Catheter ablation for atrial fibrillation is associated with reduced risk of mortality in the elderly: a prospective cohort study and propensity score analysis

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Abstract

Background It is unclear whether catheter ablation (CA) for atrial fibrillation (AF) affects the long-term prognosis in the elderly. This study aims to evaluate the relationship between CA and long-term outcomes in elderly patients with AF.

Methods Patients more than 75 years old with non-valvular AF were prospectively enrolled between August 2011 and December 2017 in the Chinese Atrial Fibrillation Registry Study. Participants who underwent CA at baseline were propensity score matched (1:1) with those who did not receive CA. The outcome events included all-cause mortality, cardiovascular mortality, stroke/transient ischemic attack (TIA), and cardiovascular hospitalization.

Results Overall, this cohort included 571 ablated patients and 571 non-ablated patients with similar characteristics on 18 dimensions. During a mean follow-up of 39.75 ± 19.98 months (minimum six months), 24 patients died in the ablation group, compared with 60 deaths in the non-ablation group (hazard ratio (HR) = 0.49, 95% confidence interval (CI): 0.30–0.79, P = 0.0024). Besides, 6 ablated and 29 non-ablated subjects died of cardiovascular disease (HR = 0.25, 95% CI: 0.11–0.61, P = 0.0022). A total of 27 ablated and 40 non-ablated patients suffered stroke/TIA (HR = 0.79, 95% CI: 0.48–1.28, P = 0.3431). In addition, 140 ablated and 194 non-ablated participants suffered cardiovascular hospitalization (HR = 0.84, 95% CI: 0.67–1.04, P = 0.1084). Subgroup analyses according to gender, type of AF, time since onset of AF, and anticoagulants exposure in initiation did not show significant heterogeneity.

Conclusions In elderly patients with AF, CA may be associated with a lower incidence of all-cause and cardiovascular mortality.

J. Geriatr. Cardiol. 2020; 17: 740–749. doi:10.11909/j.issn.1671-5411.2020.12.008

Keywords: Atrial fibrillation; Catheter ablation; Mortality; Stroke; The elderly

1 Introduction

Atrial fibrillation (AF) is the most common arrhythmia.1,2 The incidence of AF increases with age.1,3 Based on the predicted life expectancy, the incidence of AF is expected to double in the next 50 years.5 Elderly patients with AF are more likely to have comorbidities, including hypertension, diabetes mellitus (DM), heart failure (HF), and renal failure, placing them at increased risk for cardiovascular events and mortality.6,7 In addition, the effect of antiarrhythmic drugs is less predictable in aging population with more frequent side effects.8

At present, catheter ablation (CA) has proven to be an efficacious method to treat symptomatic AF.9 CA could reduce AF burden, improve exercise capacity, and ameliorate AF-related symptoms.10–12 Meanwhile, increasing studies found that CA for AF in elderly subjects was efficacious, and major complications might be more frequent in the elderly.13–18 However, few studies have evaluated the association between CA and long-term prognosis in elderly patients with AF. The objective of the current study was to access the association between CA and long-term outcomes [all-cause mortality, cardiovascular mortality, stroke/transient ischemic attack (TIA), and cardiovascular hospitalization] in elderly patients with AF.
2 Methods

2.1 Study population

The Chinese Atrial Fibrillation (China-AF) Registry is a prospective, multicenter, hospital-based, ongoing registry study of patients diagnosed with AF in Beijing, China. We have described the details of the cohort earlier. All subjects enrolled in the current study were identified from the China-AF database. Data collected between August 2011 and December 2017 were used for analyses. Eligible participants were ≥ 75 years old, with a documented AF confirmed by 12-lead electrocardiogram (ECG) or 24-hour Holter monitoring within the past six months. Exclusion criteria were as follows: follow-up of less than six months; previous ablation for AF; patients diagnosed with rheumatic mitral stenosis or having mitral valve prostheses; and data missing. Then, the subjects were divided into two groups: the ablation group and non-ablation group. The flowchart of patient selection was presented in Figure 1.

The research was approved by the Ethics Committee of Beijing Anzhen Hospital (D11110700300000) and participants were required to provide written consent in this study.

2.2 Data collection

Information on patient characteristics, including age, gender, body mass index (BMI), type of AF, time since onset of AF, insurance, education, smoking, drinking, comorbidities (DM, hypertension, HF, stroke/TIA, vascular disease, and prior bleeding), medication (rhythm/rate control drugs and anticoagulants), left ventricular ejection fraction, as well as CHA2DS2-VASc score, was collected when patients were enrolled.

2.3 Catheter ablation for atrial fibrillation

The CA strategy used in participating centers has been previously described, namely, pulmonary vein isolation for paroxysmal AF, and three additional linear ablations at the left atrial roof, cavotricuspid isthmus and mitral isthmus for persistent AF.

2.4 Medical therapy and anticoagulation management

For patients in the ablation group, warfarin or a kind of non-vitamin K antagonist oral anticoagulants (NOACs) was given to all the patients for at least three months after CA. A kind of I or III antiarrhythmic drugs would be prescribed for the eligible patients after ablation for three months. Thereafter, the choice of continuing anticoagulants and antiarrhythmic drugs was left to the physician’s discretion. Besides, for individuals in the non-ablation group, anticoagulation treatment was recommended when the CHA2DS2-VASc score was ≥ 2, and antiarrhythmic therapy for AF was at the treating physician’s discretion.

2.5 Follow-up

Each enrolled patient was followed up at three and six months and then every six months, via telephone interviews or at outpatient clinics. During each follow-up, we collected information on drug treatments, arrhythmia symptoms, clinical outcomes and results of ECG and 24-hour Holter monitoring.

Figure 1. Study flowchart. AF: atrial fibrillation.
monitoring. Additional 24-hour Holter monitoring or ECG was performed if arrhythmic symptoms occurred.

2.6 Definition of outcomes

The primary outcome was time to all-cause mortality and the secondary outcome was time to cardiovascular mortality, stroke/TIA or cardiovascular hospitalization. In this study, participants were followed up from the date of enrollment until loss of follow-up, first outcome event, or December 31, 2017.

Atrial tachyarrhythmia (AT) episode was defined as recorded AT/atrial flutter/AF ≥ 30 seconds by 12-lead ECG or 24-hour Holter monitoring. Successful CA was defined as no onset of AT episode ≥ 30 seconds beyond three months blanking period.

2.7 Statistical analysis

To eliminate the influence of selection bias in the assessment of therapeutic effect, baseline differences were adjusted by propensity score matching. The propensity score matching was based on 18 demographic and clinical variables, including age, gender, BMI, type of AF, time since onset of AF, insurance, education, smoking, drinking, hypertension, HF, DM, ischemic stroke/TIA/peripheral thromboembolism, vascular disease, prior bleeding, rhythm/rate control drugs, anticoagulants, and CHA2DS2-VASc score. Subjects in the two groups were matched in a 1:1 ratio with the caliper width of 0.1. No replacements were used.

Continuous variables were presented as mean ± SD, whereas categorical variables were shown as numbers and proportions. Continuous variables were compared using the one-way ANOVA analysis, whereas categorical variables were compared using the χ² test. Cumulative incidence rates were estimated by Kaplan-Meier method, and statistical significance was examined using the log-rank test. Cox regression analysis was used to calculate the hazard ratio (HR) and 95% confidence interval (CI) of outcomes and to assess the association between outcomes and CA. Subgroup analyses were conducted stratified by gender, type of AF, time since onset of AF, and anticoagulants exposure in initiation. In the sensitivity analyses, multivariate Cox regression models were further used to estimate the association between CA and all-cause and cardiovascular mortality. A two-sided P-value < 0.05 was considered statistically significant. All statistical analyses were conducted by using SAS 9.4 (SAS Institute, Cary, NC, USA).

3 Results

3.1 Study population

From August 2011 to December 2017, 5,005 AF patients more than 75 years old were enrolled in the China-AF registry cohort. We identified 673 patients receiving CA and 3,333 patients as controls after excluding 95 subjects diagnosed with rheumatic mitral stenosis, 130 subjects receiving ablation before enrolled in this cohort, 275 subjects with follow-up time less than six months and 499 subjects with data missing. Finally, 571 ablated and 571 non-ablated subjects at baseline were selected based on the propensity score matching (Figure 1).

3.2 Baseline characteristics

The baseline characteristics of the two groups were illustrated in Table 1. Before matching, subjects in the ablation group were younger, mostly male, with lower BMI, a higher proportion of paroxysmal AF, well educated, and well health insurance coverage. Patients in the ablation group were less likely to have a history of congestive HF, ischemic stroke/TIA/peripheral thromboembolism, and vascular disease. Besides, subjects receiving CA were more likely to use anticoagulants (92.12% vs. 39.12%, P < 0.0001). After propensity score matching, the differences between the two groups were balanced.

In this matched cohort, one-year adherence rates of the ablation and non-ablation groups were 92.03% and 94.71%, respectively. The mean number of ablations in the ablation group was 1.07 ± 0.26 per patient.

3.3 All-cause mortality

During a mean follow-up of 39.75 ± 19.98 months, 24 patients died in the ablation group (incidence rate: 1.71 per 100 person-years), and 60 patients died in the non-ablation group (incidence rate: 3.65 per 100 person-years). The cumulative incidence of mortality was lower in the ablation group than in the non-ablation group (log-rank P = 0.0024). CA was associated with a 51% lower risk of all-cause mortality (HR = 0.49, 95% CI: 0.30–0.79) (Figure 2A).

3.4 Cardiovascular mortality

Of the propensity score-matched cohort, 6 subjects died of cardiovascular disease in the ablation group (incidence rate: 0.42 per 100 person-years), and 29 subjects died of cardiovascular disease in the non-ablation group (incidence rate: 1.75 per 100 person-years). CA was associated with a lower risk of cardiovascular mortality (HR = 0.25, 95% CI: 0.11–0.61) (Figure 2B).

3.5 Stroke/TIA

During the follow-up, 27 patients receiving CA developed stroke/TIA (incidence rate: 1.96 per 100 person-years), and 40 patients receiving medical therapy developed stroke/
Table 1. Baseline characteristics of AF patients (≥ 75 years old) with and without ablation before and after propensity score matching.

| Characteristic                              | Before matching | After matching |
|---------------------------------------------|-----------------|---------------|
|                                            | Ablation (n = 673) | No ablation (n = 3,333) | P-value | Ablation (n = 571) | No ablation (n = 571) | P-value |
| Age, yrs                                   | 77.72 ± 2.68    | 79.60 ± 3.90  | < 0.0001 | 77.93 ± 2.73    | 77.94 ± 2.72  | 0.9221 |
| Male                                       | 366 (54.38%)    | 1,669 (50.08%) | 0.0342 | 300 (52.54%)      | 294 (51.49%)   | 0.7223 |
| Body mass index                            | 24.84 ± 3.39    | 24.55 ± 3.48  | 0.0478 | 24.81 ± 3.33    | 25.03 ± 3.52  | 0.2931 |
| Type of AF                                 | < 0.0001        |               |         | 0.4295           |               |         |
| Newly diagnosed                            | 42 (6.24%)      | 412 (12.36%)  |         | 37 (6.48%)       | 37 (6.48%)    |         |
| Paroxysmal                                 | 445 (66.12%)    | 1,482 (44.46%)|         | 367 (64.27%)     | 347 (60.77%)  |         |
| Persistent                                 | 186 (27.64%)    | 1,439 (43.17%)|         | 167 (29.25%)     | 187 (32.75%)  |         |
| Times since onset of AF, yrs               | 0.3475          |               |         | 0.5378           |               |         |
| < 1                                        | 230 (34.18%)    | 1,078 (32.34%)|         | 201 (35.20%)     | 211 (36.95%)  |         |
| ≥ 1                                        | 443 (65.82%)    | 2,255 (67.66%)|         | 370 (64.80%)     | 360 (63.05%)  |         |
| Health insurance coverage                  | < 0.0001        |               |         | 0.8251           |               |         |
| 100%                                       | 74 (11.00%)     | 673 (20.19%)  |         | 73 (12.78%)      | 80 (14.01%)   |         |
| Basic social medical insurance for urban employees | 353 (52.45%)    | 718 (21.54%)  |         | 287 (50.26%)     | 266 (46.58%)  |         |
| Basic social medical insurance for urban residents | 156 (23.18%)    | 1,444 (43.32%)|         | 148 (25.92%)     | 159 (27.85%)  |         |
| Cooperative medical insurance for rural residents | 22 (3.27%)      | 313 (9.39%)   |         | 19 (3.33%)       | 17 (2.98%)    |         |
| None                                       | 11 (1.63%)      | 94 (2.82%)    |         | 11 (1.93%)       | 10 (1.75%)    |         |
| Others                                     | 57 (8.47%)      | 91 (2.73%)    |         | 33 (5.78%)       | 39 (6.83%)    |         |
| Education                                  | 0.0005          |               |         | 0.6163           |               |         |
| Completed college school                   | 221 (32.84%)    | 877 (26.31%)  |         | 196 (34.33%)     | 188 (32.92%)  |         |
| Under college school                       | 452 (67.16%)    | 2,456 (73.69%)|         | 375 (65.67%)     | 383 (67.08%)  |         |
| Smoking                                    | 38 (5.65%)      | 220 (6.60%)   | 0.3604 | 33 (5.78%)       | 31 (5.43%)    | 0.7969 |
| Drinking                                   | 58 (8.62%)      | 257 (7.71%)   | 0.4213 | 51 (8.93%)       | 45 (7.88%)    | 0.5223 |
| Congestive heart failure                   | 126 (18.72%)    | 2,228 (66.85%)| < 0.0001 | 126 (22.07%)     | 145 (25.39%)  | 0.1863 |
| NYHA III-IV                                | 12 (1.78%)      | 761 (22.83%)  | < 0.0001 | 12 (2.10%)       | 18 (3.15%)    | 0.2672 |
| Hypertension                               | 519 (77.12%)    | 2,609 (78.28%)| 0.5107 | 439 (76.88%)     | 447 (78.28%)  | 0.5703 |
| Diabetes mellitus                          | 190 (28.23%)    | 988 (29.64%)  | 0.4625 | 163 (28.55%)     | 152 (26.62%)  | 0.4664 |
| Ischemic stroke/TIA/peripheral thromboembolism | 119 (17.68%)    | 816 (24.48%)  | 0.0001 | 108 (18.91%)     | 105 (18.39%)  | 0.8197 |
| Vascular disease                           | 131 (19.47%)    | 902 (27.06%)  | < 0.0001 | 106 (18.56%)     | 102 (17.86%)  | 0.7591 |
| Bleeding history                           | 38 (5.65%)      | 214 (6.42%)   | 0.4537 | 32 (5.60%)       | 32 (5.60%)    | 1.0000 |
| Rhythm/rate control drugs                  | 489 (72.66%)    | 2,433 (73.00%)| 0.8849 | 408 (71.45%)     | 411 (71.98%)  | 0.8437 |
| Anticoagulants                             | 620 (92.12%)    | 1,304 (39.12%)| < 0.0001 | 518 (90.72%)     | 524 (91.77%)  | 0.5299 |
| CHA2DS2-VASc score                         | 4.25 ± 1.31     | 5.04 ± 1.50   | < 0.0001 | 4.32 ± 1.32      | 4.35 ± 1.30   | 0.7870 |
| LVEF, %                                    | 65.00 ± 6.88    | 61.13 ± 10.03 | < 0.0001 | 64.64 ± 6.87     | 64.28 ± 7.39  | 0.3942 |

Data are presented as means ± SD or n (%). AF: atrial fibrillation; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; TIA: transient ischemic attack.

TIA (incidence rate: 2.48 per 100 person-years). There was no statistically significant difference in the cumulative incidence of stroke/TIA between the ablation group and the non-ablation group (log-rank P = 0.3431), and HR for stroke/TIA was 0.79 (95% CI: 0.48–1.28) in the ablation group compared with the non-ablation group (Figure 2C).

3.6 Cardiovascular hospitalization

Of the propensity score-matched cohort, 140 subjects developed cardiovascular hospitalization in the ablation group (incidence rate: 11.25 per 100 person-years), and 194 subjects developed cardiovascular hospitalization in the non-ablation group (incidence rate: 13.72 per 100 person-
years). There was no statistically significant difference in the cumulative incidence of cardiovascular hospitalization between ablation group and non-ablation group (log-rank $P = 0.1084$), and HR for cardiovascular hospitalization was 0.84 (95% CI: 0.67–1.04) in the ablation group compared with the non-ablation group (Figure 2D).

3.7 AT episode and anticoagulants use during each follow-up interval

The proportions of patients with AT episodes during each follow-up interval were shown in Figure 3A. In addition, during the follow-up, 341 patients (59.7%) in the ablation group remained AF-free, and 97 subjects (17.0%) in the non-ablation group remained AF-free. Ablation was associated with a 42% lower risk of AT recurrence (HR = 0.58, 95% CI: 0.49–0.68, $P < 0.0001$). The proportions of patients receiving anticoagulation therapy during each follow-up interval were illustrated in Figure 3B. The proportions of anticoagulants use in the ablation group were lower than those in the matched group.
3.8 Periprocedural complications

During the periprocedural period, stroke occurred in 2 patients, acute cardiac tamponade in 7 patients, groin hematoma in 4 patients, pseudoaneurysm in 4 patients, and arteriovenous fistula in 2 patients. No other periprocedural complications such as atro-esophageal fistula, pulmonary vein stenosis, major bleeding, or death were observed in the ablation group.

3.9 Subgroup analyses

The subgroup analyses, according to gender, type of AF, time since onset of AF, and anticoagulants exposure in initiation were shown in Figure 4. The results did not show significant heterogeneity in analyses of the subgroups, with one exception. The effect of CA on cardiovascular hospitalization differed by type of AF ($P_{interaction\text{-value}} = 0.0177$). Cardiovascular mortality was not analyzed in subgroups due to fewer events.

3.10 Sensitivity analyses

In this matched cohort, we further conducted regression analyses of factors associated with all-cause and cardiovascular mortality. Age, congestive HF, hypertension, DM, stroke/TIA, vascular disease, and prior bleeding were controlled in the analyses of all-cause and cardiovascular mortality. In multivariate Cox regression analyses, ablation remained statistically associated with a lower risk of all-cause mortality (HR = 0.49, 95% CI: 0.30–0.78) and cardiovascular mortality (HR = 0.25, 95% CI: 0.10–0.59) (supplemental material, Table 1S & Table 2S).

4 Discussion

Our main finding in the prospective observational study was that ablated elderly patients with AF had a lower risk of all-cause and cardiovascular mortality than non-ablated elderly patients. Besides, we did not find a statistical difference between propensity-matched groups in the rate of stroke/TIA and cardiovascular hospitalization. Furthermore, subgroup analyses demonstrated that the risk of all-cause mortality was not affected by gender, type of AF, time since onset of AF, and anticoagulants exposure in initiation.

AF is an arrhythmia with an increased prevalence in the elderly. Meanwhile, AF is associated with an increased risk of HF, loss of cognitive functions, and AF-related cerebrovascular accidents, all of which tend to be more devastating and debilitating in elderly patients. At present,
Figure 4. Risk of the all-cause mortality (A), stroke/transient ischemic attack (B) and cardiovascular hospitalization (C) in clinically relevant subgroups. AF: atrial fibrillation; HR: hazards ratio.
CA has been proved to be an efficacious method for AF patients.\[^9\] The beneficial effects of CA on maintaining sinus rhythm and improving quality of life were already confirmed,\[^{10,11}\] whereas the association between CA and long-term benefits was controversial. Most of patients in large trials of CA for AF were young people, and there were few data on CA for AF in elderly patients. Considering the high incidence of AF in the elderly, more attention should be paid to AF ablation in the elderly.

So far, some published studies have revealed that AF ablation was efficacious in the elderly.\[^{13-18}\] Overall, most of these studies have shown similar clinical success rates between the younger and older groups, and major complications might be more frequent in the elderly. However, few observational studies reported in the literature have assessed the long-term benefits of CA in the elderly. Hence, studies focusing on the long-term effect of CA for AF in the elderly are needed. In this study, we prospectively enrolled the AF patients more than 75 years old, collected data purposely, used the propensity score matching, and accessed the relationship between CA and long-term outcomes in elderly patients with AF.

Previous observational studies in the general population have compared outcomes between subjects who received CA and those who did not, and the outcomes were conflicting.\[^{24-27}\] CABANA randomized trial showed the strategy of CA did not significantly reduce the composite endpoint of death, disabling stroke, serious bleeding, or cardiac arrest compared to medical therapy among AF patients.\[^{28}\] However, the lower-than-expected event rates and treatment crossovers in this trial affected the treatment effect of ablation. Thus, whether CA for AF prolongs survival remains obscure. Considering that the majority of participants in previous observational studies were younger, it is unclear whether elderly patients with AF can benefit from CA. The present study showed a strong association between ablation and survival in elderly patients with AF (HR = 0.49, 95% CI: 0.30–0.79). In line with our findings, Nademanee, et al.\[^{29}\] compared CA with antiarrhythmic drugs in AF patients (age ≥ 75 years old) and found that elderly patients with AF benefited from CA, which was associated with lower mortality risk (annual mortality rate 4% in catheter group and 9.8% in non-ablation group). However, this study compared crude rates and included a limited number of individuals (261 ablated and 63 pharmacologically treated elderly patients with AF). Theoretically, the mortality risk was reduced by multiple factors, including prevented worsening of HF, restoration of sinus rhythm, and reduced AF burden.\[^{1,30}\]

Elderly patients with AF have a higher risk of stroke.\[^{31}\] The risk of stroke in patients with AF is strongly influenced by several demographic and clinical factors, including age, sex, HF, hypertension, DM, prior stroke or TIA, and vascular disease.\[^{32}\] Anticoagulant therapy was an effective therapy to prevent AF patients from suffering strokes.\[^{33}\] Meanwhile, among elderly patients with AF, anticoagulants were consistently associated with a lower risk of stroke and positive net clinical benefit, with the highest benefit in elderly patients treated with warfarin who achieved therapeutic range ≥ 60% or high dose of NOACs.\[^{34,35}\] Our previous study found that the proportion of AF patients receiving anticoagulants was only 37.5%, 32.7%, and 25.4% for patients with CHADS\(^2\) ≥ 2, 1, and 0, respectively.\[^{36}\] In recent years, with the popularization of NOACs and the improvement of doctors’ awareness of prescribing anticoagulants, the overall rate of anticoagulants initiation was increasing. In the present study, 90.72% of patients in the ablation group and 91.77% of patients in the non-ablation group were treated with anticoagulants after propensity score-matched. Therefore, it was not surprising that the risk of stroke/TIA was not significantly reduced in this study.

It has been demonstrated that AF patients were at higher risk of hospitalization. An analysis from ROCKET AF showed that the hospitalization rate was 10.2 per 100 person-years of follow-up in AF subjects, and cardiovascular causes contributed nearly a half.\[^{37}\] Mitral regurgitation was aggravated, atrial systolic function was lost and left ventricular systolic dysfunction occurred in AF patients. Therefore, elimination of AF with CA may improve HF symptoms and reduce cardiovascular hospital admissions associated with AF.\[^{38,39}\] Recently, some randomized trials explored the effect of CA on hospitalization in AF patients with HF and noted that the hospitalization rate of patients undergoing CA was significantly lower than that of the medical treatment group.\[^{12,40,41}\] However, there was limited evidence for assessing the relationship between CA for AF and cardiovascular hospitalization in elderly patients. In the present study, we found that CA for AF did not reduce cardiovascular hospitalization in elderly patients compared with medical therapy. It might be that elderly patients suffer from multiple cardiovascular diseases simultaneously, and cardiovascular hospitalization not caused by AF increased in elderly patients. Because we didn’t collect the causes of cardiovascular hospitalization, the effect of ablation on HF in elderly patients with AF remained unknown.

4.1 Limitations

This study has several limitations. Firstly, although the propensity score matching was used to ensure the consistency of baseline data between the two groups, there may
still be some residual bias due to unmeasured covariates. Secondly, among 571 subjects assigned to the medical treatment group, 48 patients (8.41%) underwent CA during the follow-up period, and intention-to-treat analysis was used in this study. Thirdly, CA techniques and medical treatments may have changed during the long-term study, which may affect the outcomes. Last but not least, because our research is an observational study, it could not determine a causal relationship.

4.2 Conclusions

In elderly patients with AF, CA may be associated with a lower incidence of mortality and does not statistically reduce the risk of stroke/TIA and cardiovascular hospitalization. Therefore, CA may be the preferred treatment for elderly patients with symptomatic and drug-refractory AF.

Acknowledgments

This study was supported by the National Key Research and Development Program of China (2017YFC0908803 & 2018YFC1312501 & 2016YFC0900901 & 2016YFC1301002 & 2020YFC2004803). All authors had no conflicts of interest to disclose. The authors gratefully acknowledge the China- AF investigators for assistance in the data collection.

References

1. Benjamin EJ, Wolf PA, D’Agostino RB, et al. Impact of atrial fibrillation on the risk of death: the Framingham Heart Study. Circulation 1998; 98: 946–952.
2. Chugh SS, Havmoeller R, Narayanam K, et al. Worldwide epidemiology of atrial fibrillation: a Global Burden of Disease 2010 Study. Circulation 2014; 129: 837–847.
3. Heeringa J, van der Kuip DA, Hofman A, et al. Prevalence, incidence and lifetime risk of atrial fibrillation: the Rotterdam study. Eur Heart J 2006; 27: 949–953.
4. Di Carlo A, Bellino L, Consoli D, et al. Prevalence of atrial fibrillation in the Italian elderly population and projections from 2020 to 2060 for Italy and the European Union: the FAF Project. Europace 2019; 21: 1468–1475.
5. Krijthe BP, Kunst A, Benjamin EJ, et al. Projections on the number of individuals with atrial fibrillation in the European Union, from 2000 to 2060. Eur Heart J 2013; 34: 2746–2751.
6. Curtis AB, Rich MW. Atrial fibrillation in the elderly: mechanisms and management. Heart Rhythm 2007; 4: 1577–1579.
7. Desai Y, El-Chami MF, Leon AR, et al. Management of atrial fibrillation in elderly adults. J Am Geriatr Soc 2017; 65: 185–193.
8. Dayer M, Hardman SM. Special problems with antiarrhythmic drugs in the elderly: safety, tolerability, and efficacy. Am J Geriatr Cardiol 2002; 11: 370–375.
9. Calkins H, Hindricks G, Cappato R, et al. 2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation. Europace 2017; 20: e1–e160.
10. Mark DB, Anstrom KJ, Sheng S, et al. Effect of catheter ablation vs. medical therapy on quality of life among patients with atrial fibrillation: the CABANA randomized clinical trial. JAMA 2019; 321: 1275–1285.
11. Blomström-Lundqvist C, Gizarunson S, Schwieler J, et al. Effect of catheter ablation vs. antiarrhythmic medication on quality of life in patients with atrial fibrillation: the CAPTAF randomized clinical trial. JAMA 2019; 321: 1059–1068.
12. Marrouche NF, Brachmann J, Andresen D, et al. Catheter ablation for atrial fibrillation with heart failure. N Engl J Med 2018; 378: 417–427.
13. Blandino A, Toso E, Scaglione M, et al. Long-term efficacy and safety of two different rhythm control strategies in elderly patients with symptomatic persistent atrial fibrillation. J Cardiovasc Electrophysiol 2013; 24: 731–738.
14. Metzner I, Wissern E, Tilz RR, et al. Ablation of atrial fibrillation in patients ≥ 75 years: long-term clinical outcome and safety. Europace 2016; 18: 543–549.
15. Bulava A, Hanis J, Dusek L. Clinical outcomes of radiofrequency catheter ablation of atrial fibrillation in octogenarians: 10-year experience of a one high-volume center. J Geriatr Cardiol 2017; 14: 575–581.
16. Kautzner J, Peichl P, Sramko M, et al. Catheter ablation of atrial fibrillation in elderly population. J Geriatr Cardiol 2017; 14: 563–568.
17. Lioni L, Letsas KP, Efremidis M, et al. Catheter ablation of atrial fibrillation in the elderly. J Geriatr Cardiol 2014; 11: 291–295.
18. Mikhailov EN, Szili-Torok T, Lebedev DS. Percutaneous interventions in elderly patients with atrial fibrillation: left atrial ablation and left atrial appendage occlusion. J Geriatr Cardiol 2017; 14: 541–546.
19. Du X, Ma C, Wu J, et al. Rationale and design of the Chinese Atrial Fibrillation Registry Study. BMC Cardiovasc Disord 2016; 16: 130.
20. Dong JZ, Sang CH, Yu RH, et al. Prospective randomized comparison between a fixed ‘2C3L’ approach vs. stepwise approach for catheter ablation of persistent atrial fibrillation. Europace 2015; 17: 1798–1806.
21. Maisel WH, Stevenson LW. Atrial fibrillation in heart failure: epidemiology, pathophysiology, and rationale for therapy. Am J Cardiol 2003; 91: 2D–3D.
22. Diener HC, Hart RG, Koudstaal PJ, et al. Atrial fibrillation and cognitive function: JACC review topic of the week. J Am Coll Cardiol 2019; 73: 612–619.
23. Freedman B, Potpara TS, Lip GY. Stroke prevention in atrial fibrillation. Lancet 2016; 388: 806–817.
24. Lin YJ, Chao TF, Tsao HM, et al. Successful catheter ablation reduces the risk of cardiovascular events in atrial fibrillation patients with CHA₂DS₂-VASc risk score of 1 and higher.
Effect of radiofrequency catheter ablation for atrial fibrillation on morbidity and mortality: a nationwide cohort study and propensity score analysis. *Circ Arrhythm Electrophysiol* 2014; 7: 76–82.

Friberg L, Tabrizi F, Englund A. Catheter ablation for atrial fibrillation is associated with lower incidence of stroke and death: data from Swedish health registries. *Eur Heart J* 2016; 37: 2478–2487.

Saliba W, Schliamser JE, Lavi I, *et al.* Catheter ablation of atrial fibrillation is associated with reduced risk of stroke and mortality: a propensity score-matched analysis. *Heart Rhythm* 2017; 14: 635–642.

Packer DL, Mark DB, Robb RA, *et al.* Effect of catheter ablation vs antiarrhythmic drug therapy on mortality, stroke, bleeding, and cardiac arrest among patients with atrial fibrillation: the CABANA randomized clinical trial. *JAMA* 2019; 321: 1261–1274.

Nademanee K, Amnueypol M, Lee F, *et al.* Benefits and risks of catheter ablation in elderly patients with atrial fibrillation. *Heart Rhythm* 2015; 12: 44–51.

Hunter RJ, McCready J, Diab I, *et al.* Maintenance of sinus rhythm with an ablation strategy in patients with atrial fibrillation is associated with a lower risk of stroke and death. *Heart* 2012; 98: 48–53.

Yii GS, Howard DP, Paul NL, *et al.* Age-specific incidence, outcome, cost, and projected future burden of atrial fibrillation-related embolic vascular events: a population-based study. *Circulation* 2014; 130: 1236–1244.

Lip GY, Nieuwlaat R, Pisters R, *et al.* Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. *Chest* 2010; 137: 263–272.

Steffel J, Verhamme P, Potpara TS, *et al.* The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation. *Eur Heart J* 2018; 39: 1330–1393.

Chao TF, Liu CJ, Lin YJ, *et al.* Oral anticoagulation in very elderly patients with atrial fibrillation: a nationwide cohort study. *Circulation* 2018; 138: 37–47.

Alnsasra H, Haim M, Senderey AB, *et al.* Net clinical benefit of anticoagulant treatments in elderly patients with nonvalvular atrial fibrillation: experience from the real world. *Heart Rhythm* 2019; 16: 31–37.

Chang SS, Dong JZ, Ma CS, *et al.* Current status and time trends of oral anticoagulation use among Chinese patients with nonvalvular atrial fibrillation: the Chinese Atrial Fibrillation Registry Study. *Stoke* 2016; 47: 1803–1810.

DeVore AD, Hellkamp AS, Becker RC, *et al.* Hospitalizations in patients with atrial fibrillation: an analysis from ROCKET AF. *Eurpaece* 2016; 18: 1135–1142.

Joy PS, Gopinathannair R, Olshansky B. Effect of ablation for atrial fibrillation on heart failure readmission rates. *Am J Cardiol* 2017; 120: 1572–1577.

Mansour M, Heist EK, Agarwal R, *et al.* Stroke and cardiovascular events after ablation or antiarrhythmic drugs for treatment of patients with atrial fibrillation. *Am J Cardiol* 2018; 121: 1192–1199.

Di Biase L, Mohanty P, Mohanty S, *et al.* Ablation versus amiodarone for treatment of persistent atrial fibrillation in patients with congestive heart failure and an implanted device: results from the AATAC multicenter randomized trial. *Circulation* 2016; 133: 1637–1644.

Prabhu S, Taylor AJ, Costello BT, *et al.* Catheter ablation versus medical rate control in atrial fibrillation and systolic dysfunction: the CAMERA-MRI study. *J Am Coll Cardiol* 2017; 70: 1949–1961.