

Original Article

Long-term clinical outcome and risk of catheter ablation in elderly with non-paroxysmal atrial fibrillation

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Received July 13, 2015; Accepted September 1, 2015; Epub September 15, 2015; Published September 30, 2015

Abstract: Background: Catheter ablation of atrial fibrillation (AF) became an effective therapy for patients with drug-refractory AF and Catheter ablation of Non-Paroxysmal AF for elderly remains a challenging task. The outcome of AF ablation in Elderly is not clear. Objective: The aim of the present study was to investigate the long-term outcomes of catheter ablation in patients with non-paroxysmal AF and the predictors of AF termination, and the clinical outcomes associated with termination and non-termination. Methods: A total of 95 non-paroxysmal AF patients who received a stepwise catheter ablation were enrolled. There were 46 patients (48.4%) suffering from recurrences (37 patients with AF and 9 patients with atrial flutter/atrial tachycardia) after single procedure during a median follow-up period of 25.6 months. AF termination by ablation was achieved in 73 of the 95 patients Results: The AF non-termination after procedure and CHA2DS2-VASc scores ≥ 3 were significant predictors of recurrences in the multivariable analysis. In AF termination group: for a CHA2DS2-VASc scores of 0, 1-2, and ≥ 3 the recurrence rates were 29% (8/28), 39% (12/31) and 64% (9/14) respectively. Similarly, In AF non-termination group: for a CHA2DS2-VASc scores of 0, 1-2, and ≥ 3 the recurrence rates were 63% (5/8), 75% (6/8), and 100% (6/6), respectively. Of the patients with CHA2DS2-VASc scores of ≥ 3 in AF non-termination group all experienced recurrences within 2 year after the single procedure. Conclusions: The catheter ablation may be effective in eliminating part of non-paroxysmal AF for elderly. In addition, the present study demonstrated that CHA2DS2-VASc scores and non-termination after procedure were useful predictors of AF recurrence.

Keywords: Catheter ablation, recurrence, long-term outcome, non-paroxysmal atrial fibrillation

Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia and its prevalence increases with age [1]. Approximately 70% of individuals with AF are between 65 and 85 years of age [2]. AF is associated with a reduced quality of life and an increased number of adverse consequences [3]. Catheter ablation targeting the pulmonary veins (PVs) has been recognized as an effective therapy for patients with AF since late 1990s [3, 4]. As techniques have improved, catheter ablation of AF has become an acceptable option for symptomatic, drug-refractory AF patients [5]. With increasing life expectancy, the elderly are the most expanding portion of our population, making AF an even more important public health problem. Several studies analyzing efficacy and out-

comes of AF ablation in septuagenarians and octogenarians have been published [6-8]. However, the patients enrolled in these 3 studies had mainly paroxysmal AF. Since the indications of AF ablation have broadened to include elderly with non-paroxysmal AF, the data on the long-term efficacy of ablation in elderly with non-paroxysmal AF have become important, but is lacking. Therefore, the purpose of this study was to evaluate the long-term outcome of catheter ablation in elderly with non-paroxysmal AF.

Methods

Study population

Patients with non-paroxysmal AF who received single catheter ablation from July 2009 - June

Table 1. Patients with and without recurrence after single procedure (n=95)

Characteristics	Recurrence (n=46)	No recurrence (n=49)	P value
Age (year)	69.2 ± 6.9	68.5 ± 7.2	0.322
Sex (male)	40 (87%)	41 (84%)	0.487
Body mass index (kg/m ²)	26.1 ± 3.8	25.7 ± 4.1	0.778
AF duration (years)	8.6 ± 7.1	5.8 ± 6.6	0.263
Fluoroscopic time (minutes)	65 ± 24	63 ± 27	0.724
Procedure time (minutes)	175 ± 66	167 ± 71	0.826
Coronary artery disease	14 (30%)	16 (32%)	0.561
Hypertension	25 (54%)	24 (49%)	0.392
Diabetes mellitus	9 (20%)	4 (8%)	0.167
Prior cerebrovascular accident	6 (13%)	8 (16%)	0.455
Congestive heart failure	9 (20%)	5 (11%)	0.311
CHA2DS2-VASc scores ≥3, n	15 (33%)	5 (11%)	0.046
LA diameter, mm	46.8 ± 6.5	42.3 ± 7.1	0.021
LVEF, %	52.0 ± 9.8	54.8 ± 10.3	0.356
Type of AF			
Persistent AF	18/46 (39%)	22/49 (43%)	0.616
Long-standing persistent AF	28/46 (61%)	27/49 (57%)	0.556

2011 were enrolled (n=122). Patients who did not receive regular follow up for at least 2 year after the ablation were excluded (n=27). Finally, there were 95 patients enrolled in this study.

All patients underwent stepwise approach which included circumferential PVs isolation (PVSI), extensive linear lesions [9, 10] and ablation of fractionated potentials [11, 12]. The long-term outcome was obtained by event recordings and office visits.

ACCF/AHA/HRS guidelines and the Venice Chart Consensus Statement [13], define persistent AF as sustained episodes beyond 7 days, necessitating pharmacological or electrical cardioversion and longstanding persistent AF as continuous AF for more than 1 year.

Stepwise catheter ablation approach

Stepwise catheter ablation included 4 steps: PVSI (circumferential isolation of the pulmonary veins), isolation of superior vena cava [SVC], ablation of atrial tissue, and LA linear ablation. Radiofrequency energy output was between 30 and 35 W with a maximum catheter tip temperature of 45°C. At each site, radiofrequency energy was applied for 20 seconds. The maximum power was limited to 35 W. The details of ablation are outlined below: (I) PVSI was per-

formed and verified as previously described as previously described using the circumferential mapping catheter [14]. Circumferential lesions were created encircling the right and left PV ostia. The end-point of ablation was the abolition or dissociation of all PVs potentials. (ii) The SVC was isolated using the same technique and endpoint as was used for the PVs. (iii) Continuous complex fractionated atrial electrogram site ablation (CFAEs) was performed in the LA. CFAEs were defined based on the following criteria [15]: (1) atrial electrograms with 2 deflections or more or with fractionated baseline complexes with continuous activity over a 10-second recording time. (2) atrial electrograms with a cycle length of 120 milliseconds over a 10-second recording time. The end point of the CFAEs ablation was to eliminate the CFAEs. (iv)

Linear ablation involved LA ablation at the LA roof joining the two superior PV and at the mitral isthmus between the left inferior PV and lateral mitral annulus. The endpoint was the creation of split potentials or an electrogram voltage reduction of >50% after each application of radiofrequency energy.

Post-ablation follow up

After the procedure, all patients received anti-arrhythmic drugs for 8 weeks to prevent any early recurrence of AF. Anticoagulation therapy was continued for at least 6 months. Patients visited the clinic or with the referring physicians every 3 months. 24-hour Holter monitoring were performed every 3 months during the 36-month follow-up. No Freedom of recurrence was defined as the absence of atrial arrhythmias after a blanking period of 3 months after the catheter ablation during the follow-up period. Thus, arrhythmia recurrence was defined as any atrial arrhythmias, lasting ≥30 seconds, recorded after the blanking period with Holter monitoring, or when patient symptoms coincided with an arrhythmia that was documented by an event recorder [16]. The long-term efficacy was assessed clinically on the basis of the symptoms, resting surface 12-lead electrocardiogram, 24-hour Holter monitoring.

Table 2. Uni- and multivariate analysis of predictors of AF recurrence

Variable	Univariate Analysis		Multivariate Analysis+	
	HR (95% CI)	P Value	HR (95% CI)	P Value
Age (year)	1.05 (1.01-1.05)	0.07		
Sex (male)	0.86 (0.26-2.29)	0.45		
Body mass index (kg/m ²)	1.01 (0.91-1.23)	0.75		
Hypertension	1.56 (1.08-2.36)	0.03	0.93 (0.61-1.35)	0.09
Diabetes mellitus	0.65 (0.32-0.99)	0.06		
Prior cerebrovascular accident	1.12 (0.48-1.72)	0.61		
Congestive heart failure	1.55 (0.82-3.69)	0.14		
CHA2DS2-VASc scores	1.08 (1.01-1.27)	<0.001	1.02 (1.01-1.57)	0.02
LA diameter (mm)	1.32 (0.81-1.79)	0.55		
AF non-termination after procedure	1.86 (1.02-2.48)	<0.001	1.65 (1.12-3.35)	0.04

+The multivariable analysis included variables whose *p* values were <0.1 in the bivariate model.

Table 3. Baseline characteristics of the patients in group I and group II

Group	N	Hypertension N (%)	Coronary artery disease N (%)	Congestive heart failure N (%)	LA diameter, mm
Group I	73	38 (52%)	22 (30%)	10 (14%)	47.3 ± 6.8
Group II	22	11 (50%)	8 (36%)	4 (18%)	41.4 ± 7.2
<i>P</i> Value		0.521	0.504	0.321	<0.001

for 9.2 ± 2.3 months in patients with persistent AF, and 7.8 ± 3.1 years in those with long-standing persistent AF.

The distribution of CHA2DS2-VASc scores ≥3 patients and LA diameter in two groups were different [patients

with recurrence, 15/46 (33%) vs. patients without recurrence, 5/49 (11%), *P*=0.311] and [patients with recurrence, 46.8 ± 6.5 vs. patients without recurrence, 42.3 ± 7.1, *P*=0.021]. No differences in age, Sex, AF duration, Procedure time, Fluoroscopic time, Medical history. The baseline characteristics are presented in **Table 1**.

Procedural characteristics and clinical outcomes

All patients received PVSI, 73 patients received SVC isolation, 70 patients received an LA linear ablation, and 52 patients underwent a continuous CFAEs ablation. There were 17 patients in whom SR was restored before LA linear ablation received PVSI, SVC isolation and CFAEs ablation. After the end of the procedure, there were 22 patients that need direct current cardioversion, The total times of radiofrequency applications for PVs, I LA linear and CFAEs ablations were 52.9 ± 11.3, 17.5 ± 8.2 and 16.5 ± 7.9 minutes, respectively. During a period of 36 months, there were 46 patients suffering from recurrences (37 patients with AF and 9 patients with atrial flutter/atrial tachycardia) after the procedure.

Statistics analysis

Statistical analysis was performed using SPSS 17.0 (SPSS, Chicago, IL, USA). Continuous variables were reported as mean ± standard deviation and compared using an unpaired 2-tailed *t* test, the Mann-Whitney test for skewed variables. Kaplan-Meier analysis was used to determine the percentage of patients free from AF after the ablation procedure. A Chi-square test was used for the categorical data. A Cox regression analysis was used to identify the factors associated with first recurrence for those variables with *P* values <0.1 between patients with and without recurrences. Variables selected to be tested in the multivariable analysis were those with a *P* value <0.1 in the bivariate models. All tests were 2-sided and a *P*-value <0.05 was considered statistically significant.

Results

Baseline characteristics

Our study consisted of consecutive 95 patients and 50 of them had long-standing persistent AF. The mean age of the population in this study was 68.7 ± 7.1 years. AF had been persistent

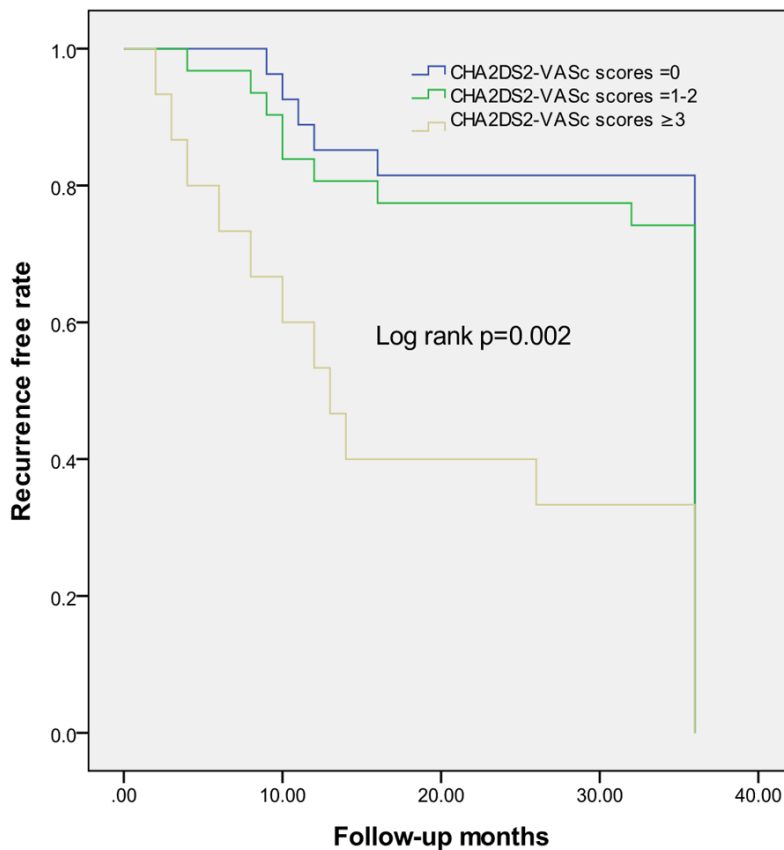


Figure 1. Kaplan-Meier analysis of the long-term freedom from recurrences of atrial arrhythmias in group I (Log rank $P=0.002$).

Clinical predictors of AF recurrence after the procedure

Clinical predictors for AF recurrence were evaluated using uni- and multivariable analyses (**Table 2**). On univariable analysis, Hypertension (Hazard Ratio [HR], 1.56; 95% CI, 1.08-2.36; $P=0.03$), CHA2DS2-VASc scores ([HR], 1.08; 95% CI, 1.01-1.27; $P<0.001$) and AF non-termination after procedure ([HR], 1.86; 95% CI, 1.02-2.48; $P<0.001$) were significant predictors for AF recurrence (**Table 3**). On multivariable analysis, Only CHA2DS2-VASc scores ([HR], 1.01; 95% CI, 1.01-1.17; $P=0.03$) and AF non-termination after procedure ([HR], 1.65; 95% CI, 1.12-3.35; $P=0.04$) remained predictors for AF recurrence (**Table 2**). There were 29 patients experienced recurrences after the Procedure in group I (AF termination group). On the other hand, there were 17 patients who needed direct current cardioversion after the Procedure experienced recurrences in group II (AF non-termination group). Compared with

group I, higher LA diameter was observed in group II patients ($P=0.02$) (**Table 3**). There was an ascending pattern of recurrence rate with higher CHA2DS2-VASc scores. In group I: for a CHA2DS2-VASc scores of 0, 1-2, and ≥ 3 the recurrence rates were 29% (8/28), 39% (12/31) and 64% (9/14), respectively (**Figure 1**). Similarly, there was an ascending pattern of recurrence rate with higher CHA2DS2-VASc scores in group II: for a CHA2DS2-VASc scores of 0, 1-2, and ≥ 3 the recurrence rates were 63% (5/8), 75% (6/8), and 100% (6/6), respectively. All recurrences happened within 2 year after the procedure in the patients with CHA2DS2-VASc scores of ≥ 3 (**Figure 2**).

Discussion

Main findings

The present data show that (1) the majority of drug-resistant symptomatic Non-paroxysmal AF in Elderly could be controlled by Stepwise Catheter Ablation Approach because the recurrence-free rate was 51.6% after a single procedure; (2) The CHA2DS2-VASc scores and AF non-termination after procedure can identify patients who will suffer from recurrences after catheter ablation.

Long-term results of catheter ablation in elderly with non-paroxysmal AF

Clinical outcome

Several studies reported the long-term effects of catheter ablation in AF [17-19]. Bhargava reported the long-term outcome in 1404 AF patients (728 had paroxysmal AF 293 had persistent AF and 383 had long-standing persistent AF), at mean follow-up of 57 ± 17 months, 84.0% patients with NPAF remained free from AF after a single ablation procedure [17]. Ouyang [18] researched 161 paroxysmal AF patients with a normal left ventricular ejection

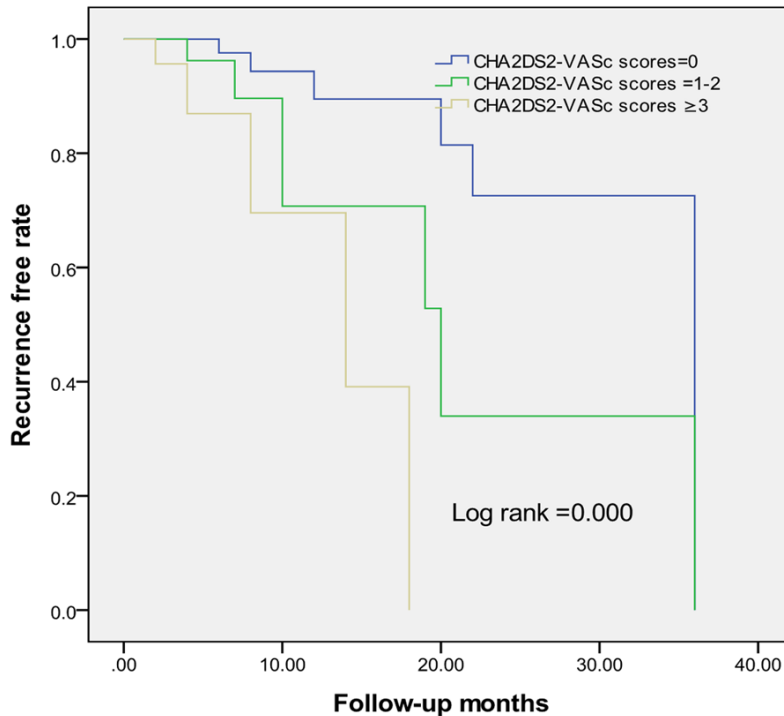


Figure 2. Kaplan-Meier analysis of the long-term freedom from recurrences of atrial arrhythmias in groupie (Log rank P=0.000).

fraction who received catheter ablation, and demonstrated that Sinus rhythm was present in 75 patients (46.6%) after the initial procedure during a median follow-up period of 4.8 years (0.33 to 5.5 years). Corrado [19] reported 174 consecutive patients over 75 years of age who underwent AF ablation from 2001 to 2006, and demonstrated that 127 (73%) maintained sinus rhythm with a single procedure, whereas 47 patients had recurrence of AF during a mean follow-up of 20 ± 14 months.

Recently, Santangeli [20] analyzed the ablation outcome in 103 (3.7%) ≥ 80 years patients undergoing RFCA of AF, and demonstrated that 71 (69%) octogenarians remained free from AF recurrence off antiarrhythmic drugs after a single procedure during a mean follow-up of 18 ± 6 months.

In comparison to these previous studies, we focused on the ablation outcomes in patients receiving the same ablation strategy during a more recent period, and may provide the information more useful in practice. Furthermore, we only enrolled old patients with non-paroxysmal AF, because the history may differ between paroxysmal and Non-Paroxysmal AF.

This study indicated that the recurrence rate after catheter ablation of non-paroxysmal AF was 48.4% after a single procedure. In addition, this study shows that the risk of recurrence in group II patients is 1.86 times in group I patients. This study is consistent with Heist [21] who found that termination of Non-paroxysmal AF by ablation was associated with favorable clinical outcomes. Therefore, catheter ablation of non-paroxysmal AF is an effective strategy for preventing AF recurrence in elderly.

CHA2DS2-VASc scores and recurrence after catheter ablation: The AF non-termination after procedure and CHA2DS2-VASc scores ≥ 3 were significant predictors

of AF recurrences after catheter ablation in this study. It has been previously recognized that stroke risk stratification scores cannot be used as standalone prognosticators for rhythm outcome [22]. In fact, CHA2DS2-scores was significant predictors for AF recurrences even after adjustment for LA diameter and AF type [23].

In group I, the median recurrence free time of patients with CHA2DS2-VASc Scores ≥ 3 was 12 months. But in group II, the median recurrence free time of patients with CHA2DS2-VASc scores of 0, 1-2, and ≥ 3 were 22 months, 12 months and 6 months. Moreover, the recurrence rate was 100% at 2 year for the group II patients who had a CHA2DS2-VASc Scores of ≥ 3 . For group II, Further analysis of the clinical data of patients found that higher LA diameter was observed (P=0.02).

These findings suggested that The LA diameter before the catheter ablation represents the severity of LA structural remodeling due to persistent AF, and the high CHA2DS2-VASc Scores may imply that the LA will still suffer from damage due to the adverse effects of systemic disease after the catheter ablation.

Study limitations: There were several limitations to this study. First, the results of the present study are not a randomized trial but rather a case control design. Second, AF recurrence may have been underestimated because the patients were not constantly monitored. Third, the CFAEs ablation was performed after PVSI and LA linear ablation; however, we did not assess the CFAEs distribution after LA linear ablation.

Conclusion

The catheter ablation may be effective in eliminating part of non-paroxysmal AF for elderly. In addition, the present study demonstrated that CHA2DS2-VASc scores and non-termination after procedure were useful predictors of AF recurrence.

Disclosure of conflict of interest

None.

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