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Long-Term Anticoagulation Discontinuation After Catheter Ablation for Atrial Fibrillation

The ALONE-AF Randomized Clinical Trial

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IMPORTANCE Data from randomized clinical trials on a long-term anticoagulation strategy for patients after catheter-based ablation for atrial fibrillation (AF) are lacking.

OBJECTIVE To evaluate whether discontinuing oral anticoagulant therapy provides superior clinical outcomes compared with continuing oral anticoagulant therapy in patients without documented atrial arrhythmia recurrence after catheter ablation for AF.

DESIGN, SETTING, AND PARTICIPANTS A randomized clinical trial including 840 adult patients (aged 19-80 years) who were enrolled and randomized from July 28, 2020, to March 9, 2023, at 18 hospitals in South Korea. Enrolled patients had at least 1 non–sex-related stroke risk factor (determined using the CHA_2DS_2-VASc score [range, 0-9]) and no documented recurrence of atrial arrhythmia for at least 1 year after catheter ablation for AF. The CHA_2DS_2-VASc score is used as an assessment of stroke risk among patients with AF (calculated using point values for congestive heart failure, hypertension, ≥75 years of age, diabetes, stroke or transient ischemic attack, vascular disease, between 65 and 74 years of age, and sex category). The date of final follow-up was June 4, 2025.

INTERVENTIONS The patients were randomly assigned in a 1:1 ratio to discontinue oral anticoagulant therapy (n = 417) or continue oral anticoagulant therapy (with direct oral anticoagulants; n = 423).

MAIN OUTCOMES AND MEASURES The primary outcome was the first occurrence of a composite of stroke, systemic embolism, and major bleeding at 2 years. Individual components of the primary outcome (such as ischemic stroke and major bleeding) were assessed as secondary outcomes.

RESULTS Of the 840 adults randomized, the mean age was 64 (SD, 8) years, 24.9% were women, the mean CHA_2DS_2-VASc score was 2.1 (SD, 1.0), and 67.6% had paroxysmal AF. At 2 years, the primary outcome occurred in 1 patient (0.3%) in the discontinue oral anticoagulant therapy group vs 8 patients (2.2%) in the continue oral anticoagulant therapy group (absolute difference, −1.9 percentage points [95% CI, −3.5 to −0.3]; P = .02). The 2-year cumulative incidence of ischemic stroke was 0.3% in the discontinue oral anticoagulant therapy group vs 0.8% in the continue oral anticoagulant therapy group (absolute difference, −0.5 percentage points [95% CI, −1.6 to 0.6]). Major bleeding occurred in 0 patients in the discontinue oral anticoagulant therapy group vs 5 patients (1.4%) in the continue oral anticoagulant therapy group (absolute difference, −1.4 percentage points [95% CI, −2.6 to −0.2]).

CONCLUSIONS AND RELEVANCE Among patients without documented atrial arrhythmia recurrence after catheter ablation for AF, discontinuing oral anticoagulant therapy resulted in a lower risk for the composite outcome of stroke, systemic embolism, and major bleeding vs continuing direct oral anticoagulant therapy.

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Visual Abstract

Editorial

Supplemental content

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Atrial fibrillation (AF) represents a major contributor to health care burden and public health challenges.[1-4] Catheter ablation for AF has demonstrated superior efficacy over medical therapy in maintaining sinus rhythm and improving quality of life.[1,2,5] However, the effect of catheter ablation on long-term thromboembolic outcomes remains uncertain.[6,7] Current guidelines advocate for continued oral anticoagulant therapy after successful ablation in patients deemed to have a significant risk of thromboembolism,[1,2,8] yet the benefits and risks of prolonged oral anticoagulant therapy (particularly regarding stroke prevention vs bleeding risk) have yet to be evaluated in randomized clinical trials. Although a lower thromboembolic risk after discontinuation of oral anticoagulant therapy following ablation has been reported in studies using registry data and in cohort studies, these findings should be interpreted cautiously due to inherent study limitations.[9-12] Further evidence, particularly from randomized clinical trials, is needed to guide optimal anticoagulation strategies in this setting.

In patients who remain free of atrial arrhythmia recurrence after ablation, the need for continued anticoagulant therapy may diminish, potentially reducing bleeding-related safety concerns. The ALONE-AF trial (Anticoagulation One year after Ablation of Atrial Fibrillation in Patients with Atrial Fibrillation) was designed to evaluate whether discontinuing oral anticoagulant therapy could lead to fewer adverse events (including stroke, systemic embolism, and major bleeding) compared with continuing direct oral anticoagulant therapy in patients without documented AF recurrence for at least 1 year after ablation.

Key Points

Question In patients without documented atrial arrhythmia recurrence after catheter ablation and at least 1 non–sex-related stroke risk factor, does discontinuing oral anticoagulant therapy result in superior clinical outcomes compared with continuing oral anticoagulant therapy?

Findings In this multicenter randomized clinical trial including 840 patients, discontinuing oral anticoagulant therapy lowered the risk of the primary outcome (composite of stroke, systemic embolism, and major bleeding) compared with continuing oral anticoagulant therapy (0.3% vs 2.2%), primarily driven by fewer major bleeding events.

Meaning In patients without atrial arrhythmia recurrence after catheter ablation for atrial fibrillation, discontinuing oral anticoagulant therapy was associated with a lower risk of stroke, systemic embolism, or major bleeding vs continuing oral anticoagulant therapy.

Methods

Study Design

This investigator-initiated, open-label, multicenter, superiority randomized clinical trial was conducted across 18 centers in South Korea. Details of the trial rationale and design appear in Supplement 1 and have been published.[13] An institutional review board at each participating institution approved the trial protocol and all trial procedures adhered to the principles outlined in the Declaration of Helsinki. An independent data and safety monitoring board periodically reviewed unblinded patient-level data to safeguard trial integrity and participant safety. This study followed the Consolidated Standards of Reporting Trials (CONSORT) reporting guideline.

Study Population

Patients aged 19 to 80 years with a history of AF who had undergone AF catheter ablation were eligible for inclusion. Enrollment was limited to individuals at intermediate or high risk of thromboembolism (defined as a CHA_2DS_2-VASc score of ≥1 for men or ≥2 for women) who remained free from atrial arrhythmia recurrence for at least 1 year after ablation. The CHA_2DS_2-VASc score is used as an assessment of stroke risk among patients with AF (calculated using point values for congestive heart failure, hypertension, ≥75 years of age, diabetes, stroke or transient ischemic attack, vascular disease, between 65 and 74 years of age, and sex category).

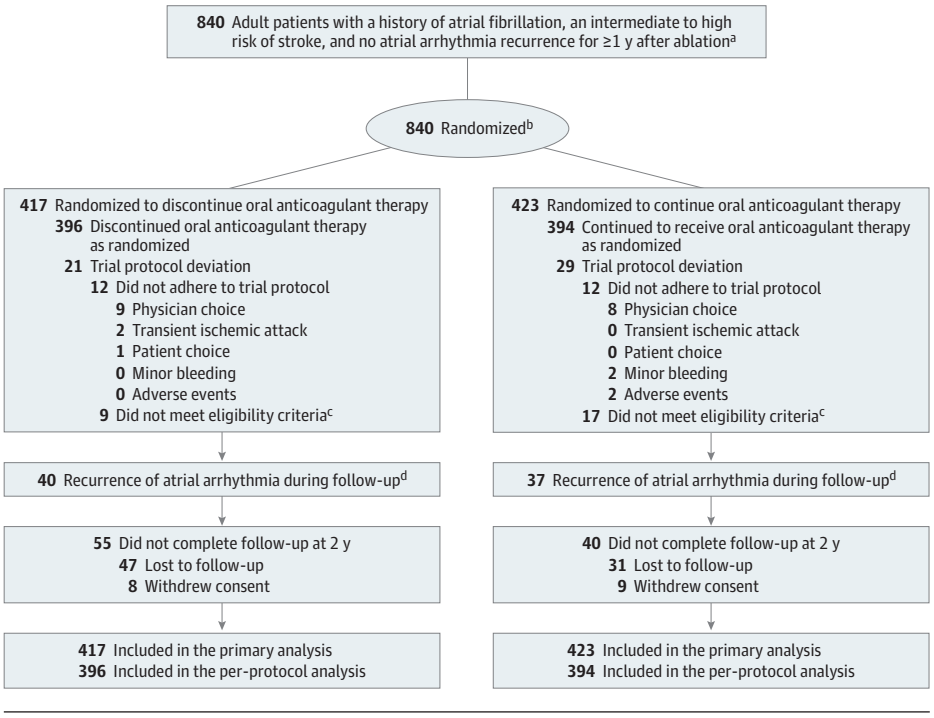
There was no upper time limit on the period from ablation to randomization. Atrial arrhythmia recurrence was defined as any documented episode lasting 30 seconds or longer for AF, atrial flutter, or atrial tachycardia, which was assessed after the ablation using at least 2 sessions of 24- to 72-hour Holter monitoring and electrocardiographic (ECG) monitoring. At least 1 of the sessions of Holter monitoring and ECG monitoring had to be performed within 2 months prior to enrollment. Full inclusion and exclusion criteria appear in eTable 1 in Supplement 2. All participants provided written informed consent before enrollment.

Randomization and Study Procedures

Eligible participants were randomized in a 1:1 ratio to either discontinue oral anticoagulant therapy or continue with this therapy (**Figure 1**). Randomization was performed using a web-based, permuted-block method with mixed block sizes of 4 and 6 at each participating site. The computer-generated allocation sequence was executed by an external programmer who was not involved in the trial. Physicians or research coordinators accessed patient allocation through a web-based response system.

Participants in the no oral anticoagulant group discontinued therapy (intervention group). Patients in the oral anticoagulant group continued to receive treatment with direct oral anticoagulants (control group); they received either 5 mg of apixaban twice daily or 20 mg of rivaroxaban once daily. The dose of apixaban was reduced to 2.5 mg twice daily in patients meeting at least 2 of the following criteria: (1) age of 80 years or older, (2) body weight of 60 kg or less, and (3) serum creatinine level of 1.5 mg/dL or greater (to convert to µmol/L, multiply by 76.25).[14] The dose of rivaroxaban was reduced to 15 mg once daily in patients with a creatinine clearance of 15 to 50 mL/min. Creatinine clearance was calculated using the Cockcroft-Gault formula.[15] In cases of intolerance to apixaban or rivaroxaban, an alternative direct oral anticoagulant could be prescribed at the investigator's discretion. Antiplatelet therapy was generally discouraged but allowed in both groups when clinically indicated (such as in

Figure 1. Flow of Patients in the ALONE-AF Trial



ALONE-AF indicates Anticoagulation One year after Ablation of Atrial Fibrillation in Patients with Atrial Fibrillation.

[a]An intermediate to high risk of stroke was defined as a CHA_2DS_2-VASc score of ≥1 for men and ≥2 for women. There were no data collected regarding screening.

[b]Randomization was performed without any adjustments or stratification.

[c]In the discontinue therapy group, 5 never underwent catheter ablation for atrial fibrillation, 2 were aged >80 years, and 2 had a CHA_2DS_2-VASc score of 0. In the continue therapy group, 10 never underwent catheter ablation for atrial fibrillation and 7 were aged >80 years.

[d]These patients were censored at the time of recurrence. Based on thromboembolic risk, anticoagulation was restarted in the discontinue therapy group or continued in the continue therapy group.

patients with percutaneous coronary intervention or acute coronary syndrome).

All patients underwent routine ECG monitoring at each follow-up visit and 24- to 72-hour Holter monitoring at least every 6 months. Additional Holter monitoring, event recorder use, or wearable ECG device use was recommended when patients reported symptoms suggestive of arrhythmia recurrence. If participants experienced a confirmed recurrence of atrial arrhythmia or underwent repeat AF ablation during the study, they were censored at the time of the event and anticoagulant therapy was reinitiated based on their thromboembolic risk.

Outcomes

The primary outcome was the first occurrence of a composite of stroke, systemic embolism, and major bleeding at 2 years. Stroke was defined as a sudden, focal neurological deficit resulting from a presumed cerebrovascular cause that persists for longer than 24 hours and was not attributable to a readily identifiable cause (such as a tumor or seizure).[16] Systemic embolism was defined as abrupt vascular insufficiency accompanied by clinical or radiological evidence of arterial occlusion, occurring in the absence of other likely mechanisms (eg, trauma, atherosclerosis, or instrumentation). Major bleeding was defined using criteria from the International Society on Thrombosis and Hemostasis.[17]

The secondary outcomes were the individual components of the primary outcome, clinically relevant nonmajor bleeding (as defined by the International Society on Thrombosis and Hemostasis criteria[18]), all-cause mortality, myocardial infarction, transient ischemic attack, and hospitalization due to any cause. Detailed definitions of the study outcomes appear in eTable 2 in Supplement 2. Adjudication of the outcomes was performed by an independent clinical event adjudication committee that remained blinded to treatment allocation and the primary outcome results of the study.

Sample Size Calculation

The study hypothesis was that discontinuing oral anticoagulant therapy would be superior to continuing oral anticoagulant therapy in reducing the incidence of the primary outcome. Assuming a dropout rate of 7%, and targeting 80% power with a 2-sided α level of .05, the total sample size required was calculated to be 840 patients with 420 patients allocated to each group.

The expected 2-year incidence rate for the primary outcome in the discontinue oral anticoagulant group was projected at 4.2%, reflecting an absolute risk reduction of 5.0% (equivalent to a relative risk reduction of 54%) that would primarily be attributable to a reduction in bleeding events.[19,20]

The expected 2-year incidence rate for the primary outcome in the continue oral anticoagulant therapy group was estimated at 9.2%, corresponding to an annual event rate of 4.6% (comprising an annual rate for stroke or systemic embolism of 1.0% after patients underwent catheter ablation to treat AF and an annual event rate of 3.6% for major bleeding, which was observed in a key randomized clinical trial of direct oral anticoagulants).[15,19,21]

Statistical Analysis

The continuous variables were summarized as means with SDs or medians with IQRs, depending on distribution. The categorical variables were presented as frequencies and percentages.

The primary outcome analysis was conducted based on the intention-to-treat population. Cumulative incidence at 2 years was estimated using the Kaplan-Meier method and 95% CIs were calculated for the between-group difference in event rates. The primary outcome was also evaluated in the per-protocol population, which excluded patients with protocol deviations such as ineligibility, lack of informed consent, or did not receive the assigned treatment.

The secondary outcomes were analyzed using cumulative incidence estimates derived from Kaplan-Meier curves, and comparisons were made accordingly. Due to the minimal amount of missing data across all variables (0.2%), a complete case analysis was performed without imputation. Patients lost to follow-up were censored at their last available assessment in the Kaplan-Meier analysis of the primary outcome. A subgroup analysis of the primary outcome was performed according to age, sex, type of AF, comorbidities, CHA_2DS_2-VASc score, and HAS-BLED score (calculated using point values for hypertension, kidney or liver disease, stroke history, prior bleeding, unstable international normalized ratio, >65 years of age, and drug or alcohol use).

For the sensitivity analysis, a multivariable Cox proportional hazards model was used to estimate the between-group difference in 2-year cumulative incidence of the primary outcome, adjusting for age and sex. To obtain marginal estimates, we predicted the 2-year event probabilities for each individual in the cohort under both treatment strategies, while holding their observed age and sex constant. The group-specific cumulative incidence was then calculated by averaging these individual-level predictions. A nonparametric bootstrap procedure with 5000 iterations was performed to account for sampling variability.

A 2-sided *P* value of <.05 was considered statistically significant. Due to the risk of type I error from multiple comparisons, the analyses for the secondary outcomes should be regarded as exploratory. All statistical analyses were performed using R version 3.5.2 (R Foundation for Statistical Computing).

Results

Between July 28, 2020, and March 9, 2023, 840 patients were randomized at 18 hospitals in South Korea (Figure 1); the mean age was 64 years (SD, 8 years), 209 (24.9%) were women, and 568 (67.6%) had paroxysmal AF. The date of final follow-up was June 4, 2025. The baseline characteristics of the patients appear in **Table 1**. The mean duration between catheter alation for AF and randomization was 3.6 years (SD, 3 years). The mean CHA_2DS_2-VASc score was 2.1 (SD, 1.0) and the mean HAS-BLED score was 1.8 (SD, 1.1). Among the 840 patients, 247 (29.4%) had a CHA_2DS_2-VASc score that was less than 2, 337 (40.1%) had a score of 2, 166 (19.8%) had a score of 3, and 90 (10.7%) had a score of 4 or greater (eFigure 1 in Supplement 2).

Radiofrequency ablation was performed in 360 of 412 patients (87.4%) in the no oral anticoagulant group vs 352 of 413 patients (85.2%) in the oral anticoagulant group after excluding patients with protocol deviations who never underwent catheter ablation for AF. The remaining patients underwent cryoballoon ablation (eTable 3 in Supplement 2). Pulmonary vein isolation was performed in all cases.

Treatments and Follow-Up

Details of the antithrombotic regimens administered after randomization appear in eTable 4 in Supplement 2. Of the 417 patients in the no oral anticoagulant group, 12 (2.9%) continued to receive oral anticoagulant therapy vs all 423 patients (100%) in the oral anticoagulant group. Of the 423 patients in the oral anticoagulant therapy group, 330 (78.0%) were prescribed 5 mg of apixaban (most common dose), 37 (8.7%) were prescribed 15 mg of rivaroxaban, and 31 (7.3%) were prescribed 20 mg of rivaroxaban. Of the 423 patients in the oral anticoagulant group, regular doses were prescribed for 362 (85.6%) and reduced doses were prescribed for 61 (14.4%). Of these 61 patients who received reduced doses of oral anticoagulant therapy, 14 (23.0%) met the criteria for dose reduction. Antiplatelet therapy was used in 36 of 417 patients (8.6%) in the no oral anticoagulant group vs 21 of 423 patients (5.0%) in the oral anticoagulant group.

At 2 years, follow-up was completed in 362 of 417 patients (86.8%) in the no oral anticoagulant group vs 383 of 423 patients (90.5%) in the oral anticoagulant group. Atrial arrhythmia recurred in 40 patients (9.6%) in the no oral anticoagulant group vs 37 patients (8.7%) in the oral anticoagulant group; the median time to recurrence after randomization was 12 months (IQR, 6.0-17.4 months) (eTable 5 in Supplement 2).

The per-protocol population analysis included 790 patients (396 in the no oral anticoagulant group vs 394 in the oral anticoagulant group) (eTable 6 in Supplement 2). The baseline characteristics of the per-protocol population appear in eTable 7 in Supplement 2.

Primary Outcome and Secondary Outcomes

At 2 years, the primary outcome occurred in 1 of 417 patients (0.3%) in the no oral anticoagulant group vs 8 of 423 patients (2.2%) in the oral anticoagulant group (absolute difference, -1.9 percentage points [95% CI, -3.5 to -0.3]; log-rank *P* = .02; **Table 2** and **Figure 2**A). To prevent 1 primary outcome event at 2 years, the number needed to treat for discontinuing oral anticoagulant vs continuing anticoagulant therapy was 53 patients (95% CI, 29 to 333 patients).

The 2-year cumulative incidence of ischemic stroke or systemic embolism was 0.3% in the no oral anticoagulant group vs 0.8% in the oral anticoagulant group (absolute difference, -0.5 percentage points [95% CI, -1.6 to 0.6]; Figure 2B). A transient ischemic attack occurred in 2 patients (0.6%) in the no oral anticoagulant group vs 0 patients in the oral anticoagulant group (absolute difference, 0.6 percentage points [95% CI, −0.2 to 1.3]).

The cumulative incidence of major bleeding was estimated at 0% in the no oral anticoagulant group vs 1.4% (n = 5) in the oral anticoagulant group (absolute difference, -1.4 percentage points [95% CI, -2.6 to -0.2]; Figure 2C). Clinically relevant nonmajor bleeding occurred in 5 patients (1.4%) in the no oral anticoagulant group vs 7 patients (1.9%) in the oral anticoagulant group. One patient in the oral anticoagulant group

Table 1. Baseline Characteristics of the Study Population

	Oral anticoagulant therapy status	
	Discontinued (n = 417)	Continued (n = 423)
Age, mean (SD), y	63 (8)	65 (8)
Sex, No. (%)[a]		
Male	321 (77.0)	310 (73.3)
Female	96 (23.0)	113 (26.7)
Type of atrial fibrillation, No. (%)[a]		
Paroxysmal	276 (66.2)	292 (69.0)
Persistent	141 (33.8)	131 (31.0)
Time from catheter ablation for atrial fibrillation to randomization, median (IQR), y	2.5 (1.4-5.2)	2.3 (1.2-4.5)
Medical history, No. (%)[a]		
Hypertension	293 (70.3)	291 (68.8)
Dyslipidemia	102 (24.5)	125 (29.6)
Diabetes	68 (16.3)	90 (21.3)
Heart failure	66 (15.8)	62 (14.7)
Stroke or transient ischemic attack	23 (5.5)	24 (5.7)
Chronic kidney disease	10 (2.4)	3 (0.7)
Myocardial infarction	4 (1.0)	8 (1.9)
Peripheral artery disease	3 (0.7)	10 (2.4)
Current, No. (%)[a]		
Drinking	121 (29.0)	107 (25.3)
Smoking	54 (12.9)	36 (8.5)
Risk assessment score, median (IQR)		
CHA_2DS_2-VASc[b]	2 (1-3)	2 (1-3)
HAS-BLED[c]	2 (1-3)	2 (1-3)
Blood pressure, median (IQR), mm Hg		
Systolic	128 (120-138)	127 (118-138)
Diastolic	77 (70-84)	75 (68-82)
Body mass index, median (IQR)[d]	25.3 (23.6-27.7)	25.0 (23.1-27.1)
Echocardiographic parameter, median (IQR)		
Left atrial dimension, mm	40 (37-43)	40 (37-44)
Left ventricle ejection fraction, %	61 (57-66)	62 (57-66)
Mitral inflow:mitral annulus tissue velocity ratio	8.9 (7.5-11.0)	9.2 (7.7-11.9)
Creatinine clearance, mean (SD), mL/min[e]	85.9 (13.1)	85.4 (14.1)

[a] Percentages may not total 100 because of rounding.

[b] Score is used as an assessment of stroke risk among patients with atrial fibrillation (calculated using point values for congestive heart failure, hypertension, ≥75 years of age, diabetes, stroke or transient ischemic attack, vascular disease, between 65 and 74 years of age, and sex category). The score range is 0 to 9; higher scores indicate a greater risk of stroke.

[c] Score is used as an assessment of major bleeding risk among patients with atrial fibrillation receiving anticoagulant therapy (calculated using point values for hypertension, kidney or liver disease, stroke history, prior bleeding, unstable international normalized ratio, >65 years of age, and drug or alcohol use). The score range is 0 to 9; higher scores indicate a greater risk of bleeding.

[d] Calculated as weight in kilograms divided by height in meters squared.

[e] Assessed using the Cockcroft-Gault formula.[15] A reference range of approximately 90 to 120 mL/min is considered appropriate in healthy adults. Lower levels are observed in older individuals.

had a hemorrhagic stroke that resulted in permanent disability (eTable 8 in Supplement 2). Detailed data on bleeding severity (as defined by various bleeding criteria and bleeding sites) appear in eTable 9 in Supplement 2. There were no reported cases of all-cause mortality or myocardial infarction in either group.

Sensitivity and Subgroup Analyses

The results for the primary outcome and the major ischemic and bleeding events in the per-protocol population (eTable 10 in Supplement 2) were generally consistent with those observed in the intention-to-treat population. For the primary outcome, the estimates at 2 years were 0.3% in the no oral anticoagulant group vs 2.3% in the oral anticoagulant group (absolute difference, −2.0 percentage points [95% CI, −3.7 to −0.3]; **Figure 3**). The treatment effect of oral anticoagulant discontinuation on the primary outcome appeared consistent across all subgroups (eFigure 2 in Supplement 2). After adjustment for age and sex, the difference in the cumulative incidence of the primary outcome remained significant (absolute difference, -2.2 percentage points [95% CI, -25.5 to 0]).

Discussion

In this multicenter randomized clinical trial evaluating long-term anticoagulation strategies in patients without documented AF recurrence after catheter ablation, the risk for the primary composite outcome of stroke, systemic embolism, and major bleeding was lower after discontinuing oral anticoagulant therapy than when oral anticoagulant therapy was continued. This result was primarily attributable to a reduction in major bleeding events, whereas the incidence of ischemic complications remained comparable between groups.

Table 2. Primary and Secondary Outcomes at 2 Years

	Oral anticoagulant therapy status, No. of patients (%)[a]		Absolute difference, percentage points (95% CI)[a]
	Discontinued (n = 417)	Continued (n = 423)	
Primary outcome			
Composite of stroke, systemic embolism, and major bleeding	1 (0.3)	8 (2.2)	−1.9 (−3.5 to −0.3)[b]
Secondary outcomes: elements of the primary outcome[c]			
Stroke	1 (0.3)	5 (1.4)	−1.1 (−2.4 to 0.3)
Ischemic	1 (0.3)	3 (0.8)	−0.5 (−1.6 to 0.6)
Hemorrhagic	0	2 (0.6)	−0.6 (−1.3 to 0.2)
Systemic embolism	0	0	
Major bleeding	0	5 (1.4)	−1.4 (−2.6 to −0.2)
Intracranial	0	2 (0.6)	−0.6 (−1.3 to 0.2)
Gastrointestinal	0	2 (0.5)	−0.5 (−1.3 to 0.2)
Other	0	1 (0.3)	−0.3 (−0.8 to 0.3)
Additional secondary outcomes[c]			
Transient ischemic attack	2 (0.6)	0	0.6 (−0.2 to 1.3)
Myocardial infarction	0	0	
Clinically relevant nonmajor bleeding	5 (1.4)	7 (1.9)	−0.5 (−2.4 to 1.4)
All-cause mortality	0	0	
Hospitalization due to any causes	30 (8.3)	38 (10.0)	−1.7 (−5.8 to 2.5)

[a] The percentages were calculated with the use of a Kaplan-Meier survival analysis of data in the intention-to-treat population; therefore, the percentages may not reflect the ratio of the numerator and the denominator.

[b] P = .02 using the log-rank test for superiority.

[c] For all of the secondary outcomes, the 95% CIs were not adjusted for multiple comparisons; therefore, inferences drawn may not be reproducible.

The current guideline recommendations[1,2,8] for continuing oral anticoagulant therapy after ablation for AF are not supported by randomized clinical trials specifically addressing this question. Although observational studies have suggested a reduced stroke risk after catheter ablation for AF,[21,22] the evidence has been inconsistent and often underpowered to confirm whether ablation alone lowers thromboembolic events. Notably, the CABANA (Catheter Ablation vs Antiarrhythmic Drug Therapy for Atrial Fibrillation) trial[6] did not demonstrate a significant reduction in stroke risk after ablation, which is consistent with findings from a systematic review and meta-analysis[23] comparing AF ablation and antiarrhythmic drug therapy that failed to show superiority of ablation in preventing strokes. Moreover, a large observational study[24] including 6866 patients undergoing AF ablation in the US reported increased stroke risk in patients with a CHA_2DS_2-VASc score of 2 or greater who discontinued anticoagulant therapy after 3 months. However, findings from Kanaoka et al[12] suggest that patients undergoing AF ablation may carry a lower thromboembolic risk than the broader AF population not receiving anticoagulant therapy, and discontinuation (even in those with a $CHADS_2$ score of 2) of therapy was not associated with a higher thromboembolic risk but was associated with a lower major bleeding risk.

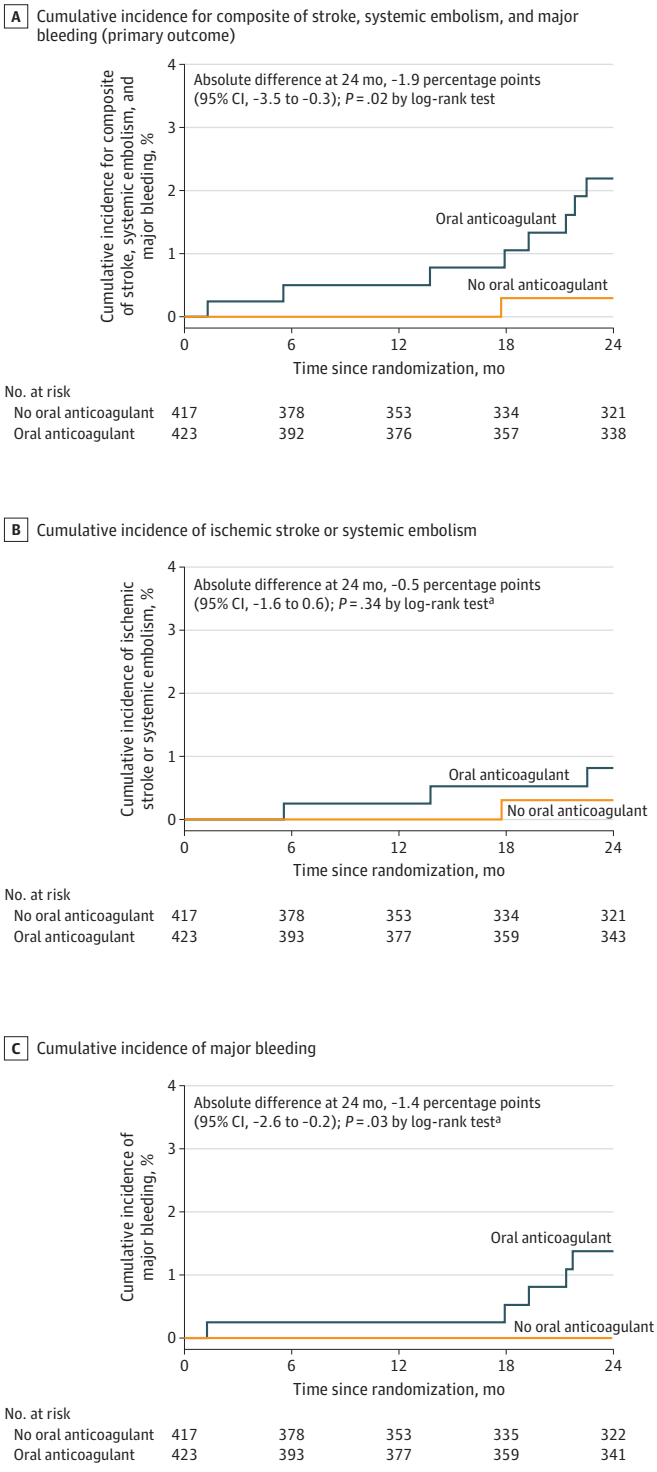
Given the limited evidence from randomized clinical trials, clinical equipoise remains that justifies further investigation. The OPTION (Comparison of Anticoagulation With Left Atrial Appendage Closure After AF Ablation) trial[25] included patients at moderate to high risk for stroke who underwent AF ablation and showed that left atrial appendage closure followed by discontinuation of anticoagulant therapy reduced bleeding complications while maintaining a low incidence of stroke compared with continuation of oral anticoagulant therapy. In the present study, the rate of ischemic stroke was low in both treatment groups, likely reflecting a reduced AF burden after ablation.

Notably, even among high-risk patients (CHA_2DS_2-VASc score ≥4) in the current study, discontinuing anticoagulation was not associated with an increased stroke risk or an increased risk for the primary composite outcome. Consistently, in the NOAH-AFNET 6 (Non-Vitamin K Antagonist Oral Anticoagulants in Patients with Atrial High Rate Episodes) trial,[26] which included patients with subclinical AF and a median CHA_2DS_2-VASc score of 4, treatment with edoxaban did not show a benefit in reducing stroke compared with placebo while increasing bleeding risk, suggesting a lower stroke risk in the setting of low AF burden.

Among patients with AF, continuation of any antithrombotic therapy exposed them to an elevated risk for bleeding, which was demonstrated in the AVERROES (Apixaban Vs Acetylsalicylic Acid to Prevent Stroke in Atrial Fibrillation Patients Who Have Failed or Are Unsuitable for Vitamin K Antagonist Treatment) trial[27] that reported annual major bleeding rates of 1.4% in the apixaban group and 1.2% in the aspirin group. In the present study, antiplatelet use was discouraged, and only 8.6% of patients in the no oral anticoagulant group received antiplatelet agents, which likely contributed to the low observed incidence of bleeding events without an associated increase in thromboembolic risk.

When discontinuation of oral anticoagulant therapy is considered, incorporating regular rhythm monitoring to detect AF recurrence is important given the poor correlation

Figure 2. Primary and Secondary Outcomes

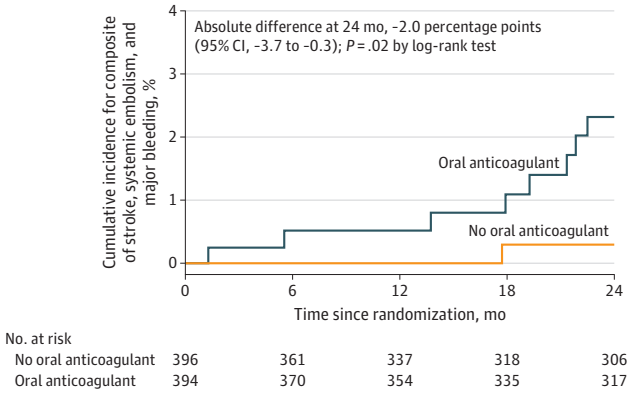


The data are presented as Kaplan-Meier curves for the primary outcome (composite of stroke, systemic embolism, and major bleeding) and for the secondary outcomes of ischemic stroke or systemic embolism and major bleeding. A total of 745 of 840 participants (88.7%) completed 2-year follow-up (median, 2 years [IQR, 2-2 years]).

[a]The *P* value was not adjusted for multiplicity and cannot be used to infer treatment effects.

between postablation AF burden and symptoms.[28] In the trial setting, continuous invasive monitoring remains the gold standard for postablation surveillance, although prolonged intermittent monitoring with ambulatory ECG devices is a practical alternative.[29] However, routine implementation of such monitoring in clinical practice is limited by cost and invasiveness. In this study, 1- to 3-day Holter monitoring every 6 months, which was supplemented by symptom-driven assessments, identified AF recurrence in approximately 10% of participants at a median of 1 year after randomization, leading to resumption of anticoagulant therapy. Although the monitoring strategy used in this trial may have underestimated AF

Figure 3. Primary Outcome in the Per-Protocol Population



No. at risk

No oral anticoagulant	396	361	337	318	306
Oral anticoagulant	394	370	354	335	317

The data are presented as Kaplan-Meier curves for the primary outcome (composite of stroke, systemic embolism, and major bleeding) at 2 years.

recurrence rates relative to continuous monitoring or longer-term ambulatory ECG monitoring, the findings suggest that discontinuation of oral anticoagulant therapy might be considered in scenarios that reflect the practical limitations of routine clinical practice.

Limitations

This trial has several limitations. First, the open-label design carries an inherent risk of reporting and ascertainment bias; however, we minimized this bias by having an independent adjudication committee evaluate all events.

Second, although the associations between discontinuation of anticoagulant therapy and improved net clinical outcomes were consistently observed in the subgroup analyses, the overall number of events was lower than anticipated, and the proportion of patients at high stroke risk may have been relatively small to detect a potential disadvantage of stopping anticoagulation.

Third, the primary outcome was a composite of stroke, systemic embolism, and major bleeding. Given the higher frequency of bleeding compared with ischemic events, the use of a net clinical outcome may have biased the results in favor of discontinuing oral anticoagulant therapy.

Fourth, because the study population consisted predominantly of East Asian patients, who have been considered at higher bleeding risk,[30] and included relatively few women, the generalizability of these findings to other populations may be limited. However, the bleeding risk gap between Asian and non-Asian patients has narrowed in the era of direct oral anticoagulant therapy and the bleeding risk is now largely comparable.[31] Consistently, in the present study, the rate for major bleeding was relatively low at approximately 1.4% over 2 years.

Conclusions

Among patients without documented atrial arrhythmia recurrence after catheter ablation for AF, discontinuing oral anticoagulant therapy resulted in a lower risk for the composite outcome of stroke, systemic embolism, and major bleeding vs continuing direct oral anticoagulant therapy.

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