

## Patterns of Anticoagulation Use and Cardioembolic Risk After Catheter Ablation for Atrial Fibrillation

Peter A. Noseworthy, MD; Xiaoxi Yao, PhD; Abhishek J. Deshmukh, MBBS; Holly Van Houten, BA; Lindsey R. Sangaralingham, MPH, PhD; Konstantinos C. Siontis, MD; Jonathan P. Piccini, Sr, MD, MHSc; Samuel J. Asirvatham, MD; Paul A. Friedman, MD; Douglas L. Packer, MD; Bernard J. Gersh, MB, ChB, DPhil; Nilay D. Shah, PhD

**Background**—There is significant practice variation in oral anticoagulation (OAC) use following catheter ablation for atrial fibrillation. It is not clear whether the risk of cardioembolism increases after discontinuation of OAC following catheter ablation.

**Methods and Results**—We identified 6886 patients within a large national administrative claims database who underwent catheter ablation for atrial fibrillation between January 1, 2005, and September 30, 2014. We assessed the effect of time off of OAC by CHA<sub>2</sub>DS<sub>2</sub>-VASc score (after adjusting for other comorbidities) on risk of cardioembolism, using Cox proportional hazards models. There was an increase in the use of non-vitamin K OAC after ablation from 0% in 2005 to 69.8% in 2014. OAC discontinuation was high, with only 60.5% and 31.3% of patients remaining on OAC at 3 and 12 months, respectively. The rate of discontinuation was higher in low-risk patients (82% versus 62.5% at 12 months for CHA<sub>2</sub>DS<sub>2</sub>-VASc 0–1 versus ≥2, respectively;  $P < 0.001$ ). Stroke occurred in 1.4% of patients with CHA<sub>2</sub>DS<sub>2</sub>-VASc ≥2 and 0.3% of those with CHA<sub>2</sub>DS<sub>2</sub>-VASc 0 or 1 over the study follow-up. The risk of cardioembolism in the first 3 months after ablation was increased among those with any time off OAC (hazard ratio 8.06 [95% CI 1.53–42.3],  $P < 0.05$ ). The risk of cardioembolism beyond 3 months was increased with OAC discontinuation among high-risk patients (hazard ratio 2.48 [95% CI 1.11–5.52],  $P < 0.05$ ) but not low-risk patients.

**Conclusion**—The overall risk of stroke in postablation patients is low; however, OAC discontinuation after ablation is common and is associated with increased risk of cardioembolism for all patients within the first 3 months and for high-risk patients in the long term. Continuing OAC for at least 3 months in all patients and indefinitely in high-risk patients appears to be the safest strategy. (*J Am Heart Assoc.* 2015;4:e002597 doi: 10.1161/JAHA.115.002597)

**Key Words:** ablation • anticoagulation • atrial fibrillation • stroke • transient ischemic attack

Catheter ablation carries a class I recommendation for the management of symptomatic, drug-refractory atrial fibrillation (AF).<sup>1</sup> Although one might expect that maintenance of sinus rhythm would lower the subsequent risk of stroke, systematic reviews of the available data do not necessarily support this notion.<sup>2</sup> Patients who undergo AF ablation may

have other stroke risk factors that persist after ablation, and asymptomatic AF recurrences are not uncommon.<sup>3,4</sup> In addition, ablation may modify electrical activation of the left atrial appendage and introduce consequent mechanical dysfunction. Accordingly, the current guidelines from the American Heart Association, American College of Cardiology, and Heart Rhythm Society state that “catheter ablation to restore sinus rhythm should not be performed with the sole intent of obviating the need for anticoagulation.”<sup>1</sup>

With limited data available on the need for and duration of anticoagulation after catheter ablation, considerable practice variation exists with respect to oral anticoagulation (OAC) after ablation. The prevailing consensus is that OAC with warfarin or non-vitamin K oral anticoagulants (NOACs) should be continued for at least 2 to 3 months after a successful ablation depending on patient preference and the estimated embolic and bleeding risks.<sup>1,5</sup>

Using data from a national administrative claims database of patients undergoing catheter ablation for AF in the United States, we sought to examine OAC practice patterns after ablation, such as rates and timing of OAC discontinuation, and

From the Heart Rhythm Section, Cardiovascular Diseases (P.A.N., A.J.D., K.C.S., S.J.A., P.A.F., D.L.P., B.J.G.) and Robert D. and Patricia E. Kern Center for Science of Health Care Delivery (P.A.N., X.Y., H.V.H., L.R.S., N.D.S.), Mayo Clinic, Rochester, MN; Optum Labs, Cambridge, MA (N.D.S.); Division of Cardiology, Duke University Medical Center, Durham, NC (J.P.P., B.J.G.).

Accompanying Figures S1 through S6 are available at <http://jaha.ahajournals.org/content/4/11/e002597suppl/DC1>

**Correspondence to:** Peter A. Noseworthy, MD, Division of Cardiovascular Diseases, Mayo Clinic College of Medicine, 200 First Street SW, Rochester, MN 55905. E-mail: [noseworthy.peter@mayo.edu](mailto:noseworthy.peter@mayo.edu)

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the extent of NOAC use. We also aimed to assess the impact of OAC discontinuation on short- and long-term risk of stroke, transient ischemic attack (TIA), and systemic embolism.

## Methods

### Data Source

We conducted a retrospective analysis using medical and pharmacy administrative claims data from the OptumLabs data warehouse, which includes persons enrolled in private insurance plans and in Medicare Advantage plans.<sup>6</sup> The database contains longitudinal health information on >100 million enrollees over the past 20 years from geographically diverse regions across the United States, with greatest representation from the South and the Midwest. The included plans provide claims for professional (eg, physician), facility (eg, hospital), and outpatient prescription medication services. Medical (professional, facility) claims include *International Classification of Diseases, 9th Revision, Clinical Modification* (ICD-9-CM) diagnosis codes, ICD-9 procedure codes, Current Procedural Terminology version 4 (CPT-4) procedure codes, Healthcare Common Procedure Coding System procedure codes, site of service codes, and provider specialty codes.<sup>7</sup>

Study data were accessed using techniques compliant with the Health Insurance Portability and Accountability Act of 1996. Because this study involved analysis of preexisting, deidentified data, it was exempt from institutional review board approval.

### Study Population

We identified all patients who underwent a catheter ablation for AF between January 1, 2005, and September 30, 2014, and were enrolled in health plan coverage at the time of and for at least 12 months before ablation. We required all patients to have at least 1 prescription for OAC filled. Because this study aimed at examining patients' use of OACs after ablation, we required that patients had continuous pharmacy plan enrollment during the 3 months prior to ablation and at least 1 month after ablation. We required that the ablation claim include an associated primary diagnosis code for AF (ICD-9-CM diagnosis code 427.31) and a procedure code (ICD-9 procedure code 37.34 and/or CPT-4 procedure codes 93651, 93656 and 93657). If a patient had >1 qualifying ablation over the study period, we considered the earliest ablation as the index procedure and following ablations as reablations. We also excluded patients with secondary diagnosis codes for Wolff-Parkinson-White syndrome (ICD-9-CM 426.7), nonparoxysmal atrioventricular nodal tachycardia (ICD-9-CM 426.89), paroxysmal supraventricular tachycardia

(ICD-9-CM 427.0), paroxysmal ventricular tachycardia (ICD-9-CM 427.1), and ventricular premature beats (ICD-9-CM 427.60, 427.61, and 427.69). Patients with diagnostic or procedural codes indicating implantation of a pacemaker or a cardioverter-defibrillator in the 12 months before or during the index procedure were also excluded to avoid inclusion of patients undergoing atrioventricular nodal ablation and pacemaker implantation for AF.<sup>8,9</sup> Similar methodology has been used previously to identify AF ablations from administrative data sets.<sup>10</sup>

### Patient Characteristics

Independent variables of interest included baseline demographics (age, sex, race, household income, and residence region), comorbidities, and CHA<sub>2</sub>DS<sub>2</sub>-VASc score. The Charlson comorbidity index was used to assess each patient's overall comorbidity burden. The CHA<sub>2</sub>DS<sub>2</sub>-VASc score was calculated for each patient, with a possible total score of 0 to 9 points (1 point for congestive heart failure, 1 point for hypertension, 1 point for diabetes, 2 points for ischemic stroke or TIA, 1 point for vascular diseases, 1 point for age 65 to 74 years, 2 points for age ≥75 years, and 1 point for female sex). All comorbidities, including the components of the Charlson comorbidity index and the CHA<sub>2</sub>DS<sub>2</sub>-VASc score (grouped into scores of 0–1 and ≥2), were defined using ICD-9-CM codes from the primary or secondary diagnoses in any physician or facility claim within the 12-month preablation period prior to the index procedure.<sup>5,11</sup>

### Oral Anticoagulation Use After Ablation or Exposure

OAC therapy after ablation was identified based on prescription claims for dabigatran, rivaroxaban, apixaban, or warfarin. The primary exposure of interest was the cumulative time that patients were not on any OAC after the initiation of OAC following the first AF catheter ablation. This was estimated using an approach similar to the percentage of days covered. The total numbers of days of supply for the medication were estimated using the prescription claims, and the number of days between fills was estimated based on the date when the prescriptions were filled. The difference between the number of days between prescription fills and the days of supply for the medication provided the number of days without an OAC.

To investigate whether ambulatory monitoring was used to guide the decision to discontinue anticoagulation, we examined the rates of ambulatory monitoring after ablation and looked among those who had continued and discontinued OAC. Because it is difficult to ascertain from claims data whether monitoring was used in the decision to discontinue anticoagulation, we also looked at the percentage of patients

who received monitoring during the 3 months before and the 3 months after the discontinuation date (defined as the date by which the last fill was supposed to be consumed by the patient).

## Outcomes

The primary outcome measures included ischemic stroke (ICD-9-CM codes 433.x1, 434.x1, and 436), TIA (ICD-9-CM codes 435.x), and systemic embolism (ICD-9-CM codes 444.x). The diagnosis codes were obtained from any diagnosis position in the inpatient claims, excluding those with a primary discharge code for rehabilitation (ICD-9-CM code V57) or any accompanying diagnoses of intracerebral hemorrhage (ICD-9-CM code 431), subarachnoid hemorrhage (ICD-9-CM 430), and trauma (ICD-9-CM codes 800–804 and 850–854).<sup>8,12,13</sup> In additional analyses, intracerebral hemorrhage (ICD-9-CM 431) and subarachnoid hemorrhage (ICD-9-CM 430) events were evaluated as secondary outcomes. Major bleeding events were assessed using previously published definitions.<sup>14</sup>

## Statistical Analysis

Descriptive analyses were conducted for the rates of utilization of NOACs as the initial OAC after ablation and the discontinuation practices of OAC within 3 and 12 months from the index ablation procedure.

Cox proportional hazards models were used to assess the patients' risk of cardioembolic events during follow-up. The resulting hazard ratios (HRs) and their 95% CIs are reported. The main independent variable, the length of time that patients were not on any OAC, was a time-varying covariate. In other words, the number of days that patients were off OAC changed over time. Models were adjusted for patients' index medication (warfarin versus NOAC), CHA<sub>2</sub>DS<sub>2</sub>-VASc score, Charlson comorbidity index, and race. Because age and sex are included in the CHA<sub>2</sub>DS<sub>2</sub>-VASc score, they were not included as separate covariates in the model. Patients were censored at the earliest date of the end of the enrollment, the end of study period, the first event, or a second ablation procedure. The proportional hazards assumption was assessed by methods based on weighted residuals. The proportional hazards assumption was valid for all models presented in the results.

We conducted 2 separate analyses to assess the risk in the first 3 months and after the first 3 months. The first analysis included all patients in the cohort and assessed their medication use and thromboembolic events within 3 months. In this analysis, time off of OAC was modeled as 0 days (reference) versus  $\geq 1$  day. The second analysis included patients who had at least 3 months of follow-up and did not

have any events in the first 3 months, and it assessed their medication use and thromboembolic events from 3 months after the index procedure until the end of follow-up or the occurrence of the outcome. Time off of OAC was modeled as follows in this analysis: 0 to 3 (reference), 3 to 6, 6 to 12, and  $>12$  months. The effects of OAC might differ between patients with high risk (CHA<sub>2</sub>DS<sub>2</sub>-VASc  $\geq 2$ ) and low risk (CHA<sub>2</sub>DS<sub>2</sub>-VASc 0–1); therefore, in each analysis, in addition to assessing the effects of the therapy and the CHA<sub>2</sub>DS<sub>2</sub>-VASc score separately, we tested the interaction effects between the time off of OACs and patients' baseline CHA<sub>2</sub>DS<sub>2</sub>-VASc scores.

The outcome for the main analysis included ischemic stroke, TIA, and systemic embolism. We also conducted a sensitivity analysis that included hemorrhagic stroke (ie, intracerebral and subarachnoid hemorrhage) as an outcome. Because previous studies demonstrated that male patients with CHA<sub>2</sub>DS<sub>2</sub>-VASc scores of 0 and female patients with CHA<sub>2</sub>DS<sub>2</sub>-VASc scores of 1 have true low risk, it is unclear whether men with CHA<sub>2</sub>DS<sub>2</sub>-VASc scores of 1 benefit from OACs.<sup>15–17</sup> An additional sensitivity test was conducted among men with CHA<sub>2</sub>DS<sub>2</sub>-VASc scores of 1.

All analyses were conducted using SAS 9.3 (SAS Institute Inc) and Stata 13.1 (Stata Corp).

## Results

### Patient Characteristics

We included 6886 patients in the analyses. Baseline characteristics are shown in Table 1. The median age was 60 years (interquartile range 54–67 years), and 71.7% of patients were male. The cohort included patients across the spectrum of CHA<sub>2</sub>DS<sub>2</sub>-VASc scores (31.3%, 23.6%, 19.8%, and 25.4% for CHA<sub>2</sub>DS<sub>2</sub>-VASc scores of 0–1, 2, 3, and  $\geq 4$ , respectively). Patients were followed for a mean of  $1.7 \pm 1.6$  years (median 1.2 years [interquartile range 0.5–2.4 years], total 11 744.8 patient-years).

### Patterns of OAC Use

For the first half of the study period, postablation OAC exclusively used warfarin; however, dabigatran, rivaroxaban, and apixaban began to be used in 2009, 2011, and 2012, respectively. Over the study period, there was an increase in NOAC use as the initial OAC after ablation from 0% in 2005 to 69.8% in 2014 (Figure 1). Specifically, the rates of dabigatran, rivaroxaban, and apixaban use in 2014—the last year of the study period—were 10.8%, 40.2%, and 17.8%, respectively.

At 3-month follow-up after the index ablation procedure, the rate of OAC discontinuation was 39.5%; however, over the study period, there was a trend toward reduction in the rate of

**Table 1.** Patient Characteristics

	First 90 Days (n=6886)		P Value	Beyond 90 Days (n=6238)		P Value
	Uninterrupted (n=1857, 27.0%)	>1 day Off OAC (n=5029, 73.0%)		<90 Days Off OAC (n=2008, 32.2%)	>90 Days Off OAC (n=4230, 67.8%)	
Age, median (IQR)	62.0 (56–69)	60.0 (53–67)	<0.0001	62.0 (55–68)	60.0 (53–67)	<0.0001
Age, n (%)			<0.0001			<0.0001
18 to 54	390 (21.0)	1477 (29.4)		457 (22.8)	1217 (28.8)	
55 to 64	717 (38.6)	2003 (39.8)		830 (41.3)	1663 (39.3)	
65 to 74	568 (30.6)	1166 (23.2)		551 (27.4)	1013 (23.9)	
≥75	182 (9.8)	383 (7.6)		170 (8.5)	337 (8.0)	
Male, n (%)	1290 (69.5)	3648 (72.5)	0.0120	1415 (70.5)	3048 (72.1)	0.1939
Race, n (%)			0.4345			0.4346
Asian	29 (1.6)	79 (1.6)		30 (1.5)	70 (1.7)	
Black	100 (5.4)	237 (4.7)		108 (5.4)	189 (4.5)	
Hispanic	70 (3.8)	193 (3.8)		73 (3.6)	167 (3.9)	
Unknown	118 (6.4)	272 (5.4)		120 (6.0)	230 (5.4)	
White	1540 (82.9)	4248 (84.5)		1677 (83.5)	3574 (84.5)	
Charlson index, n (%)			<0.0001			<0.0001
0	515 (27.7)	1707 (33.9)		545 (27.1)	1479 (35.0)	
1	512 (27.6)	1376 (27.4)		567 (28.2)	1148 (27.1)	
≥2	830 (44.7)	1946 (38.7)		896 (44.6)	1603 (37.9)	
CHA <sub>2</sub> DS <sub>2</sub> -VASc, n (%)			<0.0001			<0.0001
0 to 1	450 (24.2)	1702 (33.8)		508 (25.3)	1455 (34.4)	
2	438 (23.6)	1186 (23.6)		443 (22.1)	1015 (24.0)	
3	418 (22.5)	943 (18.8)		468 (23.3)	785 (18.6)	
≥4	551 (29.7)	1198 (23.8)		589 (29.3)	975 (23.0)	
Index medication, n (%)			0.0058			<0.0001
Apixaban	57 (3.1)	155 (3.1)		86 (4.3)	67 (1.6)	
Dabigatran	244 (13.1)	820 (16.3)		309 (15.4)	670 (15.8)	
Rivaroxaban	236 (12.7)	678 (13.5)		372 (18.5)	413 (9.8)	
Warfarin	1320 (71.1)	3376 (67.1)		1241 (61.8)	3080 (72.8)	
Follow-up years, mean (SD)	1.6 (1.6)	1.7 (1.6)	<0.0001	0.8 (0.6)	2.4 (1.6)	<0.0001

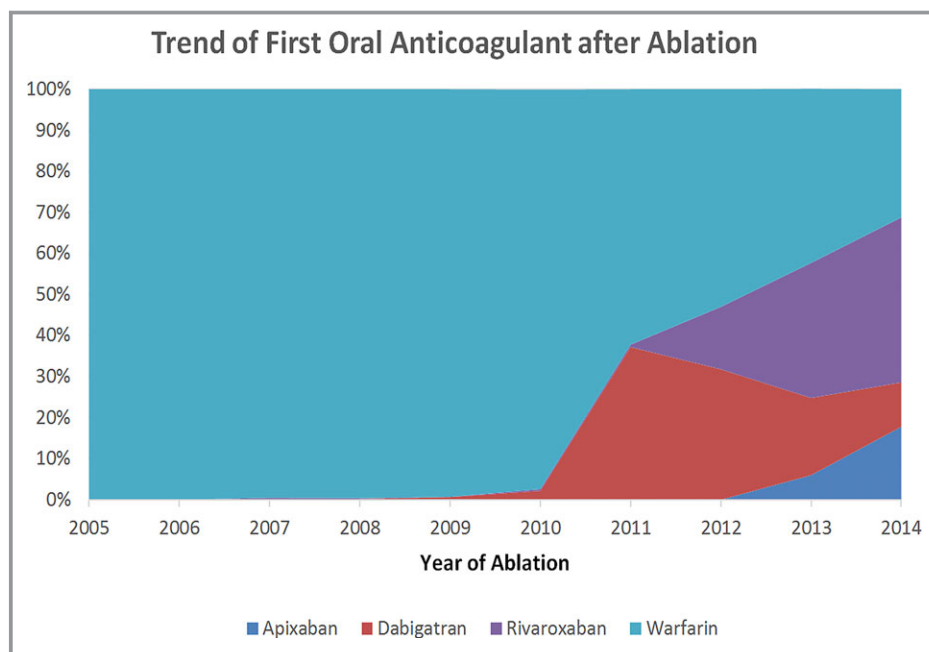
IQR indicates interquartile range; OAC, oral anticoagulation.

discontinuation at 3 months from 44% in 2005 to 31% in 2014 ( $P$  for trend <0.0001) (Figure S2). The rate of OAC discontinuation at 12-month follow-up was high, with only 31.3% of patients remaining on OAC at 12 months after the index ablation. OAC discontinuation was more common in low-risk patients (82% versus 62.5% at 12 months for CHA<sub>2</sub>DS<sub>2</sub>-VASc 0–1 versus ≥2, respectively) (Figure 2). The rates of discontinuation were similar for patients treated with warfarin, dabigatran, rivaroxaban, and apixaban as the initial postablation OAC (Figures S1 through S6). The proportion of

patients remaining on OAC at 12-month follow-up did not change significantly over the study period ( $P=0.16$ ).

### Clinical End Points

A total of 73 patients (1%) suffered an ischemic stroke, TIA, or systemic embolism. Stroke occurred in 1.4% of patients with CHA<sub>2</sub>DS<sub>2</sub>-VASc ≥2 and 0.3% of those with CHA<sub>2</sub>DS<sub>2</sub>-VASc 0 or 1 over the study follow-up. Overall, 24.6% of the events occurred in the first 3 months after ablation, whereas 21.9%



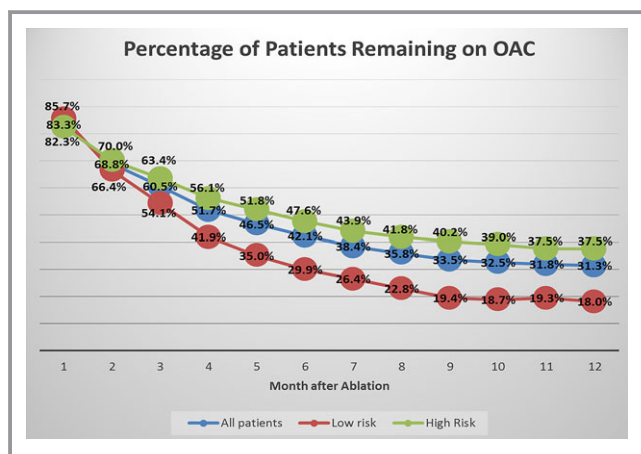
**Figure 1.** Trends of use of warfarin and non-vitamin K oral anticoagulant as initial oral anticoagulation after ablation.

occurred between 3 months and 1 year and 53.5% occurred >1 year after ablation. Median follow-up among patients who suffered an event was 1.3 years (interquartile range 0.3–2.4). A total of 34 events (46.6% of all events, 0.76 event per 100 person-years) occurred while patients were on OAC, whereas 39 (53.4% of all events, 0.56 event per 100 person-years) occurred in patients who had discontinued or interrupted OAC.

In a multivariable model considering the time off of OAC ( $\geq 1$  day), CHA<sub>2</sub>DS<sub>2</sub>-VASC score, index medication (warfarin

versus NOAC), Charlson comorbidity index, and race, the risk of embolic events in the first 3 months was markedly increased among those in whom OAC had been discontinued or interrupted for >1 day (HR 8.06 [95% CI 1.53–42.3],  $P < 0.05$ ) (Table 2). There was no difference in embolic event risk between the use of warfarin and NOAC as the initial postablation OAC strategy.

Beyond the first 3 months, there was a graded relationship between CHA<sub>2</sub>DS<sub>2</sub>-VASC score and embolic risk (Table 3). Similarly, there was a graded relationship between the time off of OAC and the risk of embolic events. There was some evidence of an interaction between CHA<sub>2</sub>DS<sub>2</sub>-VASC score and time of anticoagulation; among those at low risk (CHA<sub>2</sub>DS<sub>2</sub>-VASC 0 or 1), OAC discontinuation (defined as at least 3 months off of OAC) was not associated with increased risk of embolic events (HR 0.34 [95% CI 0.04–2.62],  $P = 0.30$ ); however, the risk beyond 3 months was increased with OAC discontinuation among high-risk patients (HR 2.48 [95% CI 1.11–5.52],  $P < 0.05$ ;  $P$  for interaction = 0.06). Use of NOAC was not a significant predictor of embolism >3 months after ablation in multivariate analysis (Table 4). In a secondary analysis, we examined the event rates beyond 3 months in patients with CHA<sub>2</sub>DS<sub>2</sub>-VASC scores of 2. There were no events in the OAC continuation group and 3 events in the OAC discontinuation group, suggesting a higher stroke rate with anticoagulation discontinuation in patients with CHA<sub>2</sub>DS<sub>2</sub>-VASC scores of 2; however, because of the low event rate, we could not perform additional regression analysis.



**Figure 2.** Percentage of patients remaining on oral anticoagulation (OAC) after ablation, stratified by all patients (blue line), low-risk patients (CHA<sub>2</sub>DS<sub>2</sub>-VASC 0, 1; red line) and high-risk patients (CHA<sub>2</sub>DS<sub>2</sub>-VASC  $\geq 2$ ; green line).



**Table 2.** Multivariable Predictors of Risk of Stroke or Systemic Embolism in the First 3 Months After Ablation (n=6886)

Risk Factor	HR (95% CI)
Time not on OAC	
0 day	Reference
≥1 day	8.06* (1.53–42.31)
CHA <sub>2</sub> DS <sub>2</sub> -VASc	
0 to 1	Reference
2	2.12 (0.43–10.46)
3	2.85 (0.56–14.47)
≥4	3.96 (0.84–18.72)
Index medication	
Warfarin	Reference
NOAC	1.79 (0.71–4.50)
Charlson comorbidity index	
0	Reference
1	0.42 (0.10–1.80)
≥2	0.62 (0.19–1.96)
Race	
White	Reference
Nonwhite	1.94 (0.70–5.36)

Omnibus *P* values for CHA<sub>2</sub>DS<sub>2</sub>-VASc and Charlson comorbidity index were both insignificant. HR indicates hazard ratio; NOAC, non-vitamin K oral anticoagulant; OAC, oral anticoagulation.

\**P*<0.05.

In our data, among the 2152 patients with CHA<sub>2</sub>DS<sub>2</sub>-VASc score 0 or 1, the majority (n=1235) were men with CHA<sub>2</sub>DS<sub>2</sub>-VASc scores of 1; in a sensitivity test looking at these men, the results remained the same as those for the whole low-risk population. There were 226 women with CHA<sub>2</sub>DS<sub>2</sub>-VASc scores of 1, and none of those women had a stroke. There were 689 men with CHA<sub>2</sub>DS<sub>2</sub>-VASc scores of 0, and 2 of them had a stroke. Our results confirmed that patients with no risk factor other than sex had true low risk, but the risk was still quite low among men with 1 additional risk factor (5 strokes, 0.4%), so these patients derived little benefit from continuing OAC beyond 3 months after ablation.

There were a total of 15 hemorrhagic strokes during the follow-up period. The risk of hemorrhagic stroke was similar between those on warfarin and NOAC; 14 hemorrhagic strokes occurred in the warfarin group (0.3% of all patients on warfarin, 0.15 per 100 patient-years), and 1 occurred in a patient on NOACs (0.05% of all patients on NOACs, 0.04 per 100 patients-years; *P*=0.21). When hemorrhagic strokes were included in the composite end point (supplemental data), the increased risk of stroke with OAC discontinuation in high-risk patients was similar (HR 2.26 [95% CI 1.11–4.60], *P*<0.05).

**Table 3.** Multivariable Predictors of Risk of Stroke or Systemic Embolism Beyond 3 Months After Ablation (n=6238)

Risk Factor	HR (95% CI)
Time not on OAC	
0 to 3 months	Reference
3 to 6 months	1.69 (0.60–4.78)
6 months to 1 year	2.74* (1.12–6.74)
>1 year	3.98** (1.56–10.12)
CHA <sub>2</sub> DS <sub>2</sub> -VASc	
0 to 1	Reference
2	0.82 (0.16–4.14)
3	2.41 (0.62–9.37)
≥4	8.50** (2.30–31.36)
Index medication	
Warfarin	Reference
NOAC	0.83 (0.37–1.86)
Charlson comorbidity index	
0	Reference
1	1.71 (0.44–6.57)
≥2	2.85 (0.78–10.37)
Race	
White	Reference
Nonwhite	2.17** (1.21–3.91)

Omnibus *P* values for length of time not on OAC, CHA<sub>2</sub>DS<sub>2</sub>-VASc, and Charlson comorbidity index were <0.05, <0.001, and not significant, respectively. HR indicates hazard ratio; NOAC, non-vitamin K oral anticoagulant; OAC, oral anticoagulation.

\**P*<0.05, \*\**P*<0.01.

There were 246 major bleeding events that occurred after OAC initiation and before the cardioembolic event or the end of follow-up, and 22 (8.9% of major bleedings and 0.3% of all

**Table 4.** The Interaction of CHA<sub>2</sub>DS<sub>2</sub>-VASc Score and Anticoagulation Use on the Risk of Stroke or Systemic Embolism Beyond 3 Months After Ablation (n=6238)

Risk Factor	HR (95% CI)
Anticoagulation use	
Low risk patients (CHA <sub>2</sub> DS <sub>2</sub> -VASc 0 or 1)	
Continuation	Reference
≥3 mo off OAC	0.34 (0.04–2.62)
High risk patients (CHA <sub>2</sub> DS <sub>2</sub> -VASc ≥2)	
Continuation	Reference
≥3 mo off OAC	2.48* (1.11–5.52)

HR indicates hazard ratio; OAC, oral anticoagulation.

\**P*<0.05, adjusted for Charlson comorbidity index, race, and index medication (age and sex included in the CHA<sub>2</sub>DS<sub>2</sub>-VASc score). *P*=0.06 for interaction.

patients) were due to intracranial bleeding. Of these, 60% (144) of the events happened while patients were on OAC. Only 42 events happened within 30 days of discontinuation.

Ambulatory monitoring was performed in 1575 (46.0%) of patients who ultimately discontinued OAC and 1472 (52.4%) of patients who continued anticoagulation until the end of follow-up. Only one-third of the patients who discontinued OACs received ambulatory monitoring during the 3 months before discontinuation, suggesting that the decision to discontinue OAC was not guided by ambulatory monitoring in the majority of patients.

## Discussion

The principle findings of this study are as follows: (1) In the first 3 months after ablation, anything short of complete and uninterrupted OAC is associated with an increased risk of stroke, and (2) beyond 3 months, OAC discontinuation is associated with increased stroke in high-risk patients (CHADS<sub>2</sub>-VASc score  $\geq 2$ ). Furthermore, we identified that a large proportion of patients may be vulnerable to stroke due to insufficient anticoagulation after ablation. Approximately 73% of patients have incomplete anticoagulation in the first 3 months after ablation, and the 65% of patients with CHA<sub>2</sub>DS<sub>2</sub>-VASc score of  $\geq 2$  discontinue OAC at any point after ablation. Our data are consistent with current guidelines and underscore the importance of uninterrupted OAC for a minimum of 3 months and indefinitely for patients at higher risk of stroke, regardless of the apparent success of the ablation. They also highlight the overall safety of ablation in this relatively young patient population.

The high rate of OAC discontinuation is striking, with approximately two-thirds of patients stopping OAC within the first year after ablation. Patients and their physicians are often eager to discontinue OAC, and the decision to do so is not without some support in the available literature. A large observational study showed that patients who discontinued OAC 3 to 6 months after ablation had comparable embolic risk to patients who continued OAC beyond that period.<sup>18</sup> Another analysis of Danish registries indicated that the bleeding risk associated with OAC beyond 3 months after ablation may outweigh the benefits of stroke risk prevention.<sup>19</sup> Several other smaller studies have also found that OAC can be safely discontinued after successful catheter ablation in selected patients with low CHA<sub>2</sub>DS<sub>2</sub>-VASc scores, without increasing the rate of stroke<sup>20–24</sup>; however, the small sample sizes and remarkably low observed stroke rates in these studies may have resulted in underpowered analyses.<sup>20,25</sup> Indeed, >10 000 patients (all of whom were at least moderate risk) were required to demonstrate the noninferiority of NOACs to warfarin in randomized clinical trials.<sup>26</sup>

Despite some observational data supportive of OAC discontinuation after ablation, current guidelines suggest continuation of OAC for a minimum of 2 to 3 months.<sup>5,27,28</sup> The high rate of OAC discontinuation within the first 3 months after ablation likely reflects evolving clinical practice over time as providers incorporate the available clinical data and assimilate to the changing guidelines. Over the study period, there was a modest increase in the proportion of patients remaining on OAC for a minimum of 3 months, but many patients are still stopping anticoagulation before the 3-month point.

Importantly, these data also illustrate the recent but widespread adoption of NOAC use after catheter ablation. Although there are no randomized clinical trials examining long-term warfarin versus NOAC use after ablation, physicians appear to be readily incorporating NOACs into their practices. Current data for NOAC use after ablation are limited to the periprocedural setting. A single study demonstrated that uninterrupted rivaroxaban was comparable to warfarin in terms of perioperative bleeding and thromboembolic events in patients undergoing AF ablation,<sup>29</sup> and authors have argued for adoption of this practice.<sup>30</sup> Our study lends further support to the idea that NOACs may be safe and effective in this population and provides the first description of long-term stroke outcomes after ablation. We demonstrated no difference in the rates of embolic stroke, TIA, or systemic embolism between NOACs and warfarin. Furthermore, hemorrhagic strokes were infrequent and occurred at similar rates with warfarin and NOAC use. Although NOACs offer improved convenience over warfarin, there does not seem to be a dramatic difference in persistence with or adherence to OAC between NOACs and warfarin.

The potential reasons for OAC discontinuation are difficult to establish from observational claims data, and this is a limitation of this form of analysis. We cannot distinguish deliberate discontinuation by the provider from nonadherence (as gauged by lack of prescription fills) on the part of the patient. It is possible that some patients developed contraindications or bleeding that prompted the stop. We note, however, that only 144 patients had significant bleeding while on OAC but 4230 patients discontinued OAC, so bleeding events alone do not explain a significant proportion of OAC discontinuation. Other clinical factors, such as the need for surgery, could confound the association between OAC discontinuation and stroke. To minimize this confounding, we defined OAC discontinuation (beyond the 3-month postablation period) as  $\geq 90$  days off of OAC in order to avoid overclassifying temporary suspension of OAC for surgery as a discontinuation. It is also important to note that although anticoagulation discontinuation was associated with an increased risk of stroke, the confidence interval of the estimate was wide. This is due to the low event rate in this

group. It is possible that the true HR is much smaller (eg, the lower bound of the 95% CI 1.53) or much larger (eg, the upper bound of the 95% CI 42.31) than the point estimate 8.06.

The other important limitations of this study are those inherent to administrative data such as under- or overcoding, unmeasured confounders, and the lack of clinical detail and outcome and diagnosis validation that is possible in clinical trials and registries. We are, for example, unable to distinguish paroxysmal and persistent AF and do not have way to definitively assess AF burden after ablation; however, the risk of stroke does not differ between patients with different patterns of AF,<sup>31,32</sup> so AF pattern does not confound the study findings. Finally, warfarin use is particularly challenging to assess with claims data because the medication is sometimes purchased without an insurance claim, and the dose may be changed without requiring a new prescription.

In summary, our study of ≈7000 patients undergoing catheter ablation for AF in the United States demonstrates that NOAC use after ablation is increasing and is now more common than warfarin use and that NOACs appear comparable to warfarin in terms of stroke prevention after ablation. Our study also illustrates that the discontinuation rate of OAC is high. Although the overall risk of stroke is low (on the order of 1%), discontinuation at any point in the first 3 months after ablation is associated with increased risk of stroke or systemic embolism. Beyond 3 months, discontinuation is associated with higher rates of stroke or systemic embolism in high- but not low-risk patients. These data support the practice of continuous anticoagulation with either warfarin or a NOAC for a minimum of 3 months for all patients after ablation and indefinitely in high-risk patients.

## Disclosures

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