Catheter ablation versus rate control in patients with atrial fibrillation and heart failure

A multicenter study

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Abstract
Many trials have shown improvements in left ventricular function, exercise capacity, and quality of life after catheter ablation (CA) of atrial fibrillation (AF) in patients with heart failure (HF). We sought to evaluate the impact of CA on hard outcomes in a retrospective cohort study. AF patients with symptomatic HF from 3 hospitals were included. Our primary endpoint was major adverse cardiac events (MACEs), a composite of all-cause mortality, stroke, and unplanned hospitalization. In total, 90 patients underwent CA and 304 ones received rate control (RaC) were included. After a mean follow-up of 13.5 ± 5.3 months, 82.2% of patients in CA group got freedom from AF; while patients receiving RaC group remained in AF. CA group had a significantly decreased risk of MACEs compared with RaC group (13.3% vs 29.3%, hazard ratio [HR] 0.51, 95% confidence interval [CI]: 0.32–0.82, P = .005). After propensity score matched for confounding factors, difference in MACEs remained significantly between groups (13.3% vs 25.6%, HR 0.50, 95% CI: 0.26–0.98, P = .044). Multivariate regression analysis also indicated that CA was significantly associated with a lower risk of MACEs in overall cohort (HR 0.486, 95% CI: 0.253–0.933, P = .030) and in propensity-matched cohort (HR 0.482, 95% CI: 0.235–0.985, P = .045). Besides, age and NYHA class were associated with an increased risk of MACEs. In conclusion, the present study demonstrated that CA for AF in HF patients could reduce the risk of MACEs in a mid-term follow-up. Thus, CA may be a reasonable option for this population.

Abbreviations: AF = atrial fibrillation, BNP = B-type natriuretic peptide, CA = catheter ablation, CI = confidence interval, HF = heart failure, HR = hazard ratio, INR = international normalized ratio, LAD = left atrial diameter, LVEDd = left ventricular end-diastolic diameter, LVEF = left ventricular ejection fraction, MACE = major adverse cardiac event, NYHA = New York Heart Association, RaC = rate control, RhC = rhythm control.

Keywords: adverse events, atrial fibrillation, catheter ablation, heart failure, rate control

1. Introduction
Atrial fibrillation (AF) and heart failure (HF) become epidemics across the world, partially due to progressive aging, reduced cardiovascular mortality and epidemiological transition in developing countries. They share similar mechanisms and underlying risk factors, and both can aggravate the severity of the other.

Patients with AF and HF have impaired quality of life, a high risk of stroke, and an increased mortality. Maintenance of sinus rhythm might decrease the risk of these public health problems. However, rhythm control (RhC) strategies have not proven to be superior to rate control (RaC) strategies in AF patients with HF. Patients receiving RhC therapy often fail to achieve freedom from AF; while patients receiving RaC therapy are often in sinus rhythm. Besides, amiodarone, a common used antiarrhythmic drug for RhC strategies presents extra-cardiac adverse effects and might increase the risk of deaths from circulatory failure. These might be the reasons for failing to identify a superior strategy from RhC and RaC.

Catheter ablation (CA), an established therapeutic option in AF patients, is superior to antiarrhythmic drug in maintaining sinus rhythm, and reducing mortality. Recent randomized controlled trials suggest that CA of AF in HF patients leads to improvements in left ventricular function, exercise capacity, and quality of life. Previous meta-analysis also got similar conclusions. We therefore hypothesized that CA may be associated with low risk of adverse events in AF patients with HF compared with medical RaC strategies and performed this retrospective cohort study to confirm this.

2. Materials and methods
2.1. Study design
This was a retrospective cohort study conducted in 3 tertiary hospitals (Nanjing Drum Tower Hospital, Hua’ian First People’s Hospital, and Jiangsu, China). The authors have no conflicts of interest to disclose.

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Hospital and Huai’an Second People’s Hospital) from January 2015 to May 2016. Before enrollment, all patients received either CA or medical RaC strategies, which were chosen by patients under recommendation of experienced doctors. The study was approved by the ethics committee at each participating hospital. All patients involved signed the informed consent. This observational study was performed according to STROBE statement and following a registered protocol at Clinical trials.gov (NCT02846922).

2.2. Patients

Patients aged >18 years, with documented AF (including paroxysmal, persistent and long-standing persistent AF), symptomatic HF (New York Heart Association [NYHA] class II to IV), and left ventricular systolic dysfunction (ejection fraction <50%) were eligible. Exclusion criteria included reversible causes of AF and/or HF, previous ablation, postoperative AF, any contra-indications to CA, anticoagulation or antiarrhythmic drugs and malignancy. Before allocation, all patients were hospitalized for the reason of HF and treated on optimal HF therapy, which was defined as taking or having tried angiotensin converting enzyme inhibitors/angiotensin receptor blockers, β-blockers, and other medications for at least 1 month.[21] All patients enrolled had anticoagulant treatment of warfarin with a target international normalized ratio (INR) of 2 to 3 or dabigatran.

2.3. Baseline assessments

Baseline variables comprised demographic and clinical data, medical history (coronary heart disease, hypertension, diabetes, and previous stroke), echocardiography results, B-type natriuretic peptide (BNP) levels, and medications of included patients. Heart rate and blood pressure were measured at rest. All patients underwent the measurement of BNP, INR, and echocardiography within 3 days before the allocation. Left atrial diameter (LAD), left ventricular end-diastolic diameter (LVEDd), and left ventricular ejection fraction (LVEF) were recorded for further analysis. LVEF was measured using the modified biplane Simpson rule in 2- and 4-chamber views. We also recorded medication information. These therapies were recommended to continue throughout the study period. We calculated CHA2DS2-Vasc score of each patient according to a recent guideline.[24] Coronary heart disease was defined as: symptoms such as angina, myocardial infarction, coronary angioplasty, or coronary artery bypass graft surgery.

2.4. Rate control

Treatment of RaC strategies (β-blockers and/or digoxin) aimed to achieve the target heart rate, which was defined as a heart rate ≤80 beats per minute at rest.[25] At baseline and during follow-up, patients were recommended for adjusted doses of β-blockers and/or digoxin until meeting the target heart rate. Patients would receive atrioventricular-node ablation with right ventricular septal pacing if the target rate was not achieved.

2.5. Catheter ablation

All patients had transoesophageal echocardiography to exclude left atrial thrombus before ablation. Under local anesthetic (lidocaine) and deep sedation (midazolam), procedures were performed by an experienced operator. A decapolar catheter was positioned into the coronary sinus. After double trans-septal punctures, a mapping catheter and ablation catheter were advanced inside the left atrium through 2 sheaths. Angiography of left and right pulmonary veins was performed. Then, we created a 3-dimensional left atrium reconstruction using the CARTO mapping system. Pulmonary vein isolation was performed within the guide of CARTO mapping system with a maximum power of 30 W, a limited temperature of 50°C, and a saline-irrigated rate of 8 to 17 mL per minute. Ablation ended with the absence of any pulmonary vein electric potential. If freedom from AF was not achieved after pulmonary vein isolation, electrical cardioversion was employed with the administration of amiodarone (150 mg) until AF converted to sinus rhythm. Ablation of linear lesions was conducted when sinus rhythm was still not restored or atrial tachycardia was found. After a 3-month blanking period postoperation, repeat procedures were considered for recurrence of AF.

2.6. Follow-up

Patients were evaluated from the discharged day until death or December 2016, from at least 1 of the following 3 methods: medical records, telephone contact, and outpatient visitation as described previously.[25] A 12-lead electrocardiogram and/or 24-hour ambulatory electrocardiogram monitoring were made for the clinical assessment. Our primary endpoint was major adverse cardiac events (MACEs), a composite of all-cause mortality, stroke and unplanned hospitalization. The secondary endpoints were all-cause mortality, stroke, and unplanned hospitalization. Stroke was determined by computed tomography scans, magnetic resonance imaging, or medical records. Unplanned hospitalization was defined as rehospitalization because of HF.

2.7. Statistical analysis

Continuous data were presented as mean ± standard deviation or medians and interquartile range according to the results of Kolmogorov-Smirnov test, and were analyzed using Student t test and Mann–Whitney U test, respectively. Categorical data were presented as numbers and percentages, with Chi-square test or Fisher exact test for the intergroup analyses. Event-free survival rates were estimated using Kaplan–Meier analysis and compared by log-rank test, which were presented as hazard ratios (HRs) and 95% confidence intervals (CIs). Cox proportional hazards regression model (forward stepwise) was further performed to evaluate the association between CA and our primary endpoint.

We additionally applied propensity score matching to adjust potential confounding factors in this study. Significant imbalanced baseline characteristics were added into a logistic regression model to calculate the propensity score of each patient. Patients in RaC group were then selected for the best match case of each subject in CA group according to the scores. In the propensity-matched cohort, we repeat the analyses mentioned above. SPSS version 22.0 (IBM SPSS, Armonk, NY) was used for the analyses. Statistical significance was considered when a 2-tailed P-value <.05.

3. Results

In total, 394 patients with AF and HF were included in this study. Of those, 90 patients chose AF ablation and the rest 304 ones received medical RaC therapy (Fig. 1). Baseline characteristics are
shown in Table 1. Patients in RaC group were older (73.0 ± 10.7 years vs 64.7 ± 9.4 years, P < .001) and had higher CHA2DS2-Vasc score (3.5 ± 1.5 vs 2.3 ± 1.5, P < .001) when compared with those in CA group. There were more patients with previous history of stroke (23.4% vs 13.3%, P = .041) and with persistent or long-standing persistent AF (81.2% vs 66.7%, P = .003) in RaC group than in CA group. Besides, patients received RaC strategies had an increased NYHA class (3.2 ± 0.7 vs 2.7 ± 0.6, P < .001), larger LAD (5.2 ± 0.8 vs 4.9 ± 0.7 cm, P < .001), and LVEDd (5.7 ± 0.9 vs 5.3 ± 0.8 cm, P = .040) compared with those underwent CA therapy. Besides, β-blockers were more often used in RaC group (71.1% vs 55.6%, 0 = 0.006). No significant difference was seen in intergroup analyses of the other variables.

We forced all imbalanced baseline characteristics (age, CHA2DS2-Vasc score, previous stroke, AF type, NYHA class, LAD, LVEDd, and β-blocker) into propensity score matching to get a propensity-matched cohort. The mean propensity score was 0.17 ± 0.17 in RaC group and was 0.41 ± 0.21 in CA group with a P-value < .001 before matching. All 90 patients in CA group were 1:1 matched with 90 patients in RaC group. After matching, the mean propensity score was 0.37 ± 0.18 in RaC group, which was comparable with that in CA group (P = .144). Moreover, no statistical significance of baseline characteristics was found between groups in propensity-matched cohort (Table 1).

During a mean follow-up of 13.5 ± 5.3 months (range, 8–24 months), 16 patients were lost to follow-up (Fig. 1). At last, 4 patients in RaC group underwent antiopeptiiod-node ablation to achieve the target rate; 30 patients underwent a second ablation procedure and 5 underwent a third in CA group. After a mean of 1.49 ± 0.61 procedures per patient, 79 patients (82.2%) got freedom from AF in CA group. While in RaC group, all patients remained in paroxysmal and persistent or long-standing persistent AF, 83.6% of whom achieved the target heart rate. At last, the mean heart rate at rest was 73.5 ± 14.5 beats per minute.

Table 1

| Baseline characteristics of patients. | Overall cohort | Propensity-matched cohort |
|--------------------------------------|---------------|---------------------------|
|                                      | Catheter ablation | Rate control | P          | Catheter ablation | Rate control | P          |
| Age, y                                | 64.7 ± 9.4      | 73.0 ± 10.7              | <.001     | 64.7 ± 9.4      | 65.4 ± 11.4              | .633     |
| Male, n (%)                           | 45 (50.0)       | 153 (50.3)               | .956     | 45 (50.0)       | 41 (45.0)               | .551     |
| Heart rate, beats/min                 | 98.2 ± 23.0     | 96.2 ± 23.4              | .482     | 98.2 ± 23.0     | 93.3 ± 20.1              | .129     |
| Systolic blood pressure, mm Hg       | 127.6 ± 18.5    | 130.8 ± 19.2             | .160     | 127.6 ± 18.5    | 124.2 ± 17.6             | .214     |
| Diastolic blood pressure, mm Hg      | 75.4 ± 9.1      | 76.2 ± 12.2              | .552     | 75.4 ± 9.1      | 75.8 ± 12.8              | .804     |
| CHA2DS2-Vasc score                    | 2.3 ± 1.5       | 3.5 ± 1.5                | <.001    | 2.3 ± 1.5       | 2.5 ± 1.3                | .254     |
| Current smoker, n (%)                 | 18 (20.0)       | 56 (18.4)                | .736     | 18 (20.0)       | 19 (21.1)                | .854     |
| Alcohol, n (%)                        | 9 (10.0)        | 26 (8.6)                 | .672     | 9 (10.0)        | 8 (8.9)                 | .799     |
| Coronary heart disease, n (%)         | 20 (22.2)       | 59 (19.4)                | .558     | 20 (22.2)       | 12 (13.3)                | .119     |
| Hypertension, n (%)                   | 49 (54.4)       | 186 (61.2)               | .252     | 49 (54.4)       | 50 (55.6)               | .881     |
| Diabetes mellitus, n (%)              | 18 (20.0)       | 81 (26.6)                | .202     | 18 (20.0)       | 12 (13.3)                | .230     |
| Previous stroke, n (%)                | 12 (13.3)       | 71 (23.4)                | .041     | 12 (13.3)       | 11 (12.2)               | .823     |
| Type of atrial fibrillation           | .003            | .012                     | .277     | .003            | .012                     | .120     |
| Paroxysmal, n (%)                     | 30 (33.3)       | 57 (18.8)                | .277     | 30 (33.3)       | 28 (31.1)               | .305     |
| Persistent or long-standing persistent, n (%) | 60 (66.7)       | 247 (81.2)               | .120     | 60 (66.7)       | 62 (68.9)               | .120     |
| Heart failure etiology                | .324            | .324                     | .324     | .324            | .324                     | .324     |
| Ischemic, n (%)                       | 8 (8.9)         | 40 (13.2)                | .277     | 8 (8.9)         | 3 (3.3)                 | .324     |
| Nons ischemic, n (%)                  | 82 (91.1)       | 264 (86.8)               | .824     | 82 (91.1)       | 87 (96.7)               | .824     |
| NYHA class                            | 2.7 ± 0.6       | 3.2 ± 0.7                | .001     | 2.7 ± 0.6       | 2.7 ± 0.7               | .820     |
| Left atrial diameter, cm              | 4.9 ± 0.7       | 5.2 ± 0.8                | <.001    | 4.9 ± 0.7       | 5.0 ± 0.7               | .273     |
| Left atrial end-diastolic diameter, cm| 5.5 ± 0.8       | 5.7 ± 0.9                | .040     | 5.5 ± 0.8       | 5.6 ± 0.8               | .320     |
| Left ventricular ejection fraction, % | 41.9 ± 6.9      | 41.1 ± 6.8               | .353     | 41.9 ± 6.9      | 41.4 ± 7.0               | .591     |
| BNP, pg/mL                            | 587 (198–826)   | 510 (273–833)            | .205     | 587 (198–826)   | 468 (236–816)            | .656     |
| International normalized ratio        | 1.83 ± 0.69     | 1.72 ± 0.74              | .200     | 1.83 ± 0.69     | 1.74 ± 0.76              | .529     |
| ACE or ARB, n (%)                     | 75 (83.3)       | 238 (78.3)               | .298     | 75 (83.3)       | 66 (73.3)               | .103     |
| β-blocker, n (%)                      | 50 (55.6)       | 216 (71.1)               | .006     | 50 (55.6)       | 49 (54.4)               | .881     |
| Digoxin, n (%)                        | 44 (48.9)       | 182 (59.9)               | .064     | 44 (48.9)       | 53 (58.9)               | .178     |
| Spirolactone, n (%)                   | 44 (48.9)       | 180 (59.2)               | .082     | 44 (48.9)       | 55 (61.1)               | .099     |

ACE = angiotensin converting enzyme inhibitor, ARB = angiotensin receptor blocker, BNP = B-type natriuretic peptide, NYHA = New York Heart Association.
in RaC group and was 71.7 ± 15.8 beats per minute in CA group (P = .312).

Table 2 presents the occurrences of our primary and secondary outcomes. In total, 29.3% patients in RaC group had MACEs, which was significantly higher than in CA group (13.3%, HR 0.51, 95% CI: 0.32–0.82, P = .005). The incidences of all-cause mortality, stroke, and unplanned hospitalization were also higher in RaC group than in CA group (7.9% vs 3.3%, 9.9% vs 4.4, and 16.1% vs 10.0%, respectively), but no statistical significance was found (Table 2). After propensity score matching, significant difference remained for the comparison of MACEs (13.3% vs 10.0%, respectively), but no statistical significance was found (Table 2). After propensity score matching, significant difference remained for the comparison of MACEs (13.3% vs 10.0%, respectively), but no statistical significance was found. Kaplan–Meier curves of MACEs-free survival in overall and propensity-matched cohort are illustrated in Figs. 2 and 3.

We additionally performed forward stepwise multivariate regression analysis to identify independent predictors of MACEs during follow-up using Cox proportional hazards regression model. Factors, such as age, gender, CHA2DS2-Vasc score, medical history, AF type, NYHA class, echocardiography indexes, BNP, and treatment of angiotensin converting enzyme inhibitor or angiotensin receptor blocker and β-blocker might have adverse effect on clinical outcomes. These factor therefore were forced into the forward stepwise regression model, which revealed that CA was significantly associated with a lower risk of MACEs (HR 0.486, 95% CI: 0.253–0.933, P = .030). LVEF seemed to be another protective factor for mid-term MACEs (HR 0.931, 95% CI: 0.902–0.960, P < .001). Moreover, elevated age, coronary heart disease, and NYHA class indicated an increased risk of MACEs (HRs, 95% CIs, and P values: 1.051 [1.024–1.078], P < .001; 1.651 [1.041–2.618], P = .034; and 1.360 [1.012–1.827], P = .042, respectively) (Table 3). In propensity-matched cohort, CA was also related with the decreased risk of MACEs (HR 0.482, 95% CI: 0.235–0.985, P = .045). Besides, age and NYHA class were also a risk factor of developing MACEs in patients with HF and AF (HRs, 95% CIs, and P values: 1.075 [1.015–1.138], P = .013 and 1.932 [1.185–3.150], P = .008).

4. Discussion
In AF patients with left ventricular dysfunction, we found that CA was associated with a low risk of MACEs during a mid-term follow-up. Our findings of propensity-matched cohort and multivariate analysis also supported this conclusion, suggesting that CA might be a more beneficial approach than medical RaC therapy in this population. However, no significant difference was found in the analyses of our secondary outcomes.

AF, characterized by irregular and rapid ventricular rate as well as loss of atrial contraction, is associated with a high risk of mortality in HF patients.26–27 RhC and RaC are 2 major ways for treatment of AF. Beta-blockers and/or digitalis are often used to achieve the target heart rate. These medications may decrease the impact of excessive ventricular rate, but cannot weaken the influence of loss of atrial contraction and irregular ventricular filling time. Theoretically, RhC can completely reverse the harmful effect of AF and may improve clinical outcomes in patients with HF and AF. However, previous studies concluded that medical RhC was similar to RaC strategies in improvement of deaths, hospitalization and the composite of deaths, stroke, and worsening HF.13–15 Several reasons might explain the

| Table 2 | Incidence of MACEs during follow-up. |
|----------------|-----------------|-----------------|-----------------|-----------------|
|                | Overall cohort  |                | Propensity-matched cohort |
|                | Catheter ablation | Rate control | HR (95%CI) | P               | Catheter ablation | Rate control | HR (95%CI) | P               |
| MACES          | (n = 90)        | (n = 304)      | .005          |                 | (n = 90)        | (n = 90)       | .044          |                 |
| All-cause mortality | 12 (13.3) | 89 (29.3) | 0.51 (0.32–0.82) | .005           | 12 (13.3) | 23 (25.6) | 0.50 (0.26–0.98) | .044           |
| Stroke         | 3 (3.3)         | 24 (7.9)       | 0.50 (0.21–1.22) | .126           | 3 (3.3) | 5 (6.8) | 0.58 (0.14–2.31) | .437           |
| Worsening heart failure | 9 (10.0) | 40 (16.1) | 0.63 (0.34–1.16) | .140           | 9 (10.0) | 14 (15.6) | 0.61 (0.27–1.40) | .243           |

CI = confidence interval; HR = hazard ratio; MACE = major adverse cardiac event.

Figure 2. The Kaplan–Meier survival curves for MACE-free survival in overall cohort.

Figure 3. The Kaplan–Meier survival curves for MACE-free survival in propensity-matcher cohort.
Catheter ablation 0.486 (0.253–b–NYHA class 1.360 (1.012–Coronary heart disease 1.651 (1.041–safety and ef
the therapy of AF in HF patients remains weak.

In these 4 randomized controlled trials. So the evidence of CA for mortality, stroke, and unplanned hospitalization were evaluated ranged 6 to 12 months. Moreover, no hard outcomes such as only 224 patients with AF and HF and the duration of follow-up similar to previous study.[19,21,22] These studies all con achieved in 82.2% of patients received AF ablation, which was
et al[20] found AF ablation did not improve LVEF (measured by cardiovascular magnetic resonance), 6-minute walk distance, N-terminal proBNP and quality of life compared with medical strategies of RaC at 6-month follow-up. These might be partially explained by the fact that sinus rhythm was restored in only 50% of patients. The ARC-HF trial investigators reported significant benefit from ablation on symptoms, exercise capacity, and neurohormonal status at 12 months.[21] LVEF change was also higher in CA group than in RaC group (10.9% vs 5.4%), however, no statistical difference was found between groups (P = 0.053), possibly because of the limited sample size. The CAMTAF trial showed that CA was superior to pharmacological RaC therapy in improving LVEF, exercise capacity, NYHA class, BNP, and quality of life at 6 months.[22] Even compared with a strict RaC strategy, atroventricular node ablation with biventricular pacing, AF ablation was still associated with significant improvement of LVEF, 6-minute walk distance, and quality of life in PABA-CHF trial.[19] Previous meta-analysis also concluded that CA was superior to RaC in cardiac function, exercise capacity, and quality of life.[23] However, these studies included only 224 patients with AF and HF and the duration of follow-up ranged 6 to 12 months. Moreover, no hard outcomes such as mortality, stroke, and unplanned hospitalization were evaluated in these 4 randomized controlled trials. So the evidence of CA for the therapy of AF in HF patients remains weak.

In the present study, maintenance of sinus rhythm was achieved in 82.2% of patients received AF ablation, which was similar to previous study.[19,21] These studies all confirmed the safety and efficacy of AF ablation except for MacDonald’s study.[20] with only 50% of patients getting freedom from AF. Despite the different success rate of AF ablation, the diverse response to CA in patients with AF and HF might also account for the different results among studies. According to the meta-regression analysis in previous study, the proportion of coronary artery disease seemed to be inversely associated the improvement in LVEF postablation, whereas the proportions of paroxysmal AF and AF recurrence had no effect on change in LVEF.[31] Recent study also suggested that CA was less effective in patients with known heart disease (defined as myocardial infarction, valvular heart disease, or hypertrophic cardiomyopathy) than in patients with idiopathic dilated cardiomyopathy.[32] Patients with “AF-induced cardiomyopathy” are more likely to benefit from RaC strategies; however, identification of patients who were most likely to respond to CA remains a challenge.[4] Recently, Bunch et al[33] included 3 cohorts of HF patients: AF patients underwent ablation, AF patients that did not receive ablation, and HF patients without AF. After a 5-year follow-up, AF and HF patients received CA had significant lower rates of deaths and HF hospitalization than those without ablation. Stroke rate was also lower in AF ablation group, but statistical analysis reached no significant difference. Patients in ablation group were healthier than those in other group according to Bunch’s data and some imbalanced baseline variables might influence long-term outcomes. However, no adjusted analysis for these potential confounding factors was performed in Bunch’s study. In the present study, patients received CA therapy also seemed to be healthier than those underwent RaC strategies, and we conducted multivariate and propensity score matching analyses to weaken the impact of the confounding factors. Notably, these 2 studies were both retrospective, and the sample size was small; therefore, although the results seemed encourag ing, high-quality large-scale randomized studies are needed to confirm these findings. Recently, an important randomized controlled trial, CASTLE-AF study ended and results were presented at ESC Congress 2017, which was similar to our results.[34] CA could significantly reduce the all-cause mortality (HR 0.53, 95% CI: 0.32–0.86, P = .011) and hospitalizations due to worsening HF (HR 0.56, 95% CI: 0.37–0.83, P = .004) during a 3-year follow-up in patients with HF and AF.[34] Another 2 important randomized controlled trials, RAFT-AF and CABANA trials, will evaluate the association between CA and hard clinical outcomes during a long-term follow-up (NCT numbers: 01420393 and 00911508). The completion of these studies will help to confirm the role of CA in patients with AF and HF.

This multicenter study had several limitations. Firstly, this is a retrospective cohort study, and some baseline characteristics were different between groups that may have influence on our outcomes. We tried to adjust for these confounding factors using multivariate and propensity score matching analyses. Secondly, only 394 patients with a mid-term follow-up were included in present study. Although we found a high risk of MACES in RaC group compared with CA group, we did not detect the differences of death, stroke, and unplanned hospitalization between groups.

Table 3

| Table 3 | Forward stepwise multiple regression analysis for predictors of MACEs during follow-up. |
|---------|-----------------------------------------------------------------------------------|
| Overall cohort | Propensity-matched cohort |
| HR (95% CI) | P | HR (95% CI) | P |
| Age, y | 1.051 (1.024–1.078) | < .001 | 1.075 (1.015–1.138) | .013 |
| Coronary heart disease | 1.651 (1.041–2.618) | .034 | 0.835 (0.328–2.125) | .705 |
| NYHA class | 1.360 (1.012–1.827) | .042 | 1.932 (1.185–3.150) | .008 |
| Left ventricular ejection fraction | 0.931 (0.902–0.960) | < .001 | 0.949 (0.898–1.004) | .068 |
| β-blocker | 0.660 (0.433–1.006) | .053 | 0.901 (0.444–1.826) | .722 |
| Catheter ablation | 0.486 (0.253–0.933) | .030 | 0.482 (0.235–0.965) | .045 |

CI = confidence interval, HR = hazard ratio, MACE = major adverse cardiac event, NYHA = New York Heart Association.
Finally, we did not evaluate the change in LVEF, 6-minute test distance, NYHA class, and quality of life, for the reason of that several studies had demonstrated the improvements of these endpoints after AF ablation.

5. Conclusions

CA resulted in a decreased risk of developing MACEs in patients with AF and HF during a mid-term follow-up. However, no significant difference between all-cause mortality, stroke, and unplanned hospitalization was found, suggesting the lack of power to detect these differences. Further high-quality studies are needed to confirm the role of CA in patients with AF and HF and to identify HF patients that respond well to CA ablation.

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