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# The Risk of Thromboembolism and Need for Oral Anticoagulation After Successful Atrial Fibrillation Ablation

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**Objectives** The aim of this multicenter study was to evaluate the safety of discontinuing oral anticoagulation therapy (OAT) after apparently successful pulmonary vein isolation.

**Background** Atrial fibrillation (AF) is associated with an increased risk of thromboembolic events (TE) and often requires OAT. Pulmonary vein isolation is considered an effective treatment for AF.

**Methods** We studied 3,355 patients, of whom 2,692 (79% male, mean age 57 ± 11 years) discontinued OAT 3 to 6 months after ablation (Off-OAT group) and 663 (70% male, mean age 59 ± 11 years) remained on OAT after this period (On-OAT group). $CHADS_2$ (congestive heart failure, hypertension, age [75 years and older], diabetes mellitus, and a history of stroke or transient ischemic attack) risk scores of 1 and ≥2 were recorded in 723 (27%) and 347 (13%) Off-OAT group patients and in 261 (39%) and 247 (37%) On-OAT group patients, respectively.

**Results** During follow-up (mean 28 ± 13 months vs. 24 ± 15 months), 2 (0.07%) Off-OAT group patients and 3 (0.45%) On-OAT group patients had an ischemic stroke ($p = 0.06$). No other thromboembolic events occurred. No Off-OAT group patient with a $CHADS_2$ risk score of ≥2 had an ischemic stroke. A major hemorrhage was observed in 1 (0.04%) Off-OAT group patient and 13 (2%) On-OAT group patients ($p < 0.0001$).

**Conclusions** In this nonrandomized study, the risk–benefit ratio favored the suspension of OAT after successful AF ablation even in patients at moderate-high risk of TE. This conclusion needs to be confirmed by future large randomized trials. (J Am Coll Cardiol 2010;55:735–43) © 2010 by the American College of Cardiology Foundation

Atrial fibrillation (AF) is a major risk factor for thromboembolism, and oral anticoagulation therapy (OAT) is usually recommended for patients at higher risk of this complication (1,2). Catheter ablation has emerged as a promising cure for AF (3,4). Reported success rates range from 45% to 95% (3). One of the potential advantages of AF ablation is the possibility of discontinuing OAT after a successful procedure. However, the safety of this strategy has not yet been demonstrated in large randomized studies.

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Two recent expert consensus documents recommended continuing OAT indefinitely, at least in patients at high

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**Abbreviations and Acronyms**

**AF** = atrial fibrillation
**CI** = confidence interval
**ECG** = electrocardiogram
**HR** = hazard ratio
**INR** = international normalized ratio of prothrombin time
**LA** = left atrial/atrium
**OAT** = oral anticoagulation therapy
**TE** = thromboembolic events
**TIA** = transient ischemic attack
**TTM** = transtelephonic monitoring

risk of thromboembolic events (TE) (3,4). Despite these recent recommendations, the use of OAT after an apparently successful ablation procedure is still controversial, and some centers implement a policy of withdrawing OAT even in the majority of patients at high risk of TE (17% of 42 centers worldwide surveyed in a recent questionnaire) (5). To clarify this issue, we conducted the present study by collecting data from 5 high-volume centers that have, over the years, implemented a consistent strategy with regard to the suspension of OAT after successful ablation.

## Methods

**Patient population.** Consecutive patients referred to the 5 participating centers between January 2001 and December 2005 who had discontinued OAT after successful AF ablation were enrolled in the study (Off-OAT group) and were compared with patients who had undergone AF ablation in the period January 2003 to December 2005 and continued OAT (On-OAT group). Patients with prosthetic valves were excluded from the study. On referral, all patient data were prospectively recorded in a computerized database. Both Off- and On-OAT groups were divided into 3 subgroups according to their TE risk profile. Patients' risk profiles were evaluated by means of the $CHADS_2$ (congestive heart failure, hypertension, age [75 years or older], diabetes mellitus, history of stroke or transient ischemic attack) score. This index is based on a points system in which 2 points are assigned for a history of TIA or stroke and 1 point for each of the other risk factors. A $CHADS_2$ score of 0 is considered to indicate a low risk of TE, a score of 1 indicates a moderate risk, and a score of 2 or more indicates a high risk (6).

All patients selected for pulmonary vein isolation had a history of symptomatic drug-resistant paroxysmal, persistent, or permanent AF (1). A follow-up of at least 1 year after the last ablation and 6 months after OAT discontinuation was required for inclusion in the study. Before the ablation procedure, all patients gave their written informed consent as approved by the institutional ethics committee, and patient data were collected in accordance with institutional ethics guidelines.

**Ablation strategy.** The ablation strategy included pulmonary vein isolation at the ostial or antral level, guided by a circular mapping catheter. Intracardiac echocardiography or angiography was used to locate the pulmonary veins and define the ostium or the antrum of the veins. Additional linear lesions, ablation of complex fractionated electrograms, and isolation of the superior vena cava were performed per institutional preference. The details of the ablation procedures have been presented elsewhere (7–9).

**Anticoagulation protocol.** All patients were monitored overnight in the hospital, and were usually discharged from 1 to 3 days after the procedure depending on institutional policy. The OAT with adjusted-dose warfarin was restarted in all patients on the evening of the ablation procedure and continued for at least 3 to 6 months to maintain the international normalized ratio of prothrombin time (INR) between 2 and 3 (10). After this period, each center decided the long-term anticoagulation strategy according to local institutional policy and the individual characteristics of each patient. As a general rule, OAT was discontinued, regardless of the $CHADS_2$ score, if patients did not experience: 1) any recurrence of atrial tachyarrhythmias (AF or atrial flutter/tachycardia longer than 1 min); 2) severe pulmonary vein stenosis (pulmonary vein narrowing >70%); and 3) severe left atrial (LA) mechanical dysfunction (absence of A-wave on pulsed Doppler transmitral recording). Patients with early recurrence of AF or episodes of atrial flutter and a $CHADS_2$ score of 1 or more were maintained on OAT for at least 6 months; subsequently, OAT was discontinued in patients without arrhythmic recurrence in the last 3 months off antiarrhythmic drugs. After OAT discontinuation, patients were treated with aspirin, 81 to 325 mg/day. Patients with a $CHADS_2$ score of 1 or more who developed a recurrence of atrial tachyarrhythmia after discontinuation were restarted on OAT. For the purpose of the present study, the data collected up to the time when these patients restarted OAT were included in the analysis.

**Post-ablation management and follow-up.** Follow-up examinations were routinely scheduled at 1 to 3, 6, and 12 months after the procedure and every 6 months thereafter. Seventy-nine percent of patients were seen up to the 1-year follow-up by the physician in the center where the ablation was performed. For all patients who were unable to be seen in the first year and thereafter, their status was assessed by a nurse practitioner via telephone and monitoring tests were obtained by the referring physician. In any case, all data collected in this way were also evaluated by the physician of the center where the ablation procedure had been performed. An electrocardiogram (ECG) was obtained routinely in all patients within 1 month after the procedure and at each follow-up examination. Each study institution had different strategies for identifying AF recurrences prior to OAT discontinuation. These included Holter recordings (at 1, 3, and 6 months) in 86% of patients and/or transtelephonic monitoring (TTM) (ranging from continuous for 5 months in 76% of patients to 1-month blocks immediately after, at 6 to 12 weeks, and at 6 months after AF ablation in 14%) in 90% of patients. Patients who underwent TTM were asked to transmit their rhythm data every time they had symptoms compatible with arrhythmias, and 1 to 3 times per day even if they were asymptomatic. Interrogation

of implanted devices was also used (when available) to confirm arrhythmia recurrence. Patients were also instructed to assess their pulse daily and report any irregularity of pulse or recurrence of symptoms immediately, at which point additional Holter monitoring or TTM was performed. The documentation of arrhythmic episodes was based on ECG and/or Holter, TTM, and implanted device recordings.

Transthoracic or transesophageal echocardiography and spiral computed tomography scan were performed during the 3-month follow-up examination for the assessment of LA function and pulmonary vein narrowing. Complete adherence to the follow-up protocol was a necessary condition for the evaluation of OAT discontinuation.

**End points of the study.** For the purpose of the study, the following events were considered as study end points: ischemic strokes and major hemorrhages. Ischemic stroke was defined as the abrupt onset of focal neurological deficit persisting for more than 24 h (11). Major hemorrhage was defined as bleeding that was intracranial or retroperitoneal, or led directly to death, or resulted in hospitalization or transfusion (12). Patients were enrolled in the study at the time when the decision regarding long-term post-ablation OAT was made, and the follow-up started from that moment. The TE and hemorrhagic events that occurred while on OAT, during the initial 3 to 6 months after ablation, were not counted.

**Statistical analysis.** All data are reported as mean ± SD for continuous variables and as percentage values for categorical variables, unless otherwise indicated. Comparison of continuous variables between 2 groups was made by means of the independent-samples Student *t* test. Categorical variables were compared by means of chi-square analysis or Fisher exact test when required. A 2-tailed p value $<0.05$ was considered statistically significant. Freedom from ischemic and hemorrhagic stroke in the Off- and On-OAT groups were estimated with Kaplan-Meier analysis and was compared by the log-rank test. Hazard ratio (HR) and relative risk from Cox regression model were used to test the effect of OAT discontinuation on the risk of TE and major hemorrhages when more than 10 events were detected. This model was adjusted for age, sex, and $CHADS_2$ score.

## Results

**Baseline characteristics and thromboembolic risk.** The Off-OAT group consisted of 2,692 patients who discontinued OAT 5 ± 3 months (median 4 months) after AF ablation. Thereafter, these patients remained off OAT for another 28 ± 13 months (median 25 months). Of these patients, 95 continued antiarrhythmic drug therapy despite the fact that they had no arrhythmic recurrences after the blanking period (first 3 months after ablation). The follow-up duration was only the minimum required for the enrollment in the study for 145 (5%) patients. In 2,477 (92%) patients, OAT was replaced with aspirin. In the other 215 (8%) patients, aspirin was not administered because of contraindication, intolerance, or patient refusal. Among the 2,692 patients in the Off-OAT group, 1,622 (60%) had a $CHADS_2$ score of 0, 723 (27%) had a $CHADS_2$ score of 1, and 347 (13%) had a $CHADS_2$ score of ≥2. The On-OAT group was made up of 663 patients who continued OAT for 24 ± 15 months (median 19 months) after the decision not to suspend this therapy. The reasons for continuing OAT were arrhythmic recurrences (n = 475, 72%), LA dysfunction (n = 66, 10%), severe pulmonary vein stenosis (n = 22, 3%), other indication for OAT (n = 19, 3%), and the decision of the referring physician or patient preference (n = 81 patients, 12%). Among the 663 patients in the On-OAT group, 155 (23%) had a $CHADS_2$ score of 0, 261 (39%) had a $CHADS_2$ score of 1, and 247 (37%) had a $CHADS_2$ score of ≥2. All patients received transthoracic or transesophageal echocardiography before the decision regarding long-term OAT was made. Ninety-eight percent of patients fulfilled the institutional monitoring protocol to assess for arrhythmic recurrences. The baseline characteristics of the whole study population, the Off-OAT group, and On-OAT group are summarized in Table 1. Patients in the Off-OAT group were more frequently male and were significantly younger than patients in the On-OAT group, more often had paroxysmal AF, and had a longer duration of AF, a lower mean $CHADS_2$ score, and a smaller LA diameter. These patients were more frequently without structural heart disease and with left ventricular ejection fraction >40%. In Table 2, patients in the Off- and On-OAT groups are further subdivided into 3 subgroups according to the $CHADS_2$ score. The mean duration of the follow-up did not differ significantly between the 2 groups for patients with $CHADS_2$ score 0, 1, and ≥2. The distribution of the various risk factors included in the $CHADS_2$ score for patients of both groups is reported in Table 3. After discussion with patients, OAT also was discontinued in 10 subjects with $CHADS_2$ scores of 5 to 6. All of these patients had a prior history of stroke or TIA associated with other TE risk factors. The OAT was discontinued only if the previous stroke or TIA was clearly related to AF and all rules for OAT withdrawal previously mentioned were satisfied.

**Arrhythmic recurrences during follow-up.** In the Off-OAT group, 77 of 2,692 patients (2.9%, 9 patients with $CHADS_2$ score ≥2) had arrhythmic recurrences 10 ± 3 months after OAT discontinuation and restarted OAT.

**TEs during follow-up.** In the Off-OAT group, only 2 of 2,692 (0.07%) patients experienced ischemic stroke during follow-up. These patients survived the TE, and only 1 suffered permanent functional disability. One patient was a 67-year-old man with a $CHADS_2$ risk score of 0 and a history of paroxysmal AF before ablation. The event occurred 6 months after OAT discontinuation while the patient was in sinus rhythm. No arrhythmic recurrences were documented before the event. After the stroke, repeat monitoring revealed both asymptomatic and symptomatic episodes of paroxysmal AF. The second patient was a 75-year-old man with a $CHADS_2$ score of 1 and a history of persistent AF before ablation. The ischemic event oc-

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**Table 1** Baseline Characteristics of the Total Population, Off-OAT Group, and On-OAT Group

| | Total Population (n = 3,355) | Off-OAT Group (n = 2,692) | On-OAT Group (n = 663) | p Value |
|---|---|---|---|---|
| Sex | | | | |
| Male | 2,579 (77) | 2,116 (79) | 463 (70) | 0.0026 |
| Female | 776 (23) | 576 (21) | 200 (30) | |
| Age, yrs | 57 ± 11 | 57 ± 11 | 59 ± 11 | <0.0001 |
| AF type | | | | |
| Paroxysmal | 2,022 (60) | 1,682 (62) | 340 (51) | <0.0001 |
| Persistent | 598 (18) | 424 (16) | 174 (26) | <0.0001 |
| Permanent | 735 (22) | 586 (22) | 149 (22) | 0.6941 |
| AF duration, months | 43 ± 40 | 44 ± 36 | 35 ± 58 | 0.0019 |
| Structural heart disease | 983 (29) | 730 (27) | 253 (38) | <0.0001 |
| Valvular | 405 (12) | 323 (12) | 82 (12) | 0.7936 |
| Ischemic | 314 (9) | 242 (9) | 72 (11) | 0.1386 |
| Dilated | 149 (4) | 90 (3) | 59 (9) | <0.0001 |
| Hypertrophic | 45 (1) | 27 (1) | 18 (3) | 0.006 |
| Others | 70 (2) | 48 (2) | 22 (3) | 0.0132 |
| Thromboembolic risk factors | | | | |
| Congestive heart failure | 266 (8) | 154 (6) | 112 (17) | <0.0001 |
| Hypertension | 1,292 (39) | 916 (34) | 376 (57) | <0.0001 |
| Age ≥75 yrs | 140 (4) | 93 (3) | 47 (7) | <0.0001 |
| Diabetes | 227 (7) | 143 (5) | 84 (13) | <0.0001 |
| Prior stroke/TIA | 230 (7) | 125 (5) | 105 (16) | <0.0001 |
| $CHADS_2$ score | | | | |
| 0 | 1,777 (53) | 1,622 (60) | 155 (23) | <0.0001 |
| 1 | 984 (29) | 723 (27) | 261 (39) | <0.0001 |
| ≥2 | 594 (18) | 347 (13) | 247 (37) | <0.0001 |
| LVEF, % | 55 ± 8 | 55 ± 8 | 55 ± 10 | 0.6590 |
| LVEF ≤40%, | 254 (8) | 188 (7) | 66 (10) | 0.0096 |
| LA diameter, mm | 44 ± 6 | 43 ± 6 | 45 ± 7 | <0.0001 |
| LA diameter ≥40 mm | 2,361 (70) | 1,857 (69) | 504 (76) | 0.0004 |

Values are n (%) and continuous variables are given as mean ± SD.

AF = atrial fibrillation; LA = left atrial/atrium; LVEF = left ventricular ejection fraction; OAT = oral anticoagulation therapy; TIA = transient ischemic attack.

cured 4 months after OAT discontinuation. Aspirin had been suspended in this patient 1 month before the event. Repeat monitoring with 24-h Holter recording and TTM performed for 1 month after the stroke was not able to document any arrhythmic recurrence. Interestingly, no patient with a $CHADS_2$ risk score ≥2 developed TE after OAT discontinuation (Table 4).

In the On-OAT group, the incidence of ischemic stroke was 0.45% (3 of 663 patients), which did not differ significantly from that of the Off-OAT group ($p = 0.06$). The strokes were not fatal. Residual neurological deficits were observed in 2 of these patients. One patient was a 78-year-old woman with a $CHADS_2$ score of 1 and a history of permanent AF. Ablation was not successful, and she remained on OAT after the procedure. The ischemic stroke occurred after 9 months of follow-up. The INR at the time of the event was 1.8. The second patient was a 77-year-old woman with a history of persistent AF and a $CHADS_2$ score of 2 because of her age and hypertension. She had AF recurrences both during and after the 3-month blanking period. One month after the decision to continue OAT, the patient underwent successful transesophageal echocardiography–guided cardioversion while on therapeutic INR. Four days later she presented in AF with aphasia and hemiplegia. Ischemic stroke was documented, and the INR value was 2.0. The third patient was a 75-year-old man with a history of hypertension and a $CHADS_2$ score of 2. He underwent unsuccessful AF ablation, and 4 months after the decision to continue OAT developed mono-ocular partial blindness with documentation of ischemic stroke. The INR value at time of the event was 2.2.

**Hemorrhagic events during follow-up.** In the Off-OAT group, only 1 of 2,692 (0.04%) patients had a major hemorrhage; this patient suffered retroperitoneal bleeding 8 months after OAT discontinuation.

In the On-OAT group, 13 of 663 (2%) patients had a major hemorrhage ($p < 0.0001$ compared with the Off-OAT group). Two (0.30%) patients had intracranial hemorrhage, and 11 (1.7%) had gastrointestinal bleeding. The hemorrhagic strokes occurred 1 and 6 months after the decision to continue OAT, respectively. The event was fatal in 1 patient and required surgical evacuation in the other. The INR at the time of the episode was not available in the first case and was 2.0 in the second. The gastrointestinal hemorrhages occurred 11 ± 6

**Table 2** Baseline Characteristics of the Whole Study Population, Off-OAT Group, and On-OAT Group According to $CHADS_2$ Score

| | Total Population | | | Off-OAT Group | | | On-OAT Group | | | p Value | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | $CHADS_2 = 0$ | $CHADS_2 = 1$ | $CHADS_2 \geq 2$ | $CHADS_2 = 0$ | $CHADS_2 = 1$ | $CHADS_2 \geq 2$ | $CHADS_2 = 0$ | $CHADS_2 = 1$ | $CHADS_2 \geq 2$ | $CHADS_2 = 0$ | $CHADS_2 = 1$ | $CHADS_2 \geq 2$ |
| Patients, n | 1,777 | 984 | 594 | 1,622 | 723 | 347 | 155 | 261 | 247 | — | — | — |
| Sex | | | | | | | | | | | | |
| Male | 1,410 (79) | 770 (78) | 399 (67) | 1,299 (80) | 575 (80) | 242 (70) | 111 (72) | 195 (75) | 157 (64) | 0.013 | 0.106 | 0.114 |
| Female | 367 (21) | 214 (22) | 195 (33) | 323 (20) | 148 (20) | 105 (30) | 44 (28) | 66 (25) | 90 (36) | | | |
| Age, yrs | 54 ± 11 | 59 ± 9 | 62 ± 11 | 54 ± 11 | 59 ± 9 | 63 ± 11 | 55 ± 11 | 60 ± 9 | 60 ± 12 | 0.110 | 0.467 | 0.004 |
| AF type | | | | | | | | | | | | |
| Paroxysmal | 1,141 (64) | 531 (54) | 350 (59) | 1,064 (65) | 407 (56) | 211 (61) | 77 (50) | 124 (47) | 139 (56) | <0.001 | 0.029 | 0.044 |
| Persistent | 243 (14) | 241 (24) | 114 (19) | 206 (13) | 163 (23) | 55 (16) | 37 (24) | 78 (30) | 59 (24) | | | |
| Permanent | 393 (22) | 212 (22) | 130 (22) | 352 (22) | 153 (21) | 81 (23) | 41 (26) | 59 (23) | 49 (20) | | | |
| AF duration, months | 42 ± 33 | 48 ± 50 | 40 ± 42 | 42 ± 31 | 49 ± 45 | 44 ± 38 | 35 ± 52 | 42 ± 72 | 41 ± 47 | 0.057 | 0.387 | 0.044 |
| SHD | 454 (26) | 265 (27) | 264 (44) | 422 (26) | 159 (22) | 149 (43) | 32 (21) | 106 (41) | 115 (47) | 0.143 | <0.001 | 0.382 |
| SHD type | | | | | | | | | | | | |
| Valvular | 247 (14) | 98 (10) | 60 (10) | 233 (14) | 65 (9) | 25 (7) | 14 (9) | 33 (14) | 35 (14) | 0.001 | 0.074 | <0.001 |
| Ischemic | 95 (5) | 91 (9) | 128 (21) | 91 (6) | 61 (8) | 90 (26) | 4 (3) | 30 (11) | 38 (15) | | | |
| Dilated | 46 (3) | 46 (5) | 57 (10) | 44 (3) | 18 (3) | 28 (8) | 2 (1) | 28 (11) | 29 (12) | | | |
| Hypertrophic | 22 (1) | 16 (2) | 7 (1) | 17 (1) | 7 (1) | 3 (1) | 5 (3) | 9 (3) | 4 (2) | | | |
| Others | 44 (3) | 14 (1) | 12 (2) | 37 (2) | 8 (1) | 3 (1) | 7 (5) | 6 (2) | 9 (4) | | | |
| LVEF, % | 56 ± 6 | 56 ± 8 | 50 ± 12 | 56 ± 6 | 56 ± 8 | 48 ± 12 | 57 ± 7 | 56 ± 9 | 53 ± 12 | 0.089 | 0.678 | <0.001 |
| LVEF ≤40% | 44 (2) | 53 (5) | 157 (26) | 40 (2) | 35 (5) | 113 (33) | 4 (3) | 18 (7) | 44 (18) | 0.790 | 0.056 | <0.001 |
| LA diameter, mm | 43 ± 7 | 44 ± 6 | 45 ± 6 | 42 ± 7 | 44 ± 6 | 45 ± 6 | 44 ± 7 | 46 ± 7 | 44 ± 7 | 0.007 | <0.001 | 0.387 |
| LA diameter ≥40 mm | 1,171 (66) | 748 (76) | 442 (74) | 1,059 (65) | 537 (74) | 261 (75) | 112 (72) | 211 (81) | 181 (73) | 0.080 | 0.033 | 0.594 |
| OAT discontinuation after ablation, months | 4 ± 2 | 5 ± 2 | 6 ± 3 | 4 ± 2 | 5 ± 2 | 6 ± 3 | — | — | — | | | |
| Follow-up after OAT discontinuation, months | 28 ± 16 | 25 ± 15 | 28 ± 16 | 29 ± 16 | 25 ± 17 | 29 ± 16 | 28 ± 9 | 26 ± 16 | 27 ± 16 | 0.402 | 0.920 | 0.406 |

Values are n (%) or mean ± SD.

SHD = structural heart disease; other abbreviations as in Table 1.

**Table 3** Thromboembolic Risk Factors According to $CHADS_2$ Score in the Off- and On-OAT Groups

| | $CHADS_2$ Score | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 0 | 1 | 2 | 3 | 4 | 5 | 6 | Total |
| Off-OAT group, n | | | | | | | | |
| Congestive HF | 0 | 40 | 70 | 26 | 8 | 8 | 2 | 154 |
| Hypertension | 0 | 644 | 175 | 72 | 15 | 8 | 2 | 916 |
| Age ≥75 yrs | 0 | 22 | 43 | 19 | 5 | 2 | 2 | 93 |
| Diabetes mellitus | 0 | 17 | 76 | 32 | 10 | 6 | 2 | 143 |
| Prior stroke/TIA | 0 | 0 | 63 | 41 | 11 | 8 | 2 | 125 |
| Total | 1,622 | 723 | 245 | 77 | 15 | 8 | 2 | |
| On-OAT group, n | | | | | | | | |
| Congestive HF | 0 | 37 | 51 | 15 | 6 | 3 | 0 | 112 |
| Hypertension | 0 | 211 | 113 | 39 | 9 | 4 | 0 | 376 |
| Age ≥75 yrs | 0 | 6 | 29 | 5 | 5 | 2 | 0 | 47 |
| Diabetes mellitus | 0 | 7 | 53 | 15 | 6 | 3 | 0 | 84 |
| Prior stroke/TIA | 0 | 0 | 68 | 26 | 7 | 4 | 0 | 105 |
| Total | 155 | 261 | 191 | 42 | 10 | 4 | 0 | |

HF = heart failure; other abbreviations as in Table 1.

months after the decision to continue OAT (range 4 to 9 months). All patients were hospitalized; of these, 9 required blood transfusion and 1 required surgery. The INR at the time of bleeding was above the normal range in 8 patients (between 4.3 and 7.6) and was unavailable in 3. One patient with unavailable INR at the time of the event had gastrointestinal bleeding due to gastric ulcers while on treatment with OAT and nonsteroidal anti-inflammatory agents. No patient died of these events.

**Comparison of event-free survival between the Off- and On-OAT group.** The annual ischemic stroke rate per 100 patient-years was 0.03 (95% confidence interval [CI]: 0.004 to 0.114) in the Off-OAT group and 0.23 (95% CI: 0.047 to 0.662) in the On-OAT group ($p = 0.049$). The annual rate for overall thromboembolic and hemorrhagic strokes per 100 patient-years was 0.03 (95% CI: 0.004 to 0.114) for the Off-OAT group and 0.38 (95% CI: 0.123 to 0.881) for the On-OAT group ($p = 0.002$). Major hemorrhages were significantly more frequent in the On-OAT group, with an annual rate per 100 patient-years of 0.98 (95% CI: 0.523 to 1.678) compared with 0.02 (95% CI: 0.001 to 0.088) in the Off-OAT group ($p < 0.0001$). The event-free survival estimates for freedom from ischemic and hemorrhagic strokes are reported in Figure 1.

In our population, HR for OAT discontinuation indicates that On-OAT group patients experienced major hemorrhage events at a rate that was about 13 times higher than that of patients in the Off-OAT group (HR: 12.9, 95% CI: 2.7 to 61.9, $p = 0.001$). Similarly, the overall hemorrhagic and TEs occurred in the On-OAT group at a rate that was about 9 times higher than that in the Off-OAT group (HR: 8.9, 95% CI: 2.7 to 28.5, $p = 0.0002$).

## Discussion

**Main findings.** The present study shows that OAT can safely be discontinued 3 to 6 months after successful ablation of AF in patients without arrhythmic recurrences off antiarrhythmic drugs, without severe pulmonary vein stenosis, and without severe LA dysfunction. Indeed, the percentage of TE in patients who suspended OAT after successful ablation of AF was not significantly different from that observed in patients who continued OAT after the procedure. In patients with $CHADS_2$ scores of 0, 1, and ≥2, the incidence of TE was 0.06%, 0.14%, and 0%, respectively, in the Off-OAT group and 0%, 0.38%, and 0.81%, respectively, in the On-OAT group. Moreover, the incidence of major hemorrhages was significantly lower among patients who suspended OAT than among those who continued ($p < 0.0001$). In our study, therefore, the risk–benefit ratio favored the discontinuation of OAT even in patients with a medium-high TE risk ($CHADS_2$ scores 1 and ≥2). Our results suggest that the $CHADS_2$ score system probably is not the most appropriate system for

**Table 4** Incidence of Thromboembolic Events and Major Hemorrhage According to $CHADS_2$ Score in Off- and On-OAT Groups

| | $CHADS_2 = 0$ | | $CHADS_2 = 1$ | | $CHADS_2 \geq 2$ | |
|---|---|---|---|---|---|---|
| | Off-OAT | On-OAT | Off-OAT | On-OAT | Off-OAT | On-OAT |
| Patients, n | 1,622 | 155 | 723 | 261 | 347 | 247 |
| TE, n (%) | 1 (0.06) | 0 | 1 (0.14) | 1 (0.38) | 0 | 2 (0.81) |
| Major hemorrhage, n (%) | 0 | 1 (0.64) | 1 (0.14) | 2 (0.8) | 0 | 10 (4) |

OAT = oral anticoagulation; TE = thromboembolic events.

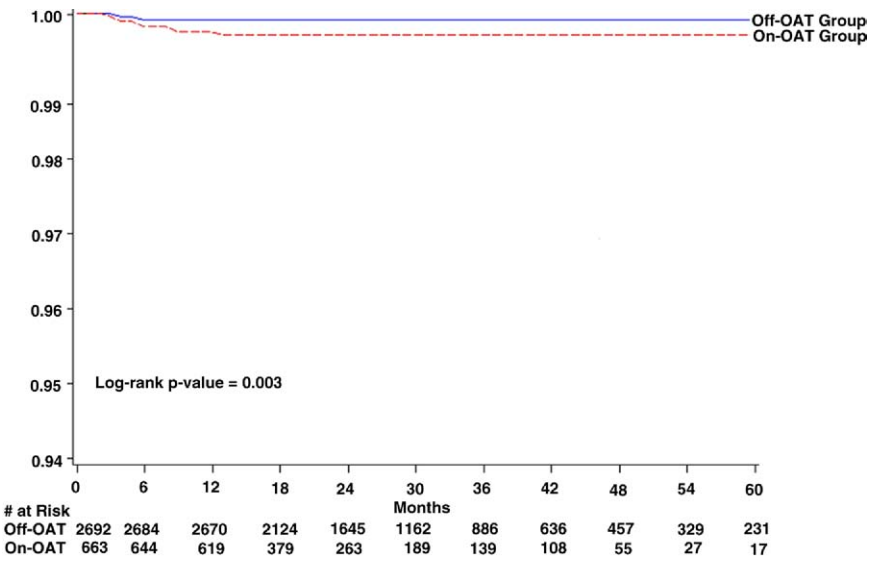


**Figure 1** **Kaplan-Meier Event-Free Survival Estimates for Freedom From Post-Ablation Thromboembolic and Hemorrhagic Strokes in the Off- and On-OAT Groups**

Data have been truncated at 5 years. OAT = oral anticoagulation therapy.

assessing TE risk and establishing an anticoagulation strategy after AF ablation.

**Comparison with previous studies.** As far as we know, this is the largest set of case records compiled on patients who have undergone long-term suspension of OAT, in terms of both the total number of patients (n = 2,692) and the number of moderate-/high-risk patients (723 patients with $CHADS_2$ score 1 and 347 patients with $CHADS_2$ score ≥2), in whom OAT is recommended or suggested by the international guidelines (1,2). Our results are substantially in line with those of other recently published retrospective studies involving smaller populations and shorter follow-up periods (13–16). In particular, they are similar to those observed by Nademanee et al. (14). In a study on long-term outcomes after AF substrate ablation guided by complex fractionated atrial electrograms, these investigators compared the incidence of TE and hemorrhages between 434 patients without arrhythmic recurrences who discontinued OAT and 118 patients requiring OAT after unsuccessful ablation. These patients were selected from a cohort of patients who were at least 65 years old or had 1 or more risk factors for stroke, including hypertension, diabetes, structural heart disease, prior history of stroke/TIA, congestive heart failure, or left ventricular ejection fraction ≤40%. In their population, the annual stroke rate was significantly lower in successfully treated patients who discontinued OAT than in patients with AF recurrences who remained on OAT (0.4% vs. 2%). However, in that study, stroke risk stratification was not based on the $CHADS_2$ score index, nor did the investigators specify the percentage of patients with $CHADS_2$ score ≥2, which identifies the group of patients at highest risk.

**Hypothesis for the low incidence of TE.** In our study, the percentage of TE observed in patients who had undergone successful ablation was decidedly low. Various explanations can be hypothesized for this finding. 1) In our population, OAT was discontinued essentially in patients who suffered no AF recurrences in the absence of antiarrhythmic drugs and after thorough, prolonged monitoring for possible asymptomatic recurrences. 2) All of our patients underwent pre-ablation transesophageal echocardiography, which excluded the presence of endocavitary thrombi, and, before OAT suspension, transthoracic or transesophageal echocardiography, which demonstrated the absence of significant LA dysfunction. 3) Patients with other causes of thromboembolic risk continued OAT. 4) Aspirin was administered indefinitely to most of our patients after OAT suspension. 5) Finally, our patients restarted OAT systematically and promptly after any arrhythmic recurrences.

**Pros and cons of OAT after successful AF ablation.** The reasons for continuing anticoagulation after ablation mainly stem from studies on drug therapy and chiefly concern the risk of asymptomatic recurrences (1,4). The data in the literature indicate that the percentage of patients who suffer exclusively asymptomatic recurrences after successful AF ablation ranges from 0% to 20% (17,18). These percentages are decidedly lower than those observed both in patients on antiarrhythmic therapy for the prevention of AF recurrences (19) and in patients with permanent pacemakers who have no history of atrial tachyarrhythmias (20) (70% and 46%, respectively). Moreover, after successful ablation, asymptomatic AF episodes are often short-lived. Indeed, in one study of patients with permanent pacemakers, the maximum duration of asymptomatic atrial tachyarrhythmias was 18 ±

12 min (21), whereas in another study, the median total arrhythmia (symptomatic and asymptomatic) duration during continuous 7-day ECG monitoring was 17 and 10 h, 6 and 12 months after ablation, respectively (22). Such short-lasting episodes seem to have little clinical significance. Indeed, according to the observations made by Capucci et al. (23), the thromboembolic risk increases only in patients in whom the duration of device-detected AF is 24 h or more.

It is important to consider that OAT involves a 1.2% per year risk of major hemorrhage (1). The decision to administer this therapy must therefore be based on a thorough assessment of the risk–benefit ratio. Patients with a thromboembolic risk of 2% per year or less do not benefit substantially from OAT, and according to the international guidelines should not be treated with this therapy (1). All of the studies, included ours, conducted to date on patients who have undergone successful AF ablation report a decidedly lower incidence of TE than that required by the guidelines (13–16). Another reason for administering OAT after AF ablation is that extensive LA lesions might impair LA function, as observed by Lemola et al. (24) on performing LA circumferential ablation in patients with paroxysmal AF. However, to the best of our knowledge, no other studies have confirmed these data. On the contrary, all of the other studies on this issue have shown significant restoration of LA function and a reduction in LA diameters (25–30). In addition, Sacher et al. (29) also found a restoration of endocrine cardiac function within 3 months in almost all patients despite extensive atrial ablation. The improvement in LA mechanical function is probably the result of inverse electroanatomic remodeling after the restoration and maintenance of sinus rhythm.

**Study limitations.** This was not a randomized prospective study, but rather a summary of a 5-center experience in which similar guidelines for OAT discontinuation were followed. To date, however, it is the observational study with the largest set of case records. The design of the study was retrospective; however, the patients' data were recorded prospectively in a computerized database. Future randomized studies involving a large population of patients at high thromboembolic risk (over 3,000 patients) will be necessary to confirm these data (3).

Another limitation of our study is the relatively scarce distribution of stroke events in the population. Moreover, our On-OAT group was smaller than our Off-OAT group, and included patients who underwent ablation in a shorter period of time (3 years vs. 5 years). Nevertheless, the number of events, particularly hemorrhagic events, was distinctly greater. For the difference existing between the 2 groups, covariate analyses were either not possible or had the risk of overfitting.

It is also important to note that data regarding being in therapeutic range over time were not systematically collected in the database. We recorded the INR at the time of the event in all patients who experienced strokes and in the majority of those who experienced hemorrhagic events. Therefore, we cannot exclude the possibility that in these patients previous INR values were outside of the range or that the time in the therapeutic range was not optimal.

After the initial 5 to 6 months post-ablation, TTM was not performed systematically. Therefore, we cannot rule out the possibility that patients may have had asymptomatic atrial tachyarrhythmias after this period. However, periodic clinical and ECG examinations and frequent Holter monitoring did not document asymptomatic recurrence and daily pulse control did not detect irregularities suggestive of AF. Moreover, prolonging a scrupulous TTM further would not be feasible in clinical practice, nor would it be readily accepted by patients. In any case, the stroke rate in our patients who maintained sinus rhythm was very low, suggesting that if any asymptomatic AF episode occurred, it was without consequence.

## Conclusions

We found that patients who discontinued OAT 3 to 6 months after successful AF ablation had a similar incidence of TE to patients who remained on OAT. Moreover, the rate of major hemorrhages was significantly lower. On the basis of these results, it seems that the risk–benefit ratio favors the discontinuation of OAT after successful AF ablation even in patients at moderate-high risk of TE based on $CHADS_2$ score alone. However, this conclusion needs to be confirmed by future large prospective randomized trials.

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