Thromboembolic Risk of Cessation of Oral Anticoagulation Post Catheter Ablation in Patients With and Without Atrial Fibrillation Recurrence

Bing Rong, MD[a,b,#], Wenqiang Han, MD[a,#], Mingjie Lin, PhD[a,c], Li Hao, MD[d], Kai Zhang, PhD, MD[a], Tongshuai Chen, PhD, MD[a], Rina Sha, MD[a], Juntao Wang, MD[a,e], Rong Wang, MD[a], and Jingquan Zhong, PhD, MD[a,e,*]

Cessation of oral anticoagulation (OAC) is common after the first 3 months of catheter ablation of atrial fibrillation (AF); however, thromboembolic risk has not been defined in patients with and without AF recurrence (RAF vs NRAF) post ablation. We identified 796 patients who discontinued OAC at 3 months post AF ablation from January 2015 to May 2018 in our center. Regular follow-up was performed to detect RAF, collect medication management and thromboembolic and major bleeding events. CHA_2DS_2-VASc score was 1.79 ± 1.50; 547 (68.7%) patients were at intermediate and high risk (i.e., CHA_2DS_2-VASc score ≥1 in male patients, or ≥2 in female patients); 169 (21.2%) were RAF. During 29.2±12.2 months follow-up, the incidence rate of thromboembolism was 1.62 per 100 patient-year (7 in 431 years) in RAF, 0.33 per 100 patient-year (5 in 1,503 years) in NRAF. After adjusting for potential confounding factors, RAF was associated with more 3.5-fold higher rate of thromboembolism compared with NRAF (adjusting HR, 4.488; 95% CI, 1.381 to 14.586). Rate of thromboembolism was even higher in patients with intermediate and high risk (2.16 per 100 patient-year [7 in 323 years] vs 0.38 per 100 patient-year [4 in 1,043 years], aHR, 5.807; 95% CI, 1.631 to 20.671). In multivariate logistic regression analysis, RAF was the only independent predictor of thromboembolism (4.837 [1.498 to 15.621], p = 0.008). In conclusion, cessation of OAC in NRAF may be reasonable, especially for patients with the contraindications for continuing OAC; however, cessation of OAC appeared unsafe in RAF with a high-risk stroke profile because of high incidence rate of thromboembolism. **(Am J Cardiol 2020;137:55−62)**

Atrial fibrillation (AF), the most common arrhythmia, is associated with an approximately five-fold increased risk of stroke.[1,2] Catheter ablation is effective as rhythm control strategy in AF patients.[3] Use of long-term oral anticoagulation (OAC) treatment, that is, after the first 3 months post ablation of AF, remains controversial. Although studies have reported a low incidence rate of thromboembolism after ablation in patients discontinuing OAC compared with those continuing OAC,[4,5] the thromboembolic risk has been inconsistent particularly in studies including patients with and without AF recurrence.[6−9] Cessation of OAC is common (from 30% to 95%) in AF patients who underwent or not underwent catheter ablation.[4,10−13] In patients with versus those without AF recurrence (RAF vs NRAF) after ablation, the incidence rate and hazard risk of thromboembolism after OAC discontinuation remains unclear. We therefore reviewed data on efficacy and complications after catheter ablation at our center to investigate the incidence rate of thromboembolic events and to identify the risk factors for thromboembolism after cessation of OAC in patients with and without AF recurrence.

Methods

This study was approved by the local institutional Ethics Committee, and written informed consent was obtained from all participants. The present analysis of events of thromboembolism and major bleeding (MB) after cessation of OAC at 3 months post ablation was based on data from a prospective observational study (Chinese Clinical Trial Registry: ChiCTR-OCH-14004674) with three-year follow-up of patients who underwent ablation for AF at our center. All patients who underwent AF catheter ablation between January 2015 and May 2018 were consecutively included

[a]The Key Laboratory of Cardiovascular Remodeling and Function Research, Chinese Ministry of Education, Chinese National Health Commission and Chinese Academy of Medical Sciences, The State and Shandong Province Joint Key Laboratory of Translational Cardiovascular Medicine, Department of Cardiology, Qilu Hospital, Cheeloo College of Medicine, Shandong University, Jinan, China; [b]Department of Geriatric Medicine, Qilu Hospital, Cheeloo College of Medicine, Shandong University, Jinan, China; [c]Department of Cardiology, Peking University First Hospital, Beijing, China; [d]Department of Health Cardiology, Shandong Provincial Qianfoshan Hospital, Shandong University, Jinan, China; and [e]Department of Cardiology, Qilu Hospital (Qingdao), Cheeloo College of Medicine, Shandong University, Qingdao, China. Manuscript received August 13, 2020; revised manuscript received and accepted September 22, 2020.

This work was supported by Natural Science Foundation of China (81970282); Biosense Webster Inc. (IIS-324); Shandong Provincial Natural Science Foundation, China, (ZR2018MH002); The Key Research and Development Plan of Shandong Province (2017GSF18165).

[#]These authors equally contributed to the study.

See page 61 for disclosure information.

*Corresponding Author: Tel: +86 18560086597; fax 86(531)86927544.

E-mail address: 18560086597@163.com (J. Zhong).

0002-9149/
https://doi.org/10.1016/j.amjcard.2020.09.036

in the study unless they met any of the following exclusion criteria: (1) valvular heart disease; (2) follow-up for <12 months; or (3) thromboembolic or MB events during the first 3 months after ablation.

Baseline data were collected before procedure. CHA_2DS_2-VASc score was used to stratify thromboembolic risk. CHA_2DS_2-VASc scores of 0, 1, ≥2 in male patients and 1, 2, ≥3 in female patients were considered to correspond to low, intermediate and high risk of thromboembolism, respectively. HAS-BLED score was used to evaluate bleeding risk; no score points were given for use of nonsteroidal anti-inflammatory drugs (except antiplatelet drugs) or labile international normalized ratio values because of incomplete information.

Medical management during the first 3 months after ablation has been previously described.[14] Heart rhythm was evaluated by electrocardiography (ECG) and 24-hour Holter monitoring at 1, 3, and 6 months and every 6 months thereafter. If the patient did not show up for scheduled follow-up monitoring visits, our follow-up office would call the patient to collect information on recurrence and complications within one month. After the 3-month observation period postablation, OAC use in patients without AF recurrence was determined in conjunction with the electrophysiologist; OAC use was encouraged in the high-risk RAF patients.

Study primary outcomes included rates of thromboembolism and MB events. Thromboembolism events included ischemic stroke, transient ischemic attack, and systemic embolism, which were diagnosed based on symptoms and computerized tomography or magnetic resonance imaging. MB events included intracranial hemorrhage and any other bleeding events requiring hospitalization. Timing and outcome of primary events were recorded during follow-up.

Data analysis was performed using SPSS 25.0 (IBM Corp.), and the significance level was set at $p < 0.05$. Crude incidence rates of thromboembolic events were expressed as rates per 100 patient-years. Cumulative survival free from thromboembolic outcome is presented as Kaplan-Meier curve. Cox hazard regression analysis was used to calculate the hazard ratio of the thromboembolic risk between RAF and NRAF groups. Factors associated with thromboembolism during follow-up were analyzed using uni- and multivariable logistic regression analyses.

Results

As shown in Figure 1, of the 871 consecutive patients who underwent catheter ablation between January 2015 and May 2018, 796 patients were included in the present analysis and underwent 826 catheter ablation procedures (average 1.04 per patient). Mean CHA_2DS_2-VASc score was 1.79 ± 1.50; 547 (68.7%) patients were at intermediate and high risk. Follow-up duration was 29.2 ± 12.2 months. During follow-up, all patients had at least one ECG or 24h Holter evaluation after 3 months post ablation, whereas only 479 (60.2%) had 24h Holter recording. Three patients died of cancer, fatal stroke, and myocardial infarction, respectively, after 12 months post ablation. 169 (21.2%) patients developed atrial tachyarrhythmia after the 3-month observational period, 24 (14.2%) developed persistent AF, and 14 (8.3%) were asymptomatic. Comparison of baseline and follow-up data between RAF and NRAF are presented in Table 1. CHA_2DS_2-VASc score, and the proportion of antiplatelet drugs and antiarrhythmic drugs were higher in RAF versus NRAF ($p < 0.05$).

Overall, 12 patients experienced thromboembolic events (Table 2) and 1 patient suffered an MB event (subarachnoid hemorrhage in patient without AF recurrence). No patient on continuous OAC experienced a thromboembolic or MB event. The rate of sequela was numerically higher in RAF versus NRAF (4/7 vs 1/5). The incidence rate of thromboembolic events was 0.33 per 100 patient-year (5 in 1,503 patient-years) in NRAF, and 1.62 per 100 patient-year (7 in

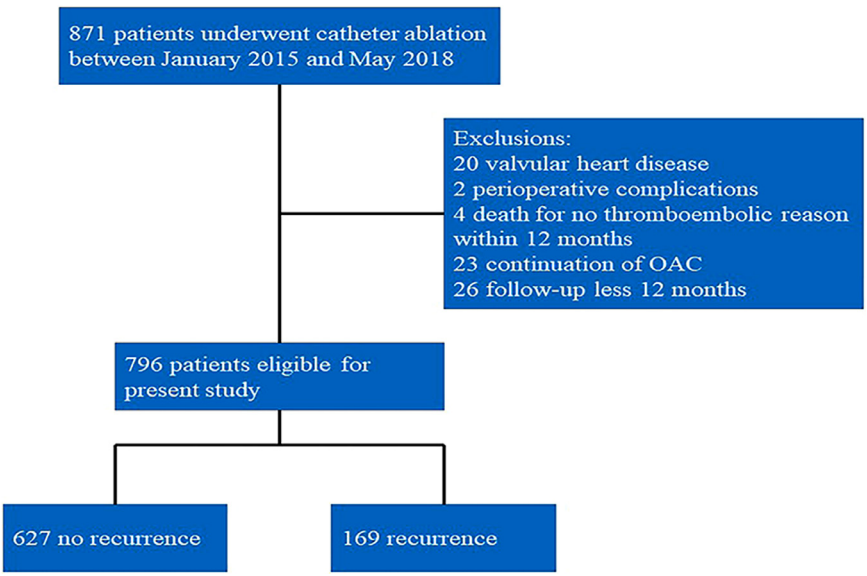

Figure 1. Flowchart of study patients with atrial fibrillation. OAC, oral anticoagulation.

Table 1
Baseline and follow-up information

	Overall (n = 796)		Intermediate or High Risk (n = 547)	
	No Recurrence (n = 627)	Recurrence (n = 169)	No Recurrence (n = 419)	Recurrence (n = 128)
Age, mean (SD) (years)	58.5(10.4)	60.1(11.0)	61.9(9.6)	63.4(9.1)
≥65	144(23.0%)	54(32.0%)*	144(34.4%)	54(42.2%)
≥75	31(4.9%)	10(5.9%)	31(7.4%)	10(7.8%)
Men	393(62.7%)	102(60.4%)	252(60.1%)	74(57.8%)
Persistent AF	244(38.9%)	62(36.7%)	169(41.9%)	52(40.6%)
Congestive heart failure	22(3.5%)	12(7.1%)*	22(5.3%)	12(9.4%)
Hypertension	298(47.5%)	84(49.7%)	298(71.1%)	84(65.6%)
Diabetes mellitus	86(13.7%)	23(13.6%)	86(20.5%)	23(18.0%)
Prior stroke/TIA/systemic embolism	53(8.5%)	16(9.5%)	53(12.6%)	16(12.5%)
Vascular disease	132(21.1%)	45(26.6%)	132(31.5%)	45(35.2%)
CHA2DS2-VASc score, mean (SD)	1.73(1.46)	1.99(1.63)*	2.43(1.27)	2.53(1.50)
HAS-BLED score, mean (SD)	0.75(0.77)	0.79(0.74)	0.97(0.80)	0.98(0.72)
Renal disease	0 (0%)	0(0%)	0(0%)	0(0%)
Liver disease	7(1.1%)	0(0%)	5(1.2%)	0(0%)
Anemia	14(2.2%)	9(5.3%)*	10(2.4%)	6(4.7%)
Alcohol consumption	171(27.3%)	44(26.0%)	115(26.3%)	36(28.1%)
Body mass index, kg/m^2, mean (SD)	26.06(4.18)	25.93(4.52)	26.15(4.29)	26.02(4.97)
LAD ≥ 40 mm	277(44.2%)	86(50.9%)	205(48.9%)	77(60.2%)†
Follow-up duration, mean(SD) (months)	28.8(12.0)	30.7(12.8)	29.9(11.6)	30.3(12.8)
24h holter monitoring	389(62.0%)	90(53.3%)*	261(62.3%)	64(50.0%)†
Antiplatelet drugs	107(17.1%)	47(27.8%)*	90(21.5%)	40(31.3%)†
Antiarrhythmic drugs	137(21.9%)	82(48.5%)*	107(25.5%)	65(50.8%)†
ACEI/ARB	99(15.8%)	26(15.4%)	94(22.4%)	25(19.5%)
Statins	11(1.8%)	3(1.8%)	9(2.1%)	3(2.3%)

Abbreviations: ACEI = angiotensin converting enzyme inhibitors; ARB = Angiotensin receptor blockers; AF = atrial fibrillation; CHA2DS2-VASc = congestive heart failure, hypertension, age 75 years or older (doubled), diabetes, stroke (doubled), vascular disease, age 65 to 74 years, sex category (female); HAS-BLED = hypertension, abnormal renal or liver function, stroke, bleeding history or predisposition, labile international normalized ratio, elderly, drugs or alcohol concomitantly; LAD = left atrial diameter.

* $p<0.05$, compared with no recurrence in total patients.

† $p<0.05$, compared with no recurrence in intermediate or high risk patients.

431 patient-years) in RAF. In patients at intermediate and high risk, the incidence rate of thromboembolic events was 0.38 per 100 patient-year (4 in 1,043 patient-years) in NRAF, and 2.16 per 100 patient-year (7 in 323 patient-years) in RAF. Compared with NRAF, after adjusting potential confounders, RAF had significantly higher incidence rate of thromboembolic events (Table 3 and Supplementary Table S1). The NRAF patients had higher cumulative survival rate from thromboembolism (Figure 2); thromboembolic events occurred 6 months after ablation and occurred post the first recording episode of recurrent AF in these patients (6/7, Table 2).

As listed in Table 4, in univariable logistic regression analysis, CHA_2DS_2-VASc score was associated with thromboembolic events in patients overall and in RAF, but not in NRAF (Supplementary Table S2). No other factors were associated with thromboembolic events in this investigation. In multivariable logistic regression analysis, after adjustment for age and gender, CHA_2DS_2-VASc score was not an independent predictor, in patients overall or in RAF (1.406 [0.920 to 2.147], $p = 0.115$; and 1.592 [0.977 to 2.594], $p = 0.062$ respectively). If adding AF recurrence as potential factor, in multivariable logistic regression analysis, AF recurrence was the only independent predictor in all patients (4.837 [1.498 to 15.621], $p = 0.008$).

Discussion

The present retrospective review of our center follow-up data, which to the best of our knowledge is the first to compare the thromboembolic risk of cessation of OAC in RAF and NRAF after catheter ablation documented: (1) a low rate of thromboembolic events after successful catheter ablation; (2) an approximately 3.5-fold higher incidence rate of thromboembolic events in RAF versus NRAF; and (3) that the efficacy of catheter ablation may impact important role on thromboembolic risk of whom OAC had been discontinued.

Catheter ablation has been associated with improvement in structural remodeling, hemodynamic function of the left atrium (LA) and intra-LA blood stasis in NRAF, which would decrease risk for thrombogenesis.[15] Results from a large prospective real-world observational registry study of Chinese patients with AF (n = 4512) indicated that compared with patients continuing long-term OAC after successful ablation, the thromboembolic risk was low in patients discontinuing long-term OAC (0.54 vs 0.86 per 100 patient-years), as was risk for MB events (0.19 vs 0.35 per 100 patient-years).[4] Similarly, for patients who had undergone successful ablation, Themistoclakis et al.[5] reported that the incidence rate of ischemic stroke and MB events was lower in patients off OAC than in those on OAC

Table 2
Characteristics of patients with thromboembolic events

	sex	Age (years)	LAD (mm)	BMI (kg/m^2)	CHA2DS2-VASc Score	Prior Thromboembolism	HAS-BLED Score	Alcohol Consumption
No recurrence	Male	66	50	27.5	2	No	2	Yes
	Male	71	30	26.8	1	No	2	Yes
	Male	45	41	41.5	0	No	0	No
	Male	62	36	25.9	1	No	0	No
	Female	61	38	38.2	4	No	0	No
Recurrence	Male	73	43	22	5	Yes	2	No
	Female	65	37	25.7	6	Yes	1	No
	Female	66	51	24.6	4	No	1	No
	Male	74	39	22.4	3	No	3	Yes
	Male	53	40	24.1	1	No	0	No
	Female	58	45	30	3	No	0	No
	Female	62	41	22.5	2	No	1	No

Type of AF at Baseline	Type of AF Post Ablation	Recurrent Time, Months	Antiplatelet Drugs Post Blank Period	Embolic Events	Embolic Time Post Ablation, Months	Sequelae
Paroxysm	NA	NA	Aspirin	Stroke	27	No
Paroxysm	NA	NA	Aspirin	Stroke	28	No
Persistence	NA	NA	No	TIA	18	No
Paroxysm	NA	NA	No	Stroke	6	No
Persistence	NA	NA	Aspirin	Stroke	14	Slurred speech
Paroxysm	Paroxysm	36	Aspirin	Stroke	24	No
Paroxysm	Paroxysm	6	Aspirin	Stroke	12	Numb thumb
Persistence	Paroxysm	3	Aspirin	Stroke	6	Death
Paroxysm	Paroxysm	3	No	Stroke	8	No
Persistence	Paroxysm	3	No	Renal embolism	13	No
Persistence	Persistence	3	No	Stroke	18	Hemiplegia
Paroxysm	Paroxysm	3	Aspirin	Stroke	13	Hemiplegia

Abbreviations: AF = atrial fibrillation; BMI = body mass index; CHA2DS2-VASc = congestive heart failure, hypertension, age 75 years or older (doubled), diabetes, stroke (doubled), vascular disease, age 65 to 74 years, sex category (female); HAS-BLED = hypertension, abnormal renal or liver function, stroke, bleeding history or predisposition, labile international normalized ratio, elderly, drugs or alcohol concomitantly; LAD = left atrial diameter; NA = not available.

(0.07% vs 0.45%, p = 0.06; 0.04% vs 2%, p < 0.0001). In the present study, in NRAF, the incidence rate of thromboembolism was 0.33 or 0.38 per 100 patient-year in the overall or intermediate and high risk populations. The annual incidence of stroke events for general Chinese population was 377 per 100,000 in 2013.[16] Therefore, consistent with study by Yang *et al.*,[4] for NRAF, thromboembolic risk was low and similar to the general population.

Table 3
Univariable and multivariable Cox regression for the incidence of thromboembolic events in all patients (n = 796)

Variable	Univariate		Multivariate	
	HR(95% CI)	p-value	HR(95% CI)	p-value
AF recurrence	5.097(1.617−16.061)	0.005	4.488(1.381−14.586)	0.013
Age	1.044(0.984−1.107)	0.155	1.046(0.935−1.170)	0.430
Female sex	1.222(0.388−3.852)	0.732	1.213(0.148−9.916)	0.857
Persistent AF	0.791(0.238−2.626)	0.701	0.716(0.190−2.689	0.620
Congestive heart failure	1.895(0.245−14.689)	0.541	1.758(0.117−26.338)	0.683
Hypertension	2.046(0.616−6.798)	0.242	2.007(0.268−15.016)	0.498
Diabetes mellitus	1.908(0.516−7.054)	0.333	1.928(0.266−14.004)	0.516
Prior stroke/TIA /systemic embolism	1.817(0.397−8.315)	0.441	2.485(0.085−72.358)	0.597
Vascular disease	2.166(0.685−6.847)	0.188	1.848(0.254−13.457)	0.544
CHA2DS2-VASc score	1.349(0.977−1.862)	0.069	0.731(0.157−3.395)	0.689
Smoking	0.723(0.196−2.670)	0.626	0.716(0.121−4.226)	0.713
Alcohol consumption	0.955(0.258−3.531)	0.945	1.350(0.225−8.118)	0.743
LAD ≥ 40 mm	1.687(0.535−5.317)	0.372	1.310(0.377−4.555)	0.671
Obesity	0.926(0.251−3.419)	0.908	0.930(0.240−3.598)	0.916

Abbreviations: AF = atrial fibrillation; CHA2DS2-VASc, congestive heart failure, hypertension, age 75 years or older (doubled), diabetes, stroke (doubled), vascular disease, age 65 to 74 years, sex category (female); HAS-BLED = hypertension, abnormal renal or liver function, stroke, bleeding history or predisposition, labile international normalized ratio, elderly, drugs or alcohol concomitantly; LAD = left atrial diameter.

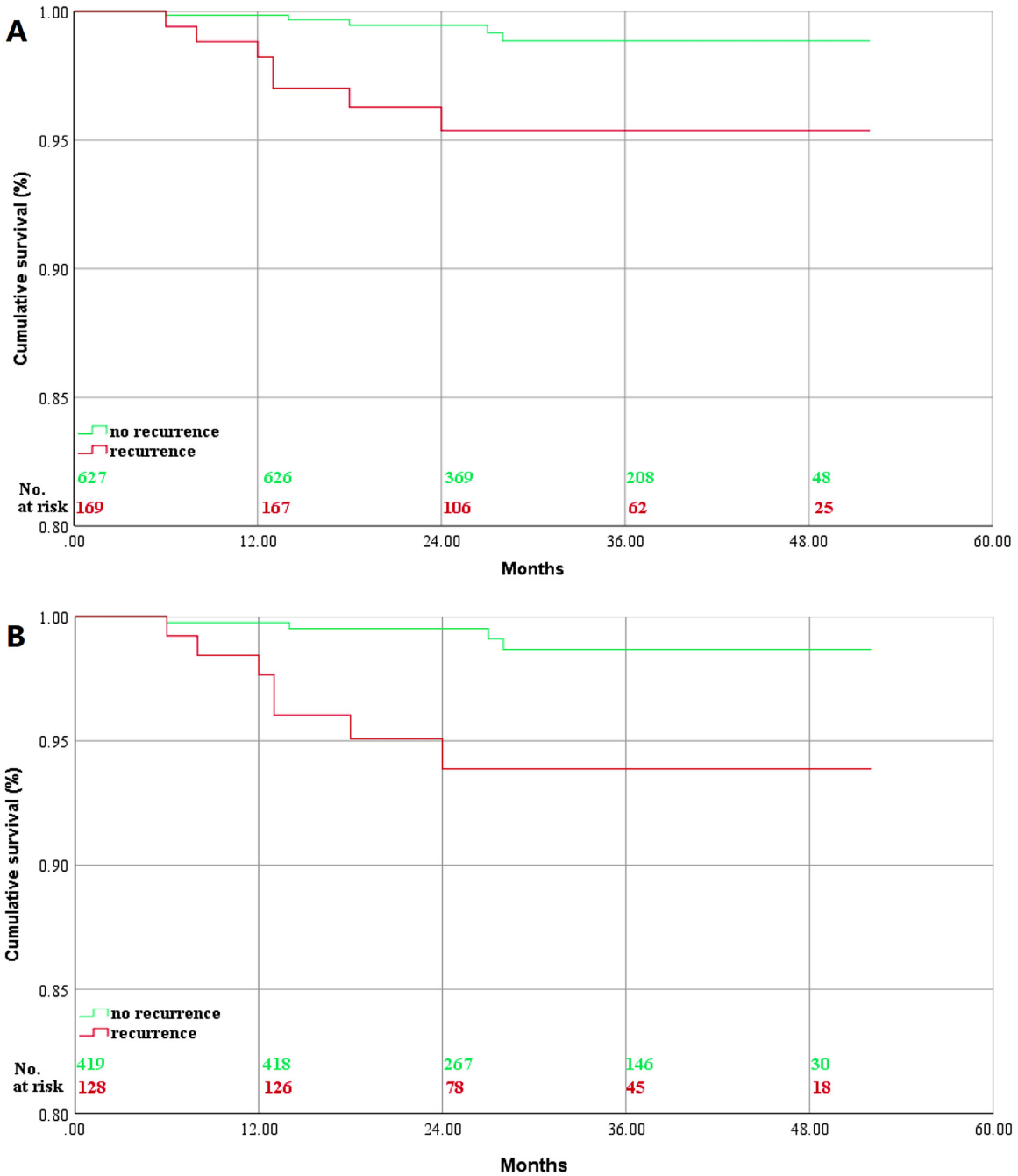

Figure 2. Kaplan-Meier curves for cumulative survival free from thromboembolic events in overall (A, p = 0.002) and in intermediate and high risk (B, p = 0.001) patient populations.

Some studies have reported on thromboembolic risk for RAF vs. NRAF. Bunch et al.[7] reported that across all $CHADS_2$ scores and ages, AF patients who underwent ablation had a similar long-term risk of stroke to that of patients without AF but lower than that of patients who did not undergo ablation. Another study based on Danish administrative registries[8] reported similar thromboembolic incidence rates in patients on and off OAC, even in those at high-risk (CHA_2DS_2-VASc score ≥2). In contrast, in the Swedish catheter ablation register,[6] patients with CHA_2DS_2-VASc score ≥2 and off warfarin treatment had a higher rate of ischemic stroke compared with those on warfarin treatment (1.6% vs 0.3% per year, p = 0.046). The inconsistency in results may result from differences in race/ethnicity, proportion of complications, follow-up duration, and incidence of recurrence. Indeed, in this study, AF recurrence was significantly associated with increased thromboembolic risk in univariate model,[8] and in the Swedish catheter ablation register[6] or Taiwanese ablated patients,[17] 8 of 11 patients with ischemic stroke events had suffered AF recurrence, which may indicate that it is not proper to evaluate the thromboembolic risk in mixed patient

Table 4
Individual risk factors associated with thromboembolism after AF ablation in all and recurrent patients

Variable	Univariate (n = 796)		Multivariate (n = 796)	
	HR(95% CI)	p-value	HR(95% CI)	p-value
Age	1.043(0.983−1.107)	0.166	1.015(0.949−1.086)	0.664
Female sex	1.178(0.370−3.744)	0.782	1.524(0.419−5.535)	0.522
Persistent AF	0.798(0.238−2.673)	0.714		
Congestive heart failure	0.483(0.061−3.856)	0.493		
Hypertension	2.193(0.655−7.341)	0.203		
Diabetes mellitus	2.132(0.568−8.002)	0.262		
Prior stroke/TIA /systemic embolism	2.140(0.459−9.971)	0.332		
Vascular disease	2.542(0.797−8.108)	0.115		
CHA2DS2-VASc score	1.399(1.008−1.942)	0.045	1.406(0.920−2.147)	0.115
Smoking	0.733(0.197−2.732)	0.644		
Alcohol consumption	0.899(0.241−3.354)	0.875		
LAD ≥ 40 mm	1.683(0.530−5.349)	0.377		
Obesity	0.935(0.251−3.488)	0.921		
Variable	Univariate (Recurrence, n = 169)		Multivariate (Recurrence, n = 169)	
	HR(95% CI)	p-value	HR(95% CI)	p-value
Age	1.044(0.965−1.130)	0.286	0.996(0.907−1.093)	0.925
Female sex	2.095(0.454−9.675)	0.343	1.079(0.907−1.093)	0.929
Persistent AF	0.680(0.128−3.614)	0.651		
Congestive heart failure	2.288(0.253−20.725)	0.462		
Hypertension	6.462(0.761−54.882)	0.087		
Diabetes mellitus	2.686(0.489−14.741)	0.255		
Prior stroke/TIA /systemic embolism	4.229(0.750−23.828)	0.102		
Vascular disease	2.143(0.460−9.972)	0.331		
CHA2DS2-VASc score	1.585(1.059−2.371)	0.025	1.592(0.977−2.594)	0.062
Smoking	0.447(0.052−3.819)	0.462		
Alcohol consumption	0.461(0.054−3.942)	0.480		
LAD ≥ 40 mm	2.500(0.417−13.260)	0.282		
Obesity	2.452(0.287−20.926)	0.412		

Abbreviations: AF = atrial fibrillation; CHA2DS2-VASc = congestive heart failure, hypertension, age 75 years or older (doubled), diabetes, stroke (doubled), vascular disease, age 65 to 74 years, sex category (female); HAS-BLED = hypertension, abnormal renal or liver function, stroke, bleeding history or predisposition, labile international normalized ratio, elderly, drugs or alcohol concomitantly; LAD = left atrial diameter.

populations with and without AF recurrence. In the present study, the incidence rate of thromboembolic events was much higher in RAF versus NRAF. In a single-center study, the estimated 5-year stroke incidence was 3% for patients discontinuing OAC after successful ablation compared with 23% for patients with AF recurrence remaining on warfarin.[18] The latter results suggest that it is reasonable to use a differential strategy in RAF versus NRAF. Noteworthy, consistent with previous studies,[5,6] in present study, all thromboembolic events happened post 6 months after ablation if cessation of OAC, which were mostly post the time of the first recording AF recurrence providing the practicable space to take timely intervention of OAC. However, the temporal association between the AF episode and need for OAC still needs further confirmation.

CHA_2DS_2-VASc score was significantly associated with increased thromboembolic risk (Table 4), as had been previously reported.[10] Of note, in the present study, CHA_2DS_2-VASc score was the only predictor of thromboembolism incidence in RAF but not in NRAF. In previous studies of patients who had undergone successful ablation or in mixed populations, previous thromboembolism was the only independent predictor in components of CHA_2DS_2-VASc score associated with thromboembolic events.[4,6,8] Although in our study, If adding AF recurrence as a potential factor, AF recurrence was the only independent strong predictor, which implies the performance of catheter ablation is a crucial factor for prognosis of AF patients after catheter ablation as previous study reported (174 ablated patients, 47 ± 23 months).[17] In accordance with the latest recommendations (2019AHA/ACC/HRS, 2017HRS/ EHRA/ECAS/APHRS/ SOLAECE expert consensus, 2020 ESC), [1,2,19] long-term continuation of OAC after 2 months post ablation should be based on the patient's stroke risk profile (i.e., CHA_2DS_2-VASc score), and not on the efficacy of ablation. Although the present study was a single-center observational study, its results underscore the need for differential management between patients with versus those without AF recurrence after ablation, which may translate into better outcomes.

Discontinuation of OAC may be reasonable in patients who had undergone successful ablation confirmed by strict post-procedure monitoring, especially for patients with poor treatment compliance or had the contraindications for continuing OAC, and low degree of atrial substrate; however, high level evidence is warranted. Patients who experience AF recurrence would appear to benefit from not

discontinuing OAC if they have a high-risk stroke profile because of high incidence rate of thromboembolic events.

The present study has the limitations inherent to its single-center observational design which may introduce selection bias; large-scale randomized studies are warranted to provide high-level evidence, such as the OCEAN trial.[20] AF recurrence may have been underestimated because of how the events were captured during follow-up which may have affected mostly the observed incidence rate of thromboembolism in AF free patients, therefore we need to interpret the results carefully. It would be better with extended ECG monitoring, like long-term daily life ECG or implantable loop recorders, to detect heart rhythm, build the relationship between AF burden and thromboembolic events, and improve medical care timely.[21–23] Moreover, the small sample size might underlie the lack of achievement of statistical significance in multivariate analysis for CHA_2DS_2-VASc score as a predictor of thromboembolic events. Finally, missing data for the components of the HAS-BLED might have led to a lower score.

Disclosures

No author has the potential conflicts of interest to any industry.

Data Availability Statements

The data underlying this article will be shared on reasonable request to the corresponding author.

Authors contribution

Bing Rong: Conceptualization, Methodology, Writing – Original Draft, Writing – Review & Editing; Wenqiang Han: Methodology, Formal analysis, Investigation, Data Curation; Mingjie Lin: Conceptualization, Writing – Original Draft, Writing – Review & Editing; Li Hao: Formal analysis, Investigation, Visualization; Kai Zhang: Methodology, Investigation, Resources; Tongshuai Chen: Investigation, Resources, Visualization; Rina Sha: Methodology, Investigation, Resources; Juntao Wang: Investigation, Resources, Visualization; Rong Wang: Investigation, Visualization, Funding acquisition; Jingquan Zhong: Conceptualization, Writing – Review & Editing, Supervision, Funding acquisition.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2020.09.036.

1. Calkins H, Hindricks G, Cappato R, Kim YH, Saad EB, Aguinaga L, Akar JG, Badhwar V, Brugada J, Camm J, Chen PS, Chen SA, Chung MK, Cosedis Nielsen J, Curtis AB, Davies DW, Day JD, d'Avila A, Natasja de Groot NMS, Di Biase L, Duytschaever M, Edgerton JR, Ellenbogen KA, Ellinor PT, Ernst S, Fenelon G, Gerstenfeld EP, Haines DE, Haissaguerre M, Helm RH, Hylek E, Jackman WM, Jalife J, Kalman JM, Kautzner J, Kottkamp H, Kuck KH, Kumagai K, Lee R, Lewalter T, Lindsay BD, Macle L, Mansour M, Marchlinski FE, Michaud GF, Nakagawa H, Natale A, Nattel S, Okumura K, Packer D, Pokushalov E, Reynolds MR, Sanders P, Scanavacca M, Schilling R, Tondo C, Tsao HM, Verma A, Wilber DJ, Yamane T, Document R. 2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation. *Europace* 2018;20:e1–e160.
2. Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, Blomstrom-Lundqvist C, Boriani G, Castella M, Dan GA, Dilaveris PE, Fauchier L, Filippatos G, Kalman JM, La Meir M, Lane DA, Lebeau JP, Lettino M, Lip GYH, Pinto FJ, Thomas GN, Valgimigli M, Van Gelder IC, Van Putte BP, Watkins CL, Group ESCSD. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS). *Eur Heart J* 2020.
3. Packer DL, Mark DB, Robb RA, Monahan KH, Bahnson TD, Poole JE, Noseworthy PA, Rosenberg YD, Jeffries N, Mitchell LB, Flaker GC, Pokushalov E, Romanov A, Bunch TJ, Noelker G, Ardashev A, Revishvili A, Wilber DJ, Cappato R, Kuck KH, Hindricks G, Davies DW, Kowey PR, Naccarelli GV, Reiffel JA, Piccini JP, Silverstein AP, Al-Khalidi HR, Lee KL, Investigators C. 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.
4. Yang WY, Du X, Jiang C, He L, Fawzy AM, Wang L, Liu C, Xia SJ, Chang SS, Guo XY, Li SN, Tang RB, Liu N, Bai R, Sang CH, Jiang CX, Yu RH, Long DY, Dong JZ, Lip GYH, Ma CS. The safety of discontinuation of oral anticoagulation therapy after apparently successful atrial fibrillation ablation: a report from the Chinese Atrial Fibrillation Registry study. *Europace* 2020;22:90–99.
5. Themistoclakis S, Corrado A, Marchlinski FE, Jais P, Zado E, Rossillo A, Di Biase L, Schweikert RA, Saliba WI, Horton R, Mohanty P, Patel D, Burkhardt DJ, Wazni OM, Bonso A, Callans DJ, Haissaguerre M, Raviele A, Natale A. The risk of thromboembolism and need for oral anticoagulation after successful atrial fibrillation ablation. *J Am Coll Cardiol* 2010;55:735–743.
6. Sjalander S, Holmqvist F, Smith JG, Platonov PG, Kesek M, Svensson PJ, Blomstrom-Lundqvist C, Tabrizi F, Tapanainen J, Poci D, Jonsson A, Sjalander A. Assessment of use vs discontinuation of oral anticoagulation after pulmonary vein isolation in patients with atrial fibrillation. *JAMA Cardiol* 2017;2:146–152.
7. Bunch TJ, May HT, Bair TL, Weiss JP, Crandall BG, Osborn JS, Mallender C, Anderson JL, Muhlestein BJ, Lappe DL, Day JD. Atrial fibrillation ablation patients have long-term stroke rates similar to patients without atrial fibrillation regardless of CHADS2 score. *Heart Rhythm* 2013;10:1272–1277.
8. Karasoy D, Gislason GH, Hansen J, Johannessen A, Kober L, Hvidtfeldt M, Ozcan C, Torp-Pedersen C, Hansen ML. Oral anticoagulation therapy after radiofrequency ablation of atrial fibrillation and the risk of thromboembolism and serious bleeding: long-term follow-up in nationwide cohort of Denmark. *Eur Heart J* 2015;36:307–314a.
9. Gallo C, Battaglia A, Anselmino M, Bianchi F, Grossi S, Nangeroni G, Toso E, Gaido L, Scaglione M, Ferraris F, Gaita F. Long-term events following atrial fibrillation rate control or transcatheter ablation: a multicenter observational study. *J Cardiovasc Med (Hagerstown)* 2016;17:187–193.
10. Bai Y, Wang YL, Shantsila A, Lip GYH. The global burden of atrial fibrillation and stroke: a systematic review of the clinical epidemiology of atrial fibrillation in Asia. *Chest* 2017;152:810–820.
11. Arai M, Okumura Y, Nagashima K, Watanabe I, Watanabe R, Wakamatsu Y, Otsuka N, Yagyu S, Kurokawa S, Ohkubo K, Nakai T, Yokoyama K, Ikeda A, Matsumoto N, Kunimoto S, Tachibana E, Iso K, Nomoto K, Tosaka T, Sonoda K, Hirayama A. Adverse clinical events during long-term follow-up after catheter ablation of atrial fibrillation. *Int Heart J* 2019;60:812–821.
12. Nuhrich JM, Kuck KH, Andresen D, Steven D, Spitzer SG, Hoffmann E, Schumacher B, Eckardt L, Brachmann J, Lewalter T, Hochadel M, Senges J, Willems S, Hoffmann BA. Oral anticoagulation is frequently discontinued after ablation of paroxysmal atrial fibrillation despite previous stroke: data from the German Ablation Registry. *Clin Res Cardiol* 2015;104:463–470.
13. Noseworthy PA, Yao X, Deshmukh AJ, Van Houten H, Sangaralingham LR, Siontis KC, Piccini JP Sr., Asirvatham SJ, Friedman PA, Packer DL, Gersh BJ, Shah ND. Patterns of anticoagulation use and cardioembolic risk after catheter ablation for atrial fibrillation. *J Am Heart Assoc* 2015;4:e002597.

14. Lin M, Hao L, Cao Y, Xie F, Han W, Rong B, Zhao Y, Zhong J. Successful radiofrequency catheter ablation of atrial fibrillation is associated with improvement in left ventricular energy loss and mechanics abnormalities. *Int J Cardiovasc Imaging* 2019;35:427–435.
15. Lin M, Hao L, Cao Y, Zhao Y, Rong B, Han W, Xie F, Zhong J. Successful catheter ablation of atrial fibrillation improves but not reverses the abnormalities of left atrial mechanics and energy loss. *Echocardiography* 2019;36:752–760.
16. Guan T, Ma J, Li M, Xue T, Lan Z, Guo J, Shen Y, Chao B, Tian G, Zhang Q, Wang L, Liu Y. Rapid transitions in the epidemiology of stroke and its risk factors in China from 2002 to 2013. *Neurology* 2017;89:53–61.
17. Lin YJ, Chao TF, Tsao HM, Chang SL, Lo LW, Chiang CE, Hu YF, Hsu PF, Chuang SY, Li CH, Chung FP, Chen YY, Wu TJ, Hsieh MH, Chen SA. Successful catheter ablation reduces the risk of cardiovascular events in atrial fibrillation patients with CHA2DS2-VASc risk score of 1 and higher. *Europace* 2013;15:676–684.
18. Nademanee K, Schwab MC, Kosar EM, Karwecki M, Moran MD, Visessook N, Michael AD, Ngarmukos T. Clinical outcomes of catheter substrate ablation for high-risk patients with atrial fibrillation. *J Am Coll Cardiol* 2008;51:843–849.
19. January CT, Wann LS, Calkins H, Chen LY, Cigarroa JE, Cleveland JC Jr., Ellinor PT, Ezekowitz MD, Field ME, Furie KL, Heidenreich PA, Murray KT, Shea JB, Tracy CM, Yancy CW. 2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. *J Am Coll Cardiol* 2019;74:104–132.
20. Verma A, Ha ACT, Kirchhof P, Hindricks G, Healey JS, Hill MD, Sharma M, Wyse DG, Champagne J, Essebag V, Wells G, Gupta D, Heidbuchel H, Sanders P, Birnie DH. The Optimal Anti-Coagulation for Enhanced-Risk Patients Post-Catheter Ablation for Atrial Fibrillation (OCEAN) trial. *Am Heart J* 2018;197:124–132.
21. Guo Y, Wang H, Zhang H, Liu T, Liang Z, Xia Y, Yan L, Xing Y, Shi H, Li S, Liu Y, Liu F, Feng M, Chen Y, Lip GYH, Investigators MI. Mobile Photoplethysmographic technology to detect atrial fibrillation. *J Am Coll Cardiol* 2019;74:2365–2375.
22. Guo Y, Lane DA, Wang L, Zhang H, Wang H, Zhang W, Wen J, Xing Y, Wu F, Xia Y, Liu T, Wu F, Liang Z, Liu F, Zhao Y, Li R, Li X, Zhang L, Guo J, Burnside G, Chen Y, Lip GYH, m AFAIITI. Mobile health technology to improve care for patients with atrial fibrillation. *J Am Coll Cardiol* 2020;75:1523–1534.
23. Chen LY, Chung MK, Allen LA, Ezekowitz M, Furie KL, McCabe P, Noseworthy PA, Perez MV, Turakhia MP. American Heart Association Council on Clinical C. Council on C. Stroke N. Council on Quality of C. Outcomes R. Stroke C. Atrial fibrillation burden: moving beyond atrial fibrillation as a binary entity: a scientific statement from the american heart association. *Circulation* 2018;137:e623–e644.