ORIGINAL ARTICLE

Left Atrial Appendage Closure after Ablation for Atrial Fibrillation

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ABSTRACT

BACKGROUND

Oral anticoagulation is recommended after ablation for atrial fibrillation among patients at high risk for stroke. Left atrial appendage closure is a mechanical alternative to anticoagulation, but data regarding its use after atrial fibrillation ablation are lacking.

METHODS

We conducted an international randomized trial involving 1600 patients with atrial fibrillation who had an elevated score (≥2 in men and ≥3 in women) on the CHA_2DS_2-VASc scale (range, 0 to 9, with higher scores indicating a greater risk of stroke) and who underwent catheter ablation. Patients were randomly assigned in a 1:1 ratio to undergo left atrial appendage closure or receive oral anticoagulation. The primary safety end point, tested for superiority, was non–procedure-related major bleeding or clinically relevant nonmajor bleeding. The primary efficacy end point, tested for noninferiority, was a composite of death from any cause, stroke, or systemic embolism at 36 months. The secondary end point, tested for noninferiority, was major bleeding, including procedure-related bleeding, through 36 months.

RESULTS

A total of 803 patients were assigned to undergo left atrial appendage closure, and 797 to receive anticoagulant therapy. The mean (±SD) age of the patients was 69.6±7.7 years, 34.1% of the patients were women, and the mean CHA_2DS_2-VASc score was 3.5±1.3. At 36 months, a primary safety end-point event had occurred in 65 patients (8.5%) in the left atrial appendage closure group (device group) and in 137 patients (18.1%) in the anticoagulation group (P<0.001 for superiority); a primary efficacy end-point event had occurred in 41 patients (5.3%) and 44 patients (5.8%), respectively (P<0.001 for noninferiority); and a secondary end-point event had occurred in 3.9% and 5.0% (P<0.001 for noninferiority). Complications related to the appendage closure device or procedure occurred in 23 patients.

CONCLUSIONS

Among patients who underwent catheter-based atrial fibrillation ablation, left atrial appendage closure was associated with a lower risk of non–procedure-related major or clinically relevant nonmajor bleeding than oral anticoagulation and was noninferior to oral anticoagulation with respect to a composite of death from any cause, stroke, or systemic embolism at 36 months. (Funded by Boston Scientific; OPTION ClinicalTrials.gov number, NCT03795298.)

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*A list of the OPTION Trial Investigators is provided in the Supplementary Appendix, available at NEJM.org.

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Catheter ablation for atrial fibrillation is an effective strategy for treating symptomatic atrial arrhythmia. However, because of the risk of recurrence of atrial fibrillation, which may be minimally symptomatic, current guidelines recommend indefinite continuation of oral anticoagulation in patients who are at moderate or high risk for stroke, regardless of the perceived outcome of the ablation procedure.[1] Oral anticoagulant therapy has important limitations, including a risk of bleeding, patient anxiety, and cost considerations, which result in a quarter of patients stopping oral anticoagulants within a year after starting treatment.[2-5]

Catheter-based left atrial appendage closure is an alternative strategy for stroke prophylaxis. The safety and efficacy of left atrial appendage closure as compared with warfarin has been established, but data comparing left atrial appendage closure devices with contemporary oral anticoagulants are limited.[6] Furthermore, because patients may have a lower risk of stroke after atrial fibrillation ablation,[7] whether the benefits of left atrial appendage closure are outweighed by the associated risks, including short-term complications related to the procedure and device-related thrombosis, is unclear.[8] Accordingly, the Comparison of Anticoagulation with Left Atrial Appendage Closure after Atrial Fibrillation Ablation (OPTION) trial was designed to determine whether left atrial appendage closure can safely decrease the risk of bleeding associated with oral anticoagulants while maintaining a low risk of stroke among patients with atrial fibrillation who have undergone catheter ablation and are at moderate or high risk for stroke.

Methods

Trial Design

The OPTION trial was a multicenter, randomized clinical trial. The trial protocol has been published previously[9] and is available with the full text of this article at NEJM.org. The trial was funded by the manufacturer of the left atrial appendage closure device (WATCHMAN FLX, Boston Scientific). The trial was designed by a steering committee (Table S1 in the Supplementary Appendix, available at NEJM.org) in collaboration with the sponsor and the Food and Drug Administration. The trial was approved by the ethics or institutional review board at each participating site, and all patients provided written consent to participate. An independent data and safety monitoring committee oversaw patient safety and trial conduct (Table S2). A clinical events committee adjudicated all outcome events (Table S3), and staff at an independent core laboratory assessed all imaging; the members of the clinical events committee and the laboratory staff were unaware of the group assignments. The sponsor collected and monitored the trial data and performed outcome analyses that were independently validated by data analysts and statisticians at the site of the principal investigator according to the statistical analysis plan (available with the protocol). The principal investigator had unrestricted access to the data and wrote the first draft of the manuscript. All the authors provided critical review of the manuscript and vouch for the accuracy and completeness of the data and for the fidelity of the trial to the protocol. Confidentiality restrictions between the sponsor and authors were in place between the time data became available and publication.

Patients

Patients who underwent catheter ablation and had a CHA_2DS_2-VASc score of at least 2 for men or at least 3 for women were eligible for randomization if the ablation had been performed 90 to 180 days before randomization or was scheduled to be performed within 10 days after randomization. Additional inclusion and exclusion criteria are shown in Table S4. The CHA_2DS_2-VASc scale is used to assess the risk of stroke among patients with atrial fibrillation; scores range from 0 to 9, with higher scores indicating a greater risk of stroke. Patients were assigned in a 1:1 ratio to undergo left atrial appendage closure (device group) or receive oral anticoagulation (anticoagulation group), with randomization stratified according to site and timing of the catheter ablation procedure.

Treatment Protocol and Follow-up

Catheter ablation was performed before the left atrial appendage closure device was implanted. After implantation, patients received oral anticoagulants and aspirin for 90 days, followed by aspirin alone until 12 months after randomization. Follow-up imaging of the device (by transesophageal echocardiography [recommended] or computed tomography) was performed at 3 months and 12 months. Patients assigned to the antico-

agulation group started or continued receiving market-approved agents. The choice of oral anticoagulant was at the discretion of the physician.

Follow-up visits occurred at 3, 12, 24, and 36 months after randomization. Clinical information was recorded at each visit, including the HAS-BLED score (an assessment of major bleeding risk among patients with atrial fibrillation receiving anticoagulants; range, 0 to 9, with higher scores indicating a greater risk of bleeding) and recurrences of atrial arrhythmia. A recurrence of atrial arrhythmia was defined as a documented episode of atrial fibrillation or new-onset atrial flutter or an atrial tachycardia event (≥30 seconds in duration or from a 10-second 12-lead electrocardiogram) or electrical or pharmacologic cardioversion for atrial flutter or atrial tachycardia since a previous visit.

END POINTS

The primary safety end point was non–procedure-related bleeding — a combination of major bleeding (as defined by the International Society on Thrombosis and Haemostasis [ISTH]) and clinically relevant nonmajor bleeding (bleeding that required medical intervention, led to hospitalization or increased level of care, or prompted a face-to-face evaluation) — through 36 months (Table S5).[10,11] The primary efficacy end point was a composite of death from any cause, stroke, or systemic embolism at 36 months after randomization. The secondary end point was ISTH major bleeding, including procedure-related bleeding, through 36 months.[11] Data on peridevice leaks and device-related thrombosis were obtained at 3 months and 12 months. The EuroQol Group 5-Dimension 5-Level questionnaire (EQ-5D-5L) and the 12-Item Short-Form Health Survey (SF-12) were completed at the time of enrollment and at 12 months and 36 months. Scores on the EQ-5D-5L index range from −0.59 to 1, with 1 indicating the best possible health state; scores on the SF-12 range from 0 to 100, with higher scores indicating better health status. Additional details regarding definitions of end point are provided in the Supplementary Appendix.

STATISTICAL ANALYSIS

For the primary safety end point, we estimated that a sample size of 1280 patients would provide the trial with 86% power to show the superiority of left atrial appendage closure to oral anticoagulation alone, assuming an incidence of bleeding of 14% in the device group and 20% in the anticoagulation group. We increased the sample size to 1600 patients to allow for withdrawals and loss to follow-up. Testing for superiority at a two-sided alpha level of 0.05 was performed in the intention-to-treat population (all patients who underwent randomization, grouped according to their assigned treatment) with the use of a log-rank P value based on the Kaplan–Meier estimation.

The trial had 85% power to detect noninferiority with respect to the primary efficacy end point in the intention-to-treat population, with a noninferiority margin of 5 percentage points. We assumed that a primary efficacy event would occur in 10% of patients in each group. A noninferiority margin of 5 percentage points, representing a relative risk of 1.5, was chosen because left atrial appendage closure is already considered to be a safe and effective alternative to oral anticoagulation for the composite of death from any cause, stroke, or systemic embolism in patients with reasons to consider an alternative to long-term anticoagulant use. The noninferiority margin in this trial is similar to that used in the trials that established noninferiority of left atrial appendage closure to oral anticoagulation.[12-14] Noninferiority was assessed with the use of the Farrington–Manning method at a one-sided type I error rate of 0.025 with the use of a one-sided z test. If the criteria were met for both superiority regarding the primary safety end point and noninferiority regarding the primary efficacy end point, the trial would be considered successful.

If the criteria for success regarding the primary end points were met, the statistical analysis plan allowed for hierarchical testing for noninferiority of the secondary end point, with a noninferiority margin of 5.25 percentage points. Noninferiority was assessed with the use of a one-sided z test. The proportional-hazards assumption for analyses reporting hazard ratios was assessed with the use of the Wald test from chi-square distribution for linearity of the log hazard ratio. Sensitivity analyses were conducted to assess the primary and secondary end points in the per-protocol population (which included patients in each treatment group regardless of adherence to anticoagulant therapy) and the on-treatment population (which included patients who had ≥80% adherence to the protocol medication until a primary or secondary end-point event oc-

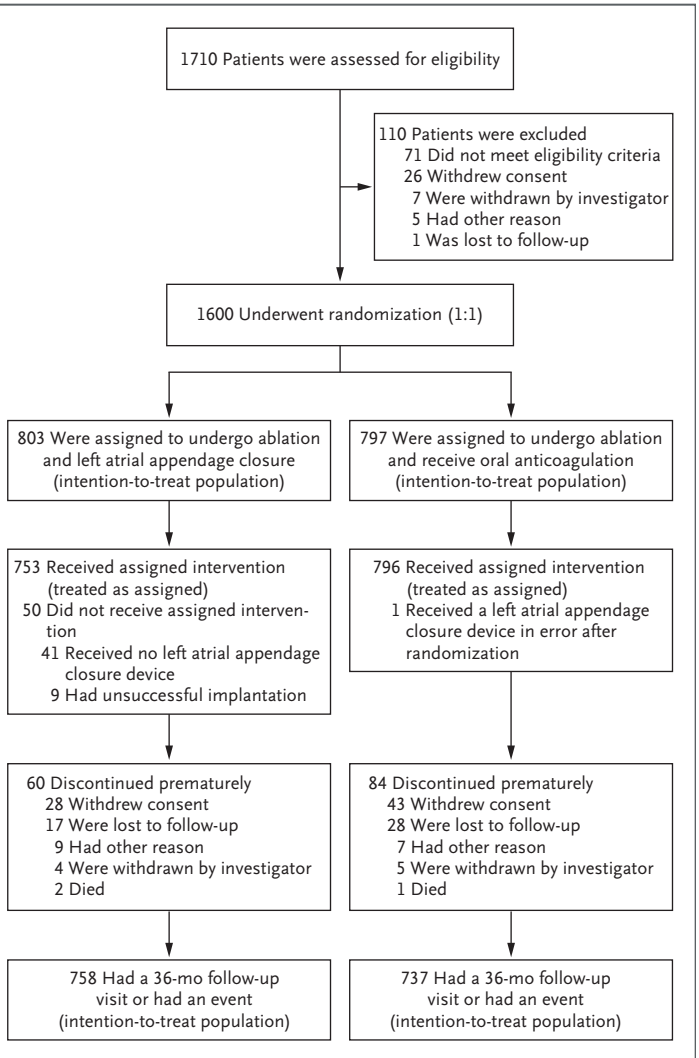


Figure 1. Eligibility, Randomization, and Follow-up.

curred or the trial ended). No statistical techniques were used to impute missing data. Additional details regarding the statistical analysis are provided in the Supplementary Appendix.

RESULTS

PATIENTS AND FOLLOW-UP

Between November 6, 2019, and June 28, 2021, a total of 1600 patients underwent randomization at 106 sites in 10 countries (a full list of sites is provided in the Supplementary Appendix). Of these patients, 803 were assigned to the device group and 797 to the anticoagulation group (Fig. 1). Fifty patients in the device group did not receive a device and continued treatment with oral anticoagulation, and 1 patient who was assigned to the anticoagulation group received a device in error. A total of 82 patients in the anticoagulation group crossed over to the device group; 67 of these patients (82%) did so after a primary end-point event occurred (Table S6).

The mean (±SD) age of the patients was 69.6±7.7 years and 34.1% were women. The mean CHA_2DS_2-VASc score was 3.5±1.3, and the mean HAS-BLED score was 1.2±0.8. Baseline characteristics appeared to be well balanced between the two trial groups (Table 1 and Table S7), and the groups were representative of patients with atrial fibrillation who undergo catheter ablation procedures (Table S8). Follow-up data at 36 months were available for 758 patients (94.4%) in the device group and 737 (92.5%) in the anticoagulation group. A total of 28 patients (3.5%) in the device group and 43 (5.4%) in the anticoagulation group withdrew consent, and 17 (2.1%) and 28 (3.5%) patients, respectively, were lost to follow-up (Fig. 1 and Table S9).

Catheter ablation was performed after randomization in 40.9% of the patients (Table 1). Radiofrequency ablation was used in 59.4% of the patients, and cryoablation in 33.2%. A return of sinus rhythm after the ablation procedure occurred in 88.1% of the patients (Table S10).

Overall, 95.0% of the patients received a non-warfarin anticoagulant (59.3% received apixaban, 27.2% rivaroxaban, 4.3% edoxaban, 3.9% dabigatran, and 0.3% other). Throughout the trial, 84.8% of the patients in the anticoagulation group continued to receive oral anticoagulation. In the device group, 10.1% of patients were receiving oral anticoagulation at 36 months (Fig. S1). The reasons for continuing treatment with anticoagulants are shown in Table S11.

In the device group, implantation was considered by investigators to be successful in 753 of the 762 patients (98.8%) in whom implantation was attempted. Complications related to the device or procedure occurred in 22 patients in the device group and in 1 patient in the anticoagulation group who crossed over to receive a device (Table S12). A complete seal of the left atrial appendage with the device was observed in 81.0% of the patients at 3 months and in 79.7% of the patients at 12 months. The 12-month incidence of device-related thrombus was 1.9% (Table S13).

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Device Group (N=803)	Anticoagulation Group (N=797)
Age — yr	69.7±7.4	69.4±7.9
Sex — no. (%)		
Male	520 (64.8)	533 (66.9)
Female	283 (35.2)	263 (33.0)
Intersex	0 (0)	1 (0.1)
Race or ethnic group — no. (%)†		
White	673 (83.8)	686 (86.1)
Black	14 (1.7)	11 (1.4)
Hispanic or Latino	13 (1.6)	12 (1.5)
Asian	4 (0.5)	1 (0.1)
American Indian or Alaskan Native	2 (0.2)	1 (0.1)
Other	3 (0.4)	3 (0.4)
Not disclosed	94 (11.7)	83 (10.4)
CHA_2DS_2-VASc score‡		
Score	3.5±1.3	3.5±1.3
Distribution — no. (%)		
1	5 (0.6)	7 (0.9)
2 to 3	428 (53.3)	422 (52.9)
4 to 5	310 (38.6)	307 (38.5)
≥6	60 (7.5)	61 (7.7)
HAS-BLED score§	1.2±0.8	1.2±0.8
Score	1.2±0.8	1.2±0.8
Distribution — no. (%)		
0	148 (18.4)	117 (14.7)
1 to 2	605 (75.3)	624 (78.3)
≥3	25 (3.1)	56 (7.0)
Atrial fibrillation pattern — no. (%)		
Persistent	326 (40.6)	296 (37.1)
Paroxysmal	477 (59.4)	501 (62.9)
Present for <1 yr	257 (32.0)	251 (31.5)
Present for ≥1 yr	546 (68.0)	546 (68.5)
Sequential LAAC: ablation 90 to 180 days before randomization — no. (%)	475 (59.2)	—
Concomitant LAAC: ablation within 10 days after randomization — no. (%)¶	328 (40.8)	—
Ablation performed 90 to 180 days before randomization — no. (%)	—	471 (59.1)
Ablation performed within 10 days after randomization — no. (%)	—	326 (40.9)

* Plus–minus values are means ±SD. LAAC denotes left atrial appendage closure.
† Race or ethnic group was reported by the patient.
‡ CHA_2DS_2-VASc scores (an assessment of the risk of stroke among patients with atrial fibrillation) range from 0 to 9, with higher scores indicating a higher risk of stroke.
§ HAS-BLED scores reflect the risk of major bleeding among patients with atrial fibrillation receiving anticoagulants and range from 0 to 9, with higher scores indicating a greater risk of bleeding.
¶ Ablation occurred within 10 days after randomization and on the same day as the left atrial appendage closure except in 3 patients.

Table 2. Primary and Secondary End Points at 36 Months (Kaplan–Meier Estimates).*

End Point	Analysis	Device Group (N=803)	Anticoagulation Group (N=797)	Difference (one-sided 97.5% upper confidence limit)	P Value
		no. of patients (%)		*percentage points*	
Primary end points					
Safety: non–procedure-related bleeding†	Superiority	65 (8.5)	137 (18.1)	—	<0.001
Efficacy: death from any cause, stroke, or systemic embolism‡	Noninferiority, with 5.0-percentage-point margin	41 (5.3)	44 (5.8)	–0.5 (1.8)	<0.001
Secondary end point					
Major bleeding event§	Noninferiority, with 5.25-percentage-point margin	30 (3.9)	38 (5.0)	–1.1 (1.0)	<0.001

* The analyses were performed in the intention-to-treat population, which included all patients who underwent randomization, grouped according to their assigned treatment group; the start time of follow-up for the intention-to-treat analysis was the day of randomization. Testing was performed in a hierarchical manner, with each step needing to reject the null hypothesis in order to proceed to the next step. Step 1 was superiority testing of the primary safety end point and noninferiority testing of the primary efficacy end point, step 2 was noninferiority testing of the secondary end point, step 3 was superiority testing of the secondary end point, and step 4 was superiority testing of the primary efficacy end point. The trial was considered to be successful if the criteria were met for both superiority regarding the primary safety end point and noninferiority regarding the primary efficacy end point.

† Non–procedure-related bleeding was a composite of ISTH major bleeding or clinically relevant nonmajor bleeding. Non–procedure-related events were those that occurred after 3 days following the procedure in the device group. The P value was calculated with the use of the log-rank test and is based on the Kaplan–Meier estimation for the superiority testing.

‡ The P value for the primary efficacy end point (a composite of stroke, all-cause death, or systemic embolism) was calculated with the use of the z test and is based on the standard normal distribution for the noninferiority testing and log-rank test for the superiority testing.

§ Major bleeding was defined as ISTH major bleeding, including procedure-related bleeding. The P value was calculated with the use of the z test and is based on the standard normal distribution for the noninferiority testing and log-rank test for the superiority testing.

END POINTS

All analyses were performed in the intention-to-treat population. Non–procedure-related major bleeding or clinically relevant nonmajor bleeding (primary safety end point) occurred in 65 patients (Kaplan–Meier estimate, 8.5%) in the device group and in 137 patients (Kaplan–Meier estimate, 18.1%) in the anticoagulation group (hazard ratio, 0.44; 95% confidence interval [CI], 0.33 to 0.59; P<0.001 for superiority) (Table 2, Fig. 2, and Table S14). Results of sensitivity analyses (assessed in the per-protocol and on-treatment populations) were consistent with the results of the primary end-point analysis (Table S15 and S16).

Death from any cause, stroke, or systemic embolism at 36 months (primary efficacy end point) occurred in 41 patients (Kaplan–Meier estimate, 5.3%) in the device group and in 44 patients (Kaplan–Meier estimate, 5.8%) in the anticoagulation group, for a difference of –0.5 percentage points (hazard ratio, 0.91; 95% CI, 0.59 to 1.39; one-sided 97.5% upper confidence limit, 1.8; P<0.001 for noninferiority) (Table 2, and Fig. 2). Results of analyses of the primary efficacy end point were similar in the per-protocol and on-treatment populations (Tables S15 and S16).

ISTH major bleeding, including procedure-related bleeding, through 36 months (secondary end point) occurred in 30 patients (Kaplan–Meier estimate, 3.9%) in the device group and in 38 patients (Kaplan–Meier estimate, 5.0%) in the anticoagulation group, for a difference of –1.1 percentage points (hazard ratio, 0.77; 95% CI, 0.48 to 1.24; one-sided 97.5% upper confidence limit, 1.0), which met the criterion for noninferiority (P<0.001) but not superiority (P=0.28) (Table 2, Fig. 2, and Fig. S2). Results of prespecified subgroup analyses of the primary and secondary end points appeared to be consistent across subgroups stratified according to age, sex, CHA_2DS_2-VASc score, HAS-BLED score, and type of atrial fibrillation (paroxysmal or persistent) (Fig. S3).

By 36 months, death from any cause had occurred in 29 patients (Kaplan–Meier estimate, 3.8%) in the device group and 34 patients (Kaplan–Meier estimate, 4.5%) in the anticoagulation group, and ischemic stroke had occurred in

9 patients (Kaplan–Meier estimate, 1.2%) and 10 patients (Kaplan–Meier estimate, 1.3%) in the two groups, respectively. Hemorrhagic stroke had occurred in 3 patients (Kaplan–Meier estimate, 0.4%) in each group. Systemic embolism had occurred in 2 patients (Kaplan–Meier estimate, 0.3%) in the device group and in 1 patient (Kaplan–Meier estimate, 0.1%) in the anticoagulation group, and pericardial effusion requiring intervention had occurred in 2 patients (Kaplan–Meier estimate, 0.3%) and 5 patients (Kaplan–Meier estimate, 0.7%), respectively. Additional safety end points through 36 months are shown in Table S17, and a full list of adverse events is provided in Table S18.

The percentage of patients with clinical recurrence of atrial fibrillation and of patients who received antiarrhythmic agents at 36 months is shown in Table S19 and Figure S4. A descriptive analysis of EQ-5D-5L and SF-12 quality-of life measures is shown in Table S20.

DISCUSSION

In this international trial involving patients at moderate-to-high risk for stroke who underwent catheter ablation for atrial fibrillation, left atrial appendage closure was associated with a lower risk of non–procedure-related bleeding than oral anticoagulation and was noninferior with respect to the composite end point of death from any cause, stroke, or systemic embolism at 36 months. The fact that left atrial appendage closure can be completed safely at the time of atrial fibrillation ablation makes it a possible alternative to long-term oral anticoagulation.

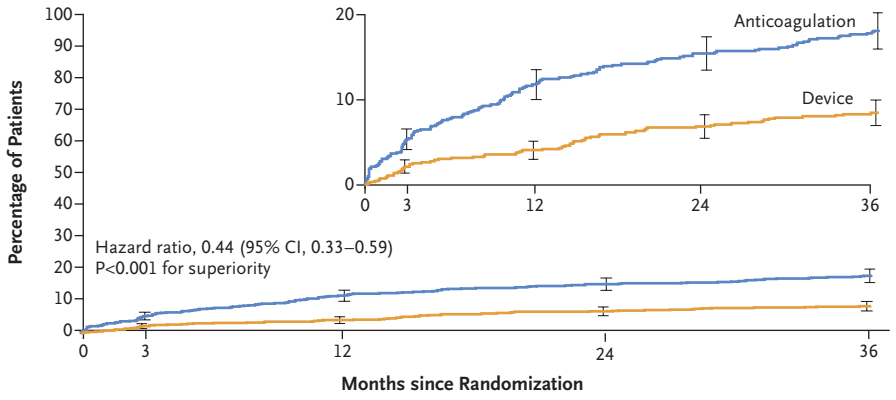
Randomized trials have shown that among patients with atrial fibrillation at elevated risk for stroke, left atrial appendage closure is associated with a lower incidence of postprocedure bleeding, hemorrhagic stroke, and death from cardiovascular causes than oral anticoagulation, with a similar incidence of ischemic stroke.[15,16] However, the oral anticoagulant used in these studies was most often warfarin and the patients who were enrolled in these trials were at high risk for stroke and bleeding. After ablation for atrial fibrillation, patients are not perceived to be at high risk for bleeding, and the results of several nonrandomized studies have suggested that catheter ablation may reduce the incidence of ischemic stroke.

The OPTION trial was designed to assess whether left atrial appendage closure would safely result in a lower incidence of bleeding than oral anticoagulation, while maintaining a low risk of stroke, in patients with atrial fibrillation who underwent catheter ablation, with the majority (95%) of patients receiving nonvitamin K antagonists (direct oral anticoagulants). The observed percentage of patients with bleeding at 36 months (18.1%) in the anticoagulation group was high despite the relatively low HAS-BLED score, which emphasizes the challenges with long-term oral anticoagulation. The 56% lower risk of non–procedure-related bleeding with left atrial appendage closure than with oral anticoagulation was driven largely by clinically relevant nonmajor bleeding (bleeding that required medical intervention, led to hospitalization or increased level of care, or prompted a face-to-face evaluation). Clinically relevant nonmajor bleeding is one of the many causes of suboptimal adherence to long-term oral anticoagulation.[17] Even with the inclusion of procedure-related bleeding events, there were numerically fewer major bleeding events with left atrial appendage closure than with oral anticoagulation.

The continued use of oral anticoagulants exposes patients to a higher risk of bleeding than the long-term aspirin therapy received by most patients who undergo left atrial appendage closure. This observation is highlighted by the results of the ARTESIA trial (Apixaban for the Reduction of Thrombo-Embolism in Patients with Device-Detected Subclinical Atrial Fibrillation). In the ARTESIA trial, in which patients had a CHA_2DS_2-VASc score of 3.9±1.1, which is similar to that in the OPTION trial, patients who received treatment with apixaban had higher rates of major bleeding than patients who received aspirin (1.71% per patient-year vs. 0.94% per patient-year; hazard ratio, 1.80; 95% CI, 1.26 to 2.57; P=0.001).[18]

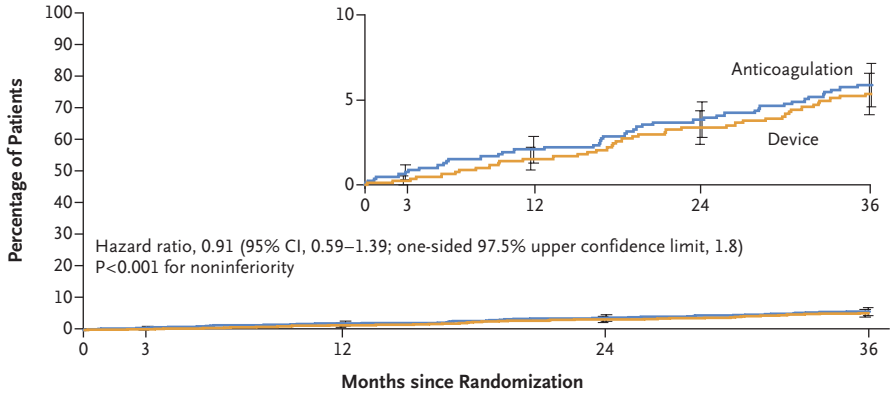
In the OPTION trial, left atrial appendage closure was noninferior to oral anticoagulation with respect to the primary efficacy composite end point of death from any cause, stroke, or systemic embolism. Deaths from any cause accounted for most of the efficacy end-point events and the incidence appeared to be similar in the two groups. None of the deaths were considered to be related to the device. The incidence of ischemic stroke was low in both trial groups.

A Non–Procedure-Related Major Bleeding or Clinically Relevant Nonmajor Bleeding (primary safety end point)



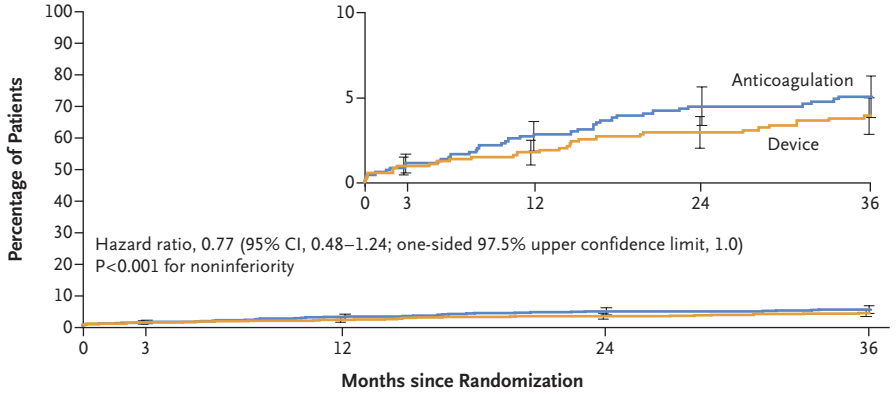
No. at Risk					
Anticoagulation	797	753	701	657	598
Device	803	776	749	728	681

B Composite of Death from Any Cause, Stroke, or Systemic Embolism (primary efficacy end point)



No. at Risk					
Anticoagulation	797	775	754	740	701
Device	803	782	772	757	722

C Major Bleeding (secondary end point)



No. at Risk					
Anticoagulation	797	772	749	726	678
Device	803	778	763	746	708

Figure 2 (facing page). Primary and Secondary End Points at 36 Months (Kaplan–Meier Analysis).

Shown is the incidence, at 36 months after randomization, of non–procedure-related major bleeding or clinically relevant nonmajor bleeding (as defined by the International Society on Thrombosis and Haemostasis [ISTH]), which was the primary safety end point (Panel A); a composite of death from any cause, stroke, or systemic embolism, which was the primary efficacy end point (Panel B); and major bleeding (as defined by the ISTH), including procedure-related bleeding, which was the secondary end point (Panel C). The two primary cohorts were patients who underwent catheter ablation and implantation of a left atrial appendage closure device and those who underwent catheter ablation and received oral anticoagulation. The insets show the same data on an expanded y axis.

The two groups appeared to be balanced with respect to sequential ablation (ablation performed 90 to 180 days before randomization), and the incidence of recurrence of atrial arrhythmias after the ablation procedure also appeared to be similar in the two groups, so it is unlikely that the outcomes could be attributed to changes in the burden of atrial fibrillation.

The relatively low risk of stroke in both treatment groups may be related to a lower burden of atrial fibrillation after ablation. Several studies have shown that a higher atrial fibrillation burden is associated with an increased risk of stroke.[19-21] Data have been mixed or underpowered to determine whether ablation reduces stroke rates.[4,22,23] Although the results of this trial appeared to be consistent across subgroups, the percentage of patients with a primary efficacy end-point event appeared to increase in both groups with increasing CHA_2DS_2-VASc score. In the absence of any compelling data, current guidelines are uniform in advocating the continuation of oral anticoagulation after ablation on the basis of underlying stroke risk and not on the basis of the perceived success of the ablation procedure.[24] In this context, the low risk of death, stroke, or systemic embolism associated with both left atrial appendage closure and oral anticoagulation provides alternatives for patients after atrial fibrillation ablation.

Complete seal of the left atrial appendage at early time points with the device used in the OPTION trial was similar to that in the PINNACLE FLX study and the SURPASS Registry.[25,26] However at 12 months, a complete seal was present in 80% of patients in the OPTION trial, as compared with 90% of patients in the PINNACLE FLX study. Most observed leaks were 3 mm or less. The difference may be attributed to the use of computed tomography for monitoring in the OPTION trial (computed tomography was used in 16% of patients at 12 months), which may be more sensitive in detecting leaks than echocardiography, which was used in the PINNACLE FLX study. The incidence of device-related thrombosis appeared to be low at 12 months. Although the percentage of patients with a complete seal was lower in the OPTION trial than the PINNACLE FLX study at 12 months, the observed incidence of ischemic stroke in our trial appeared to be similar in the two groups (occurring in 1.2% of patients assigned to undergo left atrial appendage closure and in 1.4% of those assigned to oral anticoagulation).

Left atrial appendage closure proved to be safe in this trial. Although the attribution of specific complications to left atrial appendage closure as compared with catheter ablation is confounded when these procedures are performed concomitantly, the most serious procedure-related complication, pericardial tamponade, occurred in 0.3% of patients assigned to undergo left atrial appendage closure and in 0.7% assigned to receive oral anticoagulation. The low incidence of complications is consistent with advances in device technology.[25,26]

Our trial has limitations. At the time of the trial, pulsed field ablation was not available; however, the type of ablation technology used is unlikely to alter the strategies used for stroke prevention. Patients with a left ventricular ejection fraction of 30% or less were excluded from the trial, and our results may not be applicable to these patients. Although all bleeding events were adjudicated by an independent clinical events committee, the open-label design could have led patients in the anticoagulation group to seek medical attention more frequently.

The results of this trial showed that among patients at moderate-to-high risk for stroke who underwent catheter-based ablation for atrial fibrillation, left atrial appendage closure was associated with a lower risk of non–procedure-related

major or clinically relevant nonmajor bleeding than oral anticoagulation and was noninferior to oral anticoagulation with respect to a composite end point of death from any cause, stroke, or systemic embolism at 36 months.

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A data sharing statement provided by the authors is available with the full text of this article at NEJM.org.

APPENDIX

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