34–75 years). Slight left atrial enlargement (45–53 mm) was seen in 21% of patients, and mild mitral insufficiency was seen in 34% of patients. The number of antiarrhythmic drugs used prior to ablation was 1 ± 1; only six patients were taking amiodarone at inclusion into the study. In this patient population, 15% had a history of DC cardioversion for AF. On CT, all patients had normal PV anatomy, except for 12 patients with a common left PV and for one patient with a right common PV. Mean dimensions of the separate PVs ranged from 16 to 17 mm, for the left common antra was 25 mm and the right common PV was 23 mm (Table 2).

Table 1: Patient characteristics

No. of patients	67
Age (years)	58 ± 10 (34-75)
Male/female	44 / 23
Left atrium, mild enlargement	21%
Mitral insufficiency grade 1-2	34%
Chemical/electrical cardioversion	15%
Antiarrhythmic drugs	1 ± 1
Amiodarone	6

Figure 4 shows examples of the PVAC potentials before (panel A) and after ablation inside the left inferior PV antrum (panels B). During RF application, ablation channels cannot be visualized because the duty-cycled RF energy creates noise that cannot be filtered. All the local potentials inside the antrum proximal to the ostium of all PVs were ablated according to protocol. Isolation was verified by positioning the PVAC distal to the lesion and inside the ostium to demonstrate absence of PV potentials.

Procedural results

In 67 patients, 255 PVs, including 12 left common PV and 1 right common PV, were targeted for ablation. The results of single procedure treatment are summarized in Table 3. The number of applications per vein was 6 ± 3 for the left superior PV, 4 ± 2 for the left inferior PV, 4 ± 2 for the right superior PV, and 4 ± 2 for the right inferior PV. Usually, when applications were first performed inside an upper antrum, the lower needed fewer applications and vice versa due to the electrode array overlapping previously applied lesions.

Table 2: Characteristics of pulmonary vein anatomy and ablation

	N	Size (mm)	RF applications	Range
Procedures	67	---	19 ± 5	10 - 33
Left superior PV	55	17 ± 3	6 ± 3	1 - 13
Left inferior PV	55	16 ± 3	4 ± 2	1 - 10
Left common PV	12 (18%)	25 ± 2	12 ± 4	6 - 20
Right superior PV	66	17 ± 3	4 ± 2	2 - 12
Right inferior PV	66	16 ± 3	4 ± 2	1 - 9
Right common PV	1 (1%)	23	7	7

PV = pulmonary vein; RF = radiofrequency

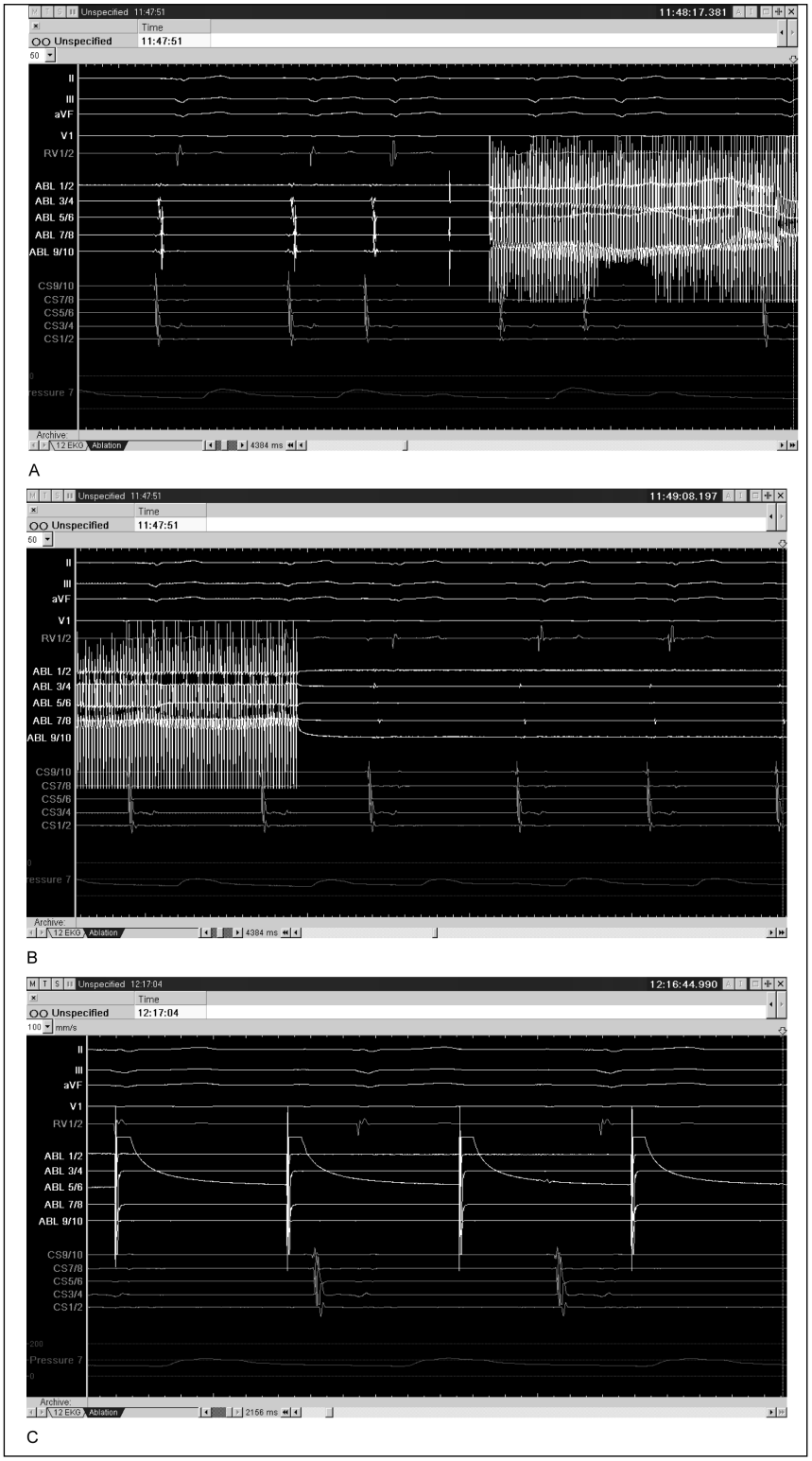

Figure 4. Pulmonary vein ablation catheter (PVAC) electrograms from left inferior pulmonary vein before ablation ***(A)*** *and left inferior pulmonary vein after ablation with PVAC* ***(B)*** *confirming isolation during PVAC pacing* ***(C)***.

Table 3: Procedural times, safety and efficacy

Procedural time	Total time (min) Fluoroscopy time (min)	85 ± 19 (53 - 145) 20 ± 7 (8 - 54)
Complications	Procedural Postprocedural	0/67 1/67 (1%)
Follow-up	Overall (month); median	5 (0-10)
AF/AT recurrence	Holter/ECG	7/52 (13%)

AF = atrial fibrillation; AT = atrial tachycardia

Table 4

Results	**Fluoroscopy Time**	**Procedural Time**	**Study**
1	44 ± 24 min	70 ± 21 min	Hocini et al. (14)
2	50 ± 17 min	156 ± 85 min	Oral et al. (6)
3	72 ± 17 min	216 ± 28 min	Cheema et al. (13)
4	72 ± 26 min	256 ± 72 min	Karch et al. (19)

In left common PV antra, the mean number of applications was about double that of a separate antrum (12 ± 4, range 6–20). The mean number of applications per patient was 19 ± 5 (range 10–33).

The PVAC itself was advanced as a mapping catheter to confirm the absence of ostial potentials or to perform an additional application if necessary. In 67 patients, all 255 targeted veins (100%) were completely isolated using the PVAC without the need for either a conventional catheter or three-dimensional mapping equipment. Total procedural time was 85 ± 19 minutes (range 53–145 minutes); fluoroscopy time was 20 ± 7 minutes (range 8–54 minutes; Table 3). In 9 patients, an additional right atrial isthmus ablation was performed. After ablation the PVAC catheter was visually inspected, and no char or thrombus was observed in any case. No procedure related complications were observed; 1 patient had an aneurysm of the femoral artery. All patients left the hospital in sinus rhythm the day after the procedure. Subsequent follow-up revealed no procedure related adverse events. Post procedural CT/MRI did not show evidence of PV stenosis (up to now data is available from 26 patients).

Freedom from AF

In total, the mean follow-up period lasted 5 months with a range 0-10 among 67 patients*. Results show that about 82% of the patients are on antiarrhythmic drugs for more than 3 months, 54% for more than 6 months. It was observed that 87% (45 of 52 patients) were free from AF according to Holter monitoring 6 months after ablation. Recurrences of AF were diagnosed in 13% (7 of 52 patients), either by the use of the ECG, event recorder, or Holter monitoring.

Discussion

Current consensus documents have found that PVI is necessary and therefore seen as the cornerstone in AF ablation (12). As a first result it can be pointed out that acute efficacy of PVAC equals or even exceeds the one of conventional-tip catheter for PV isolation. This corresponds with studies by Cheema et al. (13), Hocini et al. (14) and Verma et al. (15). The PVAC falls into the same category like balloon catheters delivering RF, ultrasound or cryoablation energies and therefore perfectly matches with novel antrum ablation techniques in general. According to a preclinical report there is evidence that the isolation in 83% of 18 targeted PVs was successful (16). In contrast, the use of ultrasound balloon for PV antrum ablation in 15 patients showed no indication for a successful isolation. Moreover, the right inferior PV was targeted in only one patient (Natale et al.) (17). While using the cryoablation balloon technique (Arctic Front, Montreal Quebec, Canada) van Belle et al. (18) demonstrated their approach. It was found that in 40% (24 of 57 patients) of the patients an additional single electrode catheter was necessary in order to complete isolation. High-intensity focused ultrasound balloon catheter (HIFU) was used by two studies. The results confirmed antral PV isolation in 57 of 67 patients and also in 41 out of 46 patients, focusing on 75% and 100% of PVs.

With a mean fluoroscopy time of 20 ± 7 min using the PVAC catheter, procedural time lasted 85 ± 19 min, in total, from femoral vein access to the complete

*Follow-up data is available of 52 patients.

withdrawal. The results shown in table 4 demonstrate the wide range of procedural and fluoroscopy times that have been recorded for complete PV isolation while using conventional single-tip catheters (19).

There was no evidence of short-term complications such as stroke problems, gastrointestinal complaints, PV stenosis, phrenic nerve damage in a series with 67 patients. The safety of conventional catheter ablation for AF has been surveyed on a worldwide basis. The report on this survey was released in 2005 and indicates major complications of 6% (20).

In summary it is feasable and safe to isolate PV by antrum ablation with a circular, multielectrode catheter (PVAC). Compared to common AF ablation techniques fluoroscopy and procedural times seem to be shorter and moreover there is no need for sophisticated mapping and steering modalities.

So far, there is no ideal definition for a successful intervention for the management of AF. The burden of AF may be cut down by antiarrhythmic and ablation therapies. Furthermore, both therapies may be able to change symptomatic episodes into asymptomatic episodes of AF (12). Despite this fact it remains questionable whether this finding is of clinical significance. Anyhow, overall results may possibly not show the truth as differences in the methods used to detect recurrence of AF were not considered but would have had an influencing impact. Many different factors have a strong impact on the efficacy of AF, for example: operator experience, volume of ablations, type of cases ablated etc. Moreover, the efficacy of AF can differ greatly within nonrandomized trial. The efficacy of a single procedure observed in paroxysmal AF varies from 38% to 78%. The average efficacy in most series was found at 60% or more. In persistent AF the efficacy showed differences from 22% to 45% with an average of 30% or less (3, 12). From an QOL perspective, asymptomatic or short episodes of symptomatic AF might be less important to the patients but in terms of preventing thromboembolic episodes it can be highly significant. Further investigation will be necessary to find out whether the abolition or notified reduction of AF will help to reduce stroke.

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