Efficacy and Safety of Catheter Ablation for Persistent or Permanent Atrial Fibrillation

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Introduction: Radiofrequency catheter ablation (RFCA) that targets pulmonary veins (PV) is an established treatment for paroxysmal atrial fibrillation (PAF). Recent studies have demonstrated that RFCA can eliminate PAF in over 90% of patients. However, the effectiveness for persistent or permanent AF has not been clarified.

Methods and Results: 27 patients (29%) had persistent or permanent AF. RFCA including PV antrum isolation (PVAI) was performed using a circular mapping catheter in the patients with persistent or permanent AF. Four patients (15%) underwent only PVAI. Thirteen patients (48%) underwent PVAI and left atrium roof and/or mitral isthmus linear ablation. Ten patients (37%) underwent PVAI and RFCA to an area with complex fractionated atrial electrograms. All patients were observed for over a year. After repeat ablation at mean follow-up of 16 ± 5 months, 23 patients (85%) had normal sinus rhythm and were free of symptomatic AF or atrial flutter. Three patients required antiarrhythmic drugs to maintain sinus rhythm during follow-up period. One patient had a transient phrenic nerve injury. Two patients were documented with sustained atrial tachycardia (AT). Mapping in 2 patients showed a macro reentry AT due to gaps in the ablation lines and further ablation was needed. No other complications including PV stenosis occurred.

Conclusions: The present study demonstrated that RFCA is an effective and feasible treatment for persistent or permanent AF.

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Key words: Catheter ablation, Atrium, Fibrillation, Arrhythmia, Cardiac function

Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia and is associated with significant morbidity and mortality in humans.1,2) Most AF is initiated by premature beats from the orifices of the pulmonary veins (PV) or from the myocardial sleeves inside the PV.3) Therefore, radiofrequency catheter ablation (RFCA) that targets PV can be an effective treatment for AF. Current RFCA strategies for AF consist of a standardized approach for PV isolation and/or encirclement with or without additional RFCA lines.3-9) However, because the pathogenesis of AF is...
multifactorial,10) a standardized RFCA approach may not be equally effective or efficient in all patients with AF. Recently, it has been suggested that AF also can be eliminated by targeting complex fractionated atrial electrograms (CFAEs) characterized by a short cycle length, fractionation, and/or continuous electric activity.11) In the present study, we evaluated whether RFCA procedures are also effective for persistent or permanent AF.

Methods

Study Subjects

The study population consisted of 27 consecutive patients (mean age, 61 ± 12 years) with symptomatic drug-refractory persistent or permanent AF who were referred for an electrophysiological study and RFCA. Patients who were recruited at our institution from January 2005 to January 2006, and had undergone a prior procedure for AF were excluded from this study. All patients were observed for over a year. AF was considered persistent when it was present for more than 7 days and when cardioversion was required to restore sinus rhythm. AF was considered permanent when it was present for more than 30 days and when cardioversion failed to convert sinus rhythm. In the present study, persistent and permanent AF were considered as chronic AF (CAF). The 27 CAF patients included 15 patients with persistent AF and 12 patients with permanent AF. Of the 27 patients, 2 patients had coronary artery disease, 3 had cardiomyopathy, and the remaining 22 patients had no structural heart disease. Echocardiography demonstrated a mean left ventricular amplitude decreased by >50% and/or 4-mm tip, deflectable quadripolar catheter (EP technologies, Navistar, Ablaze), at a target temperature of 50°C and a maximum output of 30 W for 30–60 s at each ostial site. If the activation sequence around the PV-LA junction was changed, the bipolar that showed the new earliest atrial potential was targeted. Three-dimensional images of the PVs were reconstructed by contrast-enhanced multi-detector computed tomography (MDCT) before RFCA. When AF was still present or inducible after complete PV isolation, RFCA of area with CFAEs was performed. A 3-dimensional depiction of the LA and PVs with an electroanatomical mapping system (CARTO, Biosense-Webster) was created before RFCA to detect the area with CFAEs. CFAE sites were tagged. At tagged sites, RF energy was applied until the maximum local electrogram amplitude decreased by >50% or to <0.1 mV. If AF converted to atrial tachycardia during RFCA to CFAE sites (Figure 1), AF was considered as eliminated and we converted them to sinus rhythm by external cardioversion. The endpoint of RFCA was the complete isolation of PV verified by circumferential PV mapping and no inducibility of AF. According to the study protocol, reinduction was attempted by pacing from high RA at the shortest cycle length with isoproterenol infusion, resulting in 1:1 atrial capture. AF was considered inducible if it lasted >5 minutes, and further mapping and RFCA were performed. If AF was still inducible and maintained after achievement of the procedural endpoint, transthoracic cardioversion was performed to restore sinus rhythm.

RFCA

All patients with CAF underwent PVAI. PVAI was performed as previously described12) in detail using double Lasso technique. Complete isolation of PV was considered to be bidirectional conduction block between the PV and LA based on both the inability to capture the LA during distal PV pacing and abolition of distal PV potentials. The first 4 patients underwent PVAI only. LA roof and/or mitral isthmus linear ablation were added for the other patients. RFCA to mitral isthmus was performed with a line between inferior portion of left inferior PV and lateral mitral valve annulus in the right anterior oblique position. RF energy was delivered with a temperature-controlled, 8-mm and/or 4-mm tip, deflectable quadripolar catheter (EP technologies, Navistar, Ablaze), at a target temperature of 50°C and a maximum output of 30 W for 30–60 s at each ostial site. If the activation sequence around the PV-LA junction was changed, the bipolar that showed the new earliest atrial potential was targeted. Three-dimensional images of the PVs were reconstructed by contrast-enhanced multi-detector computed tomography (MDCT) before RFCA. When AF was still present or inducible after complete PV isolation, RFCA of area with CFAEs was performed. A 3-dimensional depiction of the LA and PVs with an electroanatomical mapping system (CARTO, Biosense-Webster) was created before RFCA to detect the area with CFAEs. CFAE sites were tagged. At tagged sites, RF energy was applied until the maximum local electrogram amplitude decreased by >50% or to <0.1 mV. If AF converted to atrial tachycardia during RFCA to CFAE sites (Figure 1), AF was considered as eliminated and we converted them to sinus rhythm by external cardioversion. The endpoint of RFCA was the complete isolation of PV verified by circumferential PV mapping and no inducibility of AF. According to the study protocol, reinduction was attempted by pacing from high RA at the shortest cycle length with isoproterenol infusion, resulting in 1:1 atrial capture. AF was considered inducible if it lasted >5 minutes, and further mapping and RFCA were performed. If AF was still inducible and maintained after achievement of the procedural endpoint, transthoracic cardioversion was performed to restore sinus rhythm.
Figure 1  Ablation of CFAEs.
Case 1  65 M Permanent AF. (A) before RFCA. (B) after RFCA. (C) termination.
Follow-up
Warfarin was administered and continued for at least 3 months with an international normalized ratio level of approximately 2.0. Post-RFCA follow-up exams were performed at the same institution, initially at 1 week and subsequently at 1-month intervals. Clinical examination, 12-lead ECG, and 24-h Holter recordings were made every 3 months and when symptoms suggested recurrence of an arrhythmia. MDCT was performed at 6 months and 12 months after RFCA to assess stenosis of the PVs. A change in the PV diameter as measured by MDCT between before and 12 months after RFCA that showed a decrease in PV diameter of more than 50% was considered significant. In addition, echocardiography was performed to evaluate cardiac function after a period of sinus rhythm maintenance for same patients. Because early recurrence of AF may be transient, a blanking period of 8 weeks was used. Successful clinical outcome was defined as the absence of recurrent AF or atrial flutter (starting at 8 weeks of follow-up) without the use of antiarrhythmic drugs. The mean duration of follow-up was 16 ± 5 months after the last ablation procedure. Survival curves were estimated by the log–rank test. \( P < 0.05 \) was considered to indicate statistical significance.

Results
Lasso Mapping Catheter-Guided PV Isolation
PV isolation was performed in all 27 patients (107 targeted PVs mean 3.96 per patient), and all PVs were isolated successfully. Bidirectional conduction block between the PV and LA was confirmed by PV-LA dissociation in all PVs.

Clinical Outcome
The mean duration of follow-up was 16 ± 5 months (> 6 months) after the last RFCA procedure. Of 27 patients with CAF who underwent RFCA, PVAI alone was performed on 4 patients (15%). Three of these 4 patients (75%) were free from AF without antiarrhythmic drug therapy. The mean total procedure time for PVAI was 143 ± 33 min and the mean fluoroscopy time was 56 ± 12 min. Thirteen patients (48%) were treated with PVAI and LA roof and/or mitral isthmus linear ablation. Ten of 13 patients (77%) were free from AF without antiarrhythmic drug therapy, while the remaining 1 patient required antiarrhythmic drug treatment to maintain sinus rhythm. PVAI and LA roof and/or mitral isthmus linear ablation required a mean total procedure time of 204 ± 75 min and a mean fluoroscopy time of 78 ± 32 min. In 10 patients (37%) who underwent PVAI and RFCA to the area with CFAEs, AF was eliminated in 9 patients (90%). Seven of 10 patients (70%) were free from AF without antiarrhythmic drug therapy, while the remaining 2 patients required antiarrhythmic drug treatment to maintain sinus rhythm during the follow-up period (Figure 2). PVAI and RFCA to the area with CFAEs required a mean total procedure time of 245 ± 86 min and a mean fluoroscopy time of 90 ± 39 min.

![Figure 2](image-url)
There was no significant difference in the recurrence rate between the three groups of each methodology (Figure 3). Ablation to CFAEs eliminated AF at LA septum, crista terminalis, LA roof, RA appendage, and mitral isthmus.

After the initial RFCA procedure, a repeat RFCA was performed in 15 of the 27 patients (55%; mean sessions, 1.67 times) because of the recurrence of AF or atrial flutter. In summary, 23 of the 27 patients (85%) had normal sinus rhythm and were free of symptomatic AF or atrial flutter. Three patients required antiarrhythmic drugs to maintain sinus rhythm during follow-up period. There was no difference in the recurrence rate between persistent AF and permanent AF (Figure 3). The mean total procedure time was 198 ± 71 minutes and the mean total fluoroscopy time was 79 ± 34 minutes.

Four patients underwent echocardiography to evaluate cardiac function after a period of sinus rhythm maintenance. Cardiac function improved in all patients (Table 1).

**Complications**

One patient who underwent ablation at CFAEs developed transient phrenic nerve injury. Two patients were documented with sustained AT. Map-
ping in 2 patients showed a macro reentry AT due to gaps in the ablation lines and further ablation was needed. No PV stenoses were detected by MDCT after the RFCA procedure.

Discussion
Main Findings
The present study indicated that RFCA, including PVAI, of all PVs was effective in maintaining sinus rhythm in patients with drug-resistant persistent or permanent AF. At mean follow-up of 16 ± 5 months, 23 patients (85%) had normal sinus rhythm and were free from symptomatic AF or atrial flutter. Three patients required antiarrhythmic drugs to maintain sinus rhythm during the follow-up period. Conversion to sinus rhythm, and freedom from antiarrhythmic drugs significantly improved cardiac function. Transient phrenic nerve injury occurred in 1 patient after the RFCA procedure, but there were no other complications including PV stenosis during follow-up period. Thus, RFCA is an effective and safe treatment for persistent or permanent AF.

RFCA Strategy
In patients with CAF, the PVs are also the dominant trigger for initiating AF after electrical cardioversion.12) PVs may have an important role not only in the onset, but also the maintenance of AF.13) However, they do not always lead to AF. RFCA technique that targets only the PV ostium have had modest efficacy in CAF.3,4,16) Consistent with the multifactorial nature of AF,10) autonomic innervation of the LA, non-PV arrhythmogenicity, multiple reentrant wavelets, and anisotropic reentry leading to rotors were all implicated in the genesis of AF. Therefore, elimination of only PV input may not be sufficient in all patients with CAF. Although the significance of CFAEs are still unknown, it may be associated with the mechanism of AF maintenance. Animal studies demonstrated that rotors drive AF in the LA.17,18) The central core of these rotors may have high-frequency electric activity, whereas the periphery of the rotors may display complex electrograms because of wave break and fibrillatory conduction.19–21) CFAEs may also indicate the sites of wave collision, slow conduction, or pivot points for reentrant circuits,22) and may facilitate multiple wavelet reentry. It is also possible that CFAEs reflect underlying ganglionated plexi, providing another potential reason for these RFCA sites.23) We performed RFCA of area with CFAEs for the patients who did not respond to the electrical PV disconnection from the atrium. RFCA of area with CFAEs are effective for a greater part of these patients. It is suggested that RFCA to CFAEs could be the next option for the patients with CAF who did not respond to PVAI. In the present study, RFCA to CFAEs sites led to restoration to sinus rhythm and improvement of cardiac function. It has been demonstrated that restoration and maintenance of sinus rhythm by catheter ablation in patients with CAF without drugs improved cardiac function.24) Thus, the adaptation of RFCA can expand to persistent or permanent AF. Further clinical data will justify the indication of invasive RFCA for persistent or permanent AF.

Study limitation
There were a few limitations in this study. First, although the study reached some conclusions, only a relatively small number of patients were evaluated. Second, the clinical outcome of RFCA procedure to CAF was judged based on the symptoms of the patients, serial ECG recordings over a limited time, and 24-hour Holter data. Thus, the patients with asymptomatic AF recurrence might have been underestimated. Further studies are needed to answer these questions.

Conclusions
The present study demonstrated that RFCA is an effective and feasible treatment for persistent or permanent AF. RFCA to CFAEs could be the next option for the patients with CAF who did not respond to PVAI, resulting in improvement of cardiac function. These results suggest that RFCA is highly effective in patients with CAF.

References