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Bleeding Outcomes After Left Atrial Appendage Closure Compared With Long-Term Warfarin

A Pooled, Patient-Level Analysis of the WATCHMAN Randomized Trial Experience

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ABSTRACT

OBJECTIVES The purpose of this study was to compare the relative risk of major bleeding with left atrial appendage (LAA) closure compared with long-term warfarin therapy.

BACKGROUND LAA closure is an alternative approach to chronic oral anticoagulation for the prevention of thromboembolism in patients with atrial fibrillation (AF).

METHODS We conducted a pooled, patient-level analysis of the 2 randomized clinical trials that compared WATCHMAN (Boston Scientific, Natick, Massachusetts) LAA closure with long-term warfarin therapy in AF.

RESULTS A total of 1,114 patients were included, with a median follow-up of 3.1 years. The overall rate of major bleeding from randomization to the end of follow-up was similar between treatment groups (3.5 events vs. 3.6 events per 100 patient-years; rate ratio [RR]: 0.96; 95% confidence interval [CI]: 0.66 to 1.40; $p = 0.84$). LAA closure significantly reduced bleeding >7 days post-randomization (1.8 events vs. 3.6 events per 100 patient-years; RR: 0.49; 95% CI: 0.32 to 0.75; $p = 0.001$), with the difference emerging 6 months after randomization (1.0 events vs. 3.5 events per 100 patient-years; RR: 0.28; 95% CI: 0.16 to 0.49; $p < 0.001$), when patients assigned to LAA closure were able to discontinue adjunctive oral anticoagulation and antiplatelet therapy. The reduction in bleeding with LAA closure was directionally consistent across all patient subgroups.

CONCLUSIONS There was no difference in the overall rate of major bleeding in patients assigned to LAA closure compared with extended warfarin therapy over 3 years of follow-up. However, LAA closure significantly reduced bleeding beyond the procedural period, particularly once adjunctive pharmacotherapy was discontinued. The favorable effect of LAA closure on long-term bleeding should be considered when selecting a stroke prevention strategy for patients with nonvalvular AF. (WATCHMAN Left Atrial Appendage System for Embolic PROTECTion in Patients With Atrial Fibrillation; NCT00129545; and Evaluation of the WATCHMAN LAA Closure Device in Patients With Atrial Fibrillation Versus Long Term Warfarin Therapy [PREVAIL]; NCT01182441) (J Am Coll Cardiol Intv 2015;8:1925–32) © 2015 by the American College of Cardiology Foundation. Published by Elsevier. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation

LAA = left atrial appendage

NOAC = non-vitamin K–dependent oral anticoagulant

OAC = oral anticoagulant

RRR = relative risk reduction

Atrial fibrillation (AF) is associated with a 4- to 5-fold increased risk of ischemic stroke after adjustment for other risk factors (1). Oral anticoagulant (OAC) therapy reduces this risk but increases the risk of bleeding (2), which contributes to underutilization and frequent discontinuation (3–5). Despite the established efficacy of the non-vitamin K-antagonist oral anticoagulant agents (NOACs), the randomized clinical trials of these agents excluded patients with previous bleeding or those with conditions associated with a high bleeding risk (6–10). Therefore, there is an unmet clinical need for alternative therapeutic approaches that reduce thromboembolic events but are associated with less long-term bleeding.

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The left atrial appendage (LAA) is the probable source of most thromboembolic events in patients with nonvalvular AF (11,12). The results of the PROTECT-AF (WATCHMAN Left Atrial Appendage System for Embolic Protection in Patients with Atrial Fibrillation) and PREVAIL (Prospective Randomized Evaluation of the Watchman LAA Closure Device In Patients with Atrial Fibrillation Versus Long Term Warfarin Therapy) trials demonstrated that transcatheter LAA closure followed by discontinuation of long-term OAC is a safe and effective alternative to long-term warfarin anticoagulation for the prevention of stroke, systemic embolism, and cardiovascular death in AF patients at moderate-to-high thromboembolic risk (13,14). Differences in bleeding outcomes between mechanical closure and long-term warfarin therapy could help inform the selection of the appropriate management strategy for stroke prevention in patients with AF. The goal of this study was to assess the relative risks of bleeding over time with a strategy of transcatheter LAA closure compared with long-term warfarin therapy among OAC-eligible patients.

METHODS

PATIENT POPULATION AND STUDY PROCEDURES. This was a pooled, patient-level analysis of the PROTECT-AF and PREVAIL randomized clinical trials. The study designs of these trials have been described previously (13,15). In brief, the PROTECT-AF trial randomly assigned 707 AF patients with $CHADS_2$ (congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, stroke) score ≥1 who were eligible for long-term OAC to either LAA closure with the WATCHMAN device (Boston Scientific, Natick, Massachusetts) or warfarin in a 2:1 ratio; the PREVAIL trial randomly assigned 407 OAC-eligible AF patients with $CHADS_2$ scores ≥2 (and selected patients with $CHADS_2 = 1$ and an additional risk factor) to either WATCHMAN LAA closure or warfarin in a 2:1 ratio. The inclusion and exclusion criteria of the 2 trials were otherwise similar, except that patients requiring clopidogrel therapy at baseline were eligible for PROTECT-AF but not PREVAIL. In both trials, patients who were randomly assigned to LAA closure continued warfarin and aspirin for approximately 6 weeks post-procedure, when transesophageal echocardiography was performed to confirm LAA sealing. If the LAA was adequately sealed (peridevice leak <5 mm in diameter), patients discontinued warfarin and were treated with aspirin and clopidogrel for 6 months post-procedure, followed by indefinite aspirin therapy (**Figure 1**).

ENDPOINTS AND DEFINITIONS. The primary efficacy endpoint of both trials was a composite of cardiovascular or unexplained death, stroke, and systemic embolism. Major bleeding was defined as an adverse event that was assigned 1 of several bleeding codes and was adjudicated by the clinical events committee as significant (life-threatening or resulting in hospitalization, prolongation of hospitalization, substantial disability, or death). $CHADS_2$ and CHA_2DS_2-VASc (congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, stroke/transient ischemic attack, vascular disease, age 65 to 74 years, sex category) scores were calculated according to Gage et al. (16) and Lip et al. (17), respectively. Modified HAS-BLED scores were calculated according to Pisters et al. (18), except that no points were assigned for liver dysfunction or labile international normalized ratio values, as these data were not systematically collected. High baseline bleeding risk was defined as a modified HAS-BLED score ≥3, consistent with society guidelines (19).

STATISTICAL ANALYSIS. Patient-level data were pooled from the PROTECT-AF and PREVAIL trials at 2,717 and 860 patient-years of follow-up, respectively, and were analyzed using a frequentist

Scientific; and the LAA closure technology has been licensed to Boston Scientific, and both Mayo Clinic and Dr. Holmes have contractual rights to receive future royalties from this license.

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FIGURE 1 Timeline of Adjunctive Pharmacotherapy in Patients Randomly Assigned to Device Therapy

From implant to 45 days, patients were treated with a combination of aspirin and warfarin, and if TEE then documented a seal (leak <5 mm), patients were treated with a combination of aspirin and clopidogrel from 45 days to 6 months. After this period of adjunctive pharmacotherapy, patients were treated with aspirin monotherapy ("destination therapy"). ASA = aspirin; TEE = transesophageal echocardiography.

statistical approach. The PREVAIL patients were assessed without the informative prior. Post-hoc landmark analyses were performed at 7 days, 45 days, and 6 months post-procedure to assess the influence of procedural complications and adjunctive pharmacotherapy on rates of bleeding. Log-rank tests were used to compare Kaplan-Meier curves for overall follow-up and beyond 7 days, because the proportional hazards assumption was not met for these periods. Events per 100 patient-years were compared using Poisson regression models including random study effects. Cox proportional hazards models were used to compare groups beyond 45 days and beyond 6 months, as the proportional hazard assumption was met for these periods ($p = 0.20$ and $p = 0.23$, respectively). Cox proportional hazards models were used to test subgroup-by-treatment interactions. All Cox models used a marginal models approach to account for intrastudy correlation. Categorical variables are reported as counts (percentages), and continuous variables are reported as the mean ± SD or median and interquartile range (IQR) where appropriate. Statistical significance was accepted at the 95% confidence level ($p < 0.05$).

RESULTS

A total of 1,114 patients were included in the analysis, of which 732 and 382 were randomly assigned to device and warfarin therapy, respectively. Baseline characteristics are summarized in Table 1. Overall, the mean age was 72.9 ± 8.5 years, the mean CHA_2DS_2-VASc score was 3.7 ± 1.4, and the mean modified HAS-BLED score was 1.9 ± 1.0. A CHA_2DS_2-VASc score ≥2 was present in 95.6% of patients, and a modified HAS-BLED score ≥3 in 22.1%. The mean CHA_2DS_2-VASc score was slightly higher and previous myocardial infarction more frequent in the long-term warfarin group ($p = 0.02$ for both). Patients were followed for a median of 3.1 years (IQR: 2.0 to 5.0 years). Cumulative follow-up was 2,422 patient-years for the device group and 1,249 patient-years for the warfarin group. The time within therapeutic range among patients assigned to warfarin therapy was 69%. Among patients receiving the device, the median duration of warfarin treatment was 50 days (IQR: 43 to 57 days), and 89.5% permanently discontinued warfarin over the course of the trial.

BLEEDING RATES. The distribution of bleeding risk and the observed rates of bleeding according to treatment group are shown in Tables 2 and 3. The bleeding rates from randomization to the end of follow-up were similar between patients randomly assigned to device and long-term warfarin therapy (3.5 events vs. 3.6 events per 100 patient-years; rate ratio (RR): 0.96; 95% CI: 0.66 to 1.40; $p = 0.84$). Approximately one-half of the bleeding events in the

TABLE 1 Baseline Characteristics of the Study Population

	Treatment Arm		
	LAA Closure (n = 732)	Long-Term Warfarin (n = 382)	p Value
Age, yrs	72.5 ± 8.4	73.5 ± 8.6	0.09
Age >65 yrs	616 (84.2)	329 (86.1)	0.38
Male	508 (69.4)	274 (71.7)	0.45
Hypertension	653 (89.2)	354 (92.7)	0.07
Diabetes mellitus	204 (27.9)	113 (29.6)	0.58
Previous myocardial infarction	105 (14.3)	77 (20.2)	0.02
Previous stroke	104 (14.2)	61 (16.0)	0.43
Previous major bleeding	96 (13.1)	52 (13.6)	0.82
$CHADS_2$	2.3 ± 1.1	2.4 ± 1.2	0.06
CHA_2DS_2-VASc	3.6 ± 1.4	3.8 ± 1.5	0.02
CHA_2DS_2-VASc ≥2	692 (94.9)	367 (96.8)	0.17
Modified HAS-BLED	1.9 ± 0.9	1.9 ± 1.0	NS

Values are mean ± SD or n (%). Patients were randomized in a 2:1 fashion to either LAA closure or long-term warfarin. The modified HAS-BLED score provided zero points for liver disease and labile international normalized ratio.

$CHADS_2$ = congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, stroke; CHA_2DS_2-VASc = congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, stroke/transient ischemic attack, vascular disease, age 65–74 years, sex category; LAA = left atrial appendage; NS = not significant.

TABLE 2 Distribution of Modified HAS-BLED Scores Among the Patient Population

Modified HAS-BLED Score	LAA Closure (n = 732)	Warfarin (n = 382)
0	34 (4.6)	17 (4.5)
1	220 (30.1)	123 (32.2)
2	284 (38.8)	151 (39.5)
3	124 (16.9)	66 (17.2)
4	31 (4.2)	19 (5.0)
5	0	6 (1.6)

Values are n (%). Patients were randomized in a 2:1 fashion to either LAA closure or long-term warfarin The modified HAS-BLED score provided no points for liver disease and labile international normalized ratio.

LAA = left atrial appendage.

device group (48%) occurred within the first 7 days after randomization, that is, during the periprocedural period. LAA closure significantly reduced the rate of major bleeding compared with long-term warfarin beyond 7 days post-randomization (1.8 events vs. 3.6 events per 100 patient-years; RR: 0.49; 95% CI: 0.32 to 0.75; $p = 0.001$), beyond 45 days (1.3 events vs. 3.6 events per 100 patient-years; RR: 0.37; 95% CI: 0.23 to 0.60; $p < 0.001$); and beyond 6 months (1.0 events vs. 3.5 events per 100 patient-years; RR: 0.28; 95% CI: 0.16 to 0.49; $p < 0.001$). The decrease in bleeding with LAA closure was driven by reductions in both gastrointestinal bleeding and hemorrhagic stroke (Table 4).

The difference in survival free from bleeding increased with continued follow-up (Figure 2). Landmark analyses across several intervals (Figures 2 and 3) suggest that the reduction in bleeding with LAA closure began 6 months after randomization, consistent with when patients in the device group could discontinue adjunctive pharmacotherapy (warfarin and aspirin followed by dual antiplatelet therapy).

SUBGROUP ANALYSES. The relationships between clinical characteristics and bleeding beyond 6 months post-randomization are shown in Table 5. LAA closure significantly reduced bleeding irrespective of age, sex, baseline bleeding risk, or thromboembolic risk score. The relative magnitude of benefit was significantly greater in females, patients ≤75 years of age, and those with modified HAS-BLED scores <3.

DISCUSSION

The main findings of this study are that among OAC-eligible patients with AF: 1) the overall rate of major bleeding over a median follow-up of 3 years was similar with a strategy of LAA closure compared with long-term warfarin; and 2) LAA closure led to a significant and substantial reduction in major bleeding once the required period of adjunctive anticoagulant and dual antiplatelet pharmacotherapy for the device was completed. Furthermore, LAA closure significantly reduced nonprocedural bleeding across risk and age strata. These findings have important implications for the selection of a management strategy for stroke prevention in patients with nonvalvular AF.

Although the clinical efficacy of OAC is well established, concerns about long-term bleeding are a major driver of OAC prescribing patterns as well as treatment discontinuation in patients who have already initiated therapy (3–5). The current analysis demonstrates that, although the overall rate of bleeding was similar between groups at a median follow-up duration of 3 years beyond the immediate procedural period, the risk of bleeding was substantially lower after LAA closure than with long-term warfarin therapy. Indeed, beyond 6 months after the procedure, when all adjunctive pharmacotherapy other than aspirin could be discontinued, LAA closure provided a 72% relative risk reduction (RRR) in major bleeds. This reduction was driven mainly by gastrointestinal bleeding and to a lesser extent by hemorrhagic stroke. Although the NOACs also reduce hemorrhagic stroke compared with warfarin, their use is associated with greater or similar rates of

TABLE 3 Observed Rates of Major Bleeding Over Time According to Treatment Group

	LAA Closure (n = 732)		Long-Term Warfarin (n = 382)			
	Bleeding Rate (n events/N at risk)	Event Rate/100 pt-yrs (n events/pt-years)	Bleeding Rate (n events/N at risk)	Event Rate/100 pt-yrs (n events/pt-years)	Rate Ratio (95% CI)	p Value
Overall	10.8 (79/732)	3.5 (79/2,268)	11.3 (43/382)	3.6 (43/1,187)	0.96 (0.66–1.40)	0.84
Post-procedural	5.9 (40/682)	1.8 (40/2,255)	11.3 (43/381)	3.6 (43/1,180)	0.49 (0.32–0.75)	0.001
Destination therapy	3.2 (19/601)	1.0 (19/1,958)	9.7 (35/360)	3.5 (35/1,004)	0.28 (0.16–0.49)	<0.001

Values are % (n/N). The *overall* period was defined as after randomization to the end of follow-up; *post-procedural* period as >7 days after randomization to the end of follow-up, thereby isolating nonprocedural related bleeding events; and *destination therapy* period as beyond 180 days post-randomization, when patients assigned to LAA closure were eligible to receive aspirin alone. Patients were randomized in a 2:1 fashion to either LAA closure or long-term warfarin.

LAA = left atrial appendage; Pt-yrs = patient-years.

TABLE 4 Types and Frequencies of Major Bleeding Events That Occurred After the Period of Adjunctive Pharmacotherapy (OAC and DAPT) in the Device Group (>6 Months Post-Randomization)

	LAA Closure (n = 732)	Warfarin (n = 382)	p Value
Gastrointestinal bleeding	10 (1.4)	21 (5.5)	<0.001
Epistaxis	1 (0.1)	1 (0.3)	1.0
Hematuria	0 (0)	2 (0.5)	0.12
Hemorrhagic stroke	2 (0.3)	7 (1.8)	0.01
Cranial bleed	3 (0.4)	1 (0.3)	1.0
Anemia requiring transfusion	2 (0.3)	1 (0.3)	1.0
Major bleed requiring transfusion	1 (0.1)	1 (0.3)	1.0
Other bleeding	0 (0)	1 (0.3)	0.35

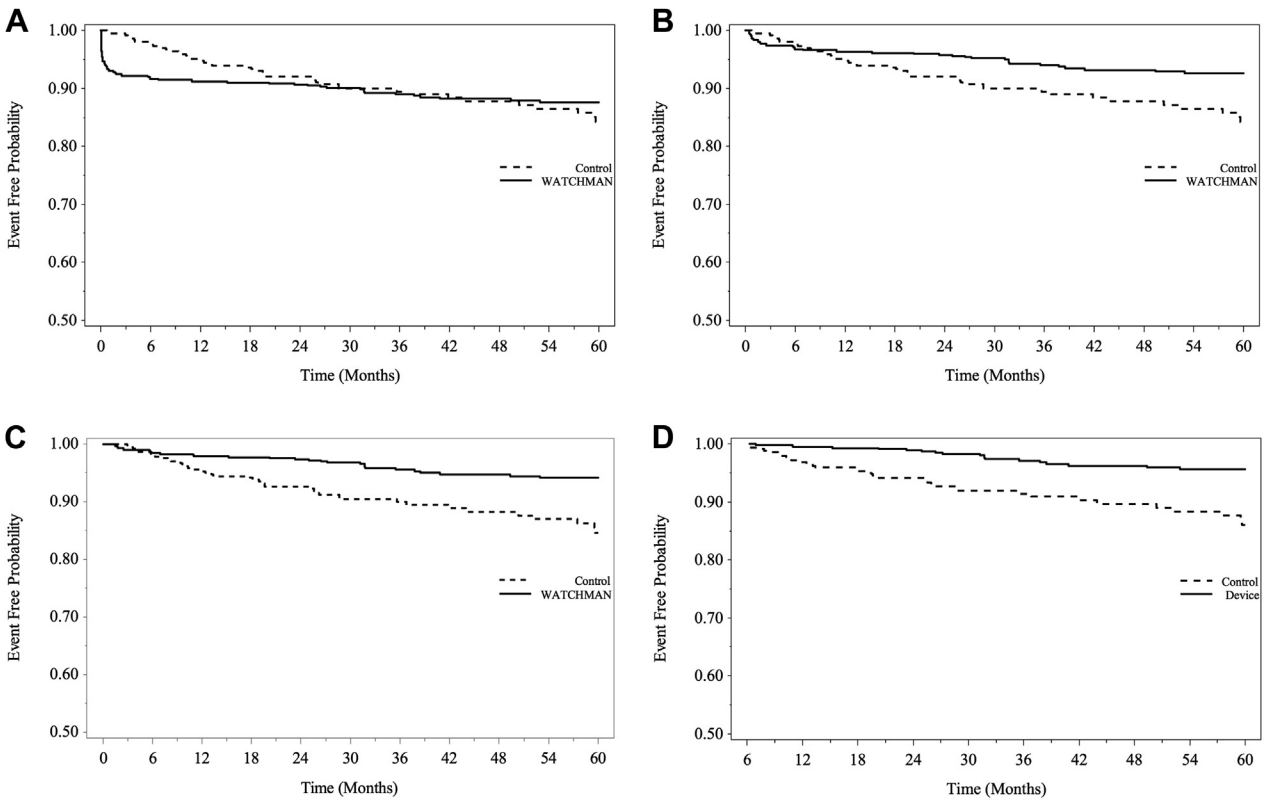
Values are n (%). Note that patients were randomly assigned to LAA closure or warfarin therapy in a 2:1 fashion.

DAPT = dual antiplatelet therapy; LAA = left atrial appendage; OAC = oral anticoagulation.

gastrointestinal bleeding (6,7,9,10). Although LAA closure is associated with a significant procedural hazard, there is an important practical distinction between bleeding that occurs at the time of the device implantation (e.g., pericardial effusion or groin hematoma) and nonprocedural, anticoagulation-related bleeding: the former occurs in the hospital setting where medical care is immediately available, whereas the latter may occur when prompt care is not rapidly accessible.

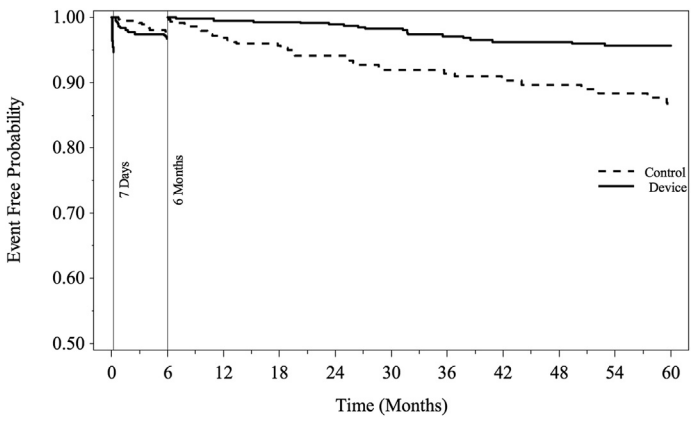
The reduction in bleeding with LAA closure compared with chronic warfarin was directionally consistent among all patient subgroups examined. Paradoxically, we observed a particular advantage for LAA closure in patients with lower HAS-BLED scores, possibly because the bleeding risk score also predicts bleeding in patients who are not anticoagulated (18). Patients with high HAS-BLED scores may, therefore,

FIGURE 2 Kaplan-Meier Curves for Major Bleeding



(A) Freedom from first major bleed from randomization to the end of follow-up ($p = 0.97$). **(B)** Freedom from first major bleed from 8 days post-randomization to the end of follow-up (the post-procedural period) ($p = 0.002$). **(C)** Freedom from first major bleed from 45 days post-randomization to the end of follow-up) (hazard ratio: 0.38; 95% confidence interval: 0.33 to 0.44; $p < 0.001$). **(D)** Freedom from first major bleed from 6 months post-randomization to the end of follow-up (hazard ratio: 0.28; 95% confidence interval: 0.23 to 0.35; $p < 0.001$).

FIGURE 3 Landmark Analysis of the Freedom From Major Bleeding Over 3 Intervals of Follow-Up



3 intervals: from randomization to day 7, representing the periprocedural period for patients randomly assigned to left atrial appendage closure; 8 days to 6 months post-randomization, during which device-treated patients received warfarin and aspirin followed by dual antiplatelet therapy; and beyond 6 months, when device-treated patients were eligible to receive aspirin alone.

face a continued risk of bleeding even after discontinuation of post-procedural anticoagulation, diminishing the absolute benefit of LAA closure. Even so, the absolute and relative reductions in bleeding >6 months after LAA closure were substantial and clinically relevant in patients at high bleeding risk (RRR: 45%; absolute risk reduction: 6.8%) and in those ≥75 years of age (RRR: 57%; absolute risk reduction: 6.5%). These observations suggest that the long-term safety benefit of LAA closure over warfarin applies across the spectrum of bleeding risk.

TABLE 5 Major Bleeds Beyond 6 Months Post-Randomization According to Subgroup

	LAA Closure	Warfarin	Hazard Ratio (95% Confidence Interval)	p Value	p Interaction
Age ≤75 yrs	1.4 (6/436)	7.8 (17/217)	0.17 (0.147–0.196)	<0.001	0.005
Age >75 yrs	4.4 (13/296)	10.9 (18/165)	0.43 (0.264–0.701)	0.001	
CHA_2DS_2-VASc ≤4	1.8 (10/551)	8.5 (22/258)	0.21 (0.138–0.321)	<0.001	0.28
CHA_2DS_2-VASc >4	5.1 (9/178)	10.7 (13/121)	0.47 (0.161–1.378)	0.17	
Modified HAS-BLED <3	1.4 (8/561)	7.9 (23/291)	0.17 (0.173–0.174)	<0.001	0.001
Modified HAS-BLED ≥3	6.4 (11/171)	13.2 (12/91)	0.55 (0.282–1.070)	0.078	
No history of TIA/stroke	2.3 (13/570)	8.9 (26/292)	0.26 (0.216–0.305)	<0.001	0.67
History of TIA/stroke	3.7 (6/162)	10.0 (9/90)	0.35 (0.102–1.225)	0.10	
Female	1.8 (4/224)	12.0 (13/108)	0.17 (0.074–0.369)	<0.001	0.02
Male	3.0 (15/508)	8.0 (22/274)	0.35 (0.320–0.393)	<0.001	

Values are % (n/N) unless otherwise specified.
LAA = left atrial appendage; TIA = transient ischemic attack.

In this patient-level, pooled analysis of the randomized clinical trial experience of the WATCHMAN device, procedure-related events were the major driver of bleeding in the device group, highlighting the importance of procedural safety in determining the overall risk to benefit ratio of LAA closure as an alternative management strategy for stroke prevention in patients with AF. However, the event curves continued to diverge over time, consistent with the increased hazard of bleeding with warfarin compared to aspirin alone even in OAC-eligible patients (20). The risk of major bleeding is expected to persist or increase in patients treated with chronic OAC as they age. Therefore, although the overall major bleeding rates were similar between LAA closure and chronic warfarin therapy, improved safety (13) and longer follow-up seems likely to favor LAA closure. Our findings may not be extrapolated to other methods of LAA closure, which have been associated with higher rates of procedural bleeding or other procedure-related complications (21,22), or to anticoagulation with agents other than warfarin, such as the NOACs.

The adjunctive pharmacotherapy after WATCHMAN implantation used in the current trials was empirical. The results of this analysis suggest that the risk of bleeding during the period of adjunctive pharmacotherapy in the device arm was similar to that in the warfarin arm (**Figure 2**), consistent with previous observations that the risk of bleeding increases when aspirin is given concurrently with warfarin and is similar with dual antiplatelet therapy compared with warfarin alone (19,23). Whether a shorter period of post-procedural dual antiplatelet therapy or warfarin could reduce nonprocedural bleeding and improve the post-procedural risk profile of LAA closure deserves further evaluation, particularly in patients at very high bleeding risk (24).

STUDY LIMITATIONS. Major bleeding was not a prospectively defined endpoint in the clinical trial protocols. However, the bleeding events included in this analysis were all site-reported and adjudicated by a clinical events committee. The reduction in bleeding with LAA closure compared with continued warfarin therapy may be underestimated, as it does not account for patients in the warfarin group who discontinued the drug. We used a modified HAS-BLED score, because certain characteristics included in the originally described score (18) were not systematically collected. Although the prognostic strength of this modified score has not been validated, it was associated with bleeding rates during follow-up. Slight differences in clinical characteristics in the randomized

arms, likely due to chance, may have influenced treatment effects. These analyses were post-hoc and are therefore exploratory and hypothesis-generating. Finally, this analysis does not address the comparative risk of bleeding with NOACs, which have been associated with similar (6) or lower rates of all-cause bleeding (7,9,10) compared with warfarin.

CONCLUSIONS

In this pooled, patient-level analysis of the WATCHMAN randomized clinical trial experience, there was no difference in the overall rate of major bleeding (procedural and nonprocedural) over 3 years of follow-up in patients assigned to LAA closure compared with extended warfarin therapy. However, LAA closure significantly reduced the rate of major bleeding beyond the periprocedural period, particularly beyond 6 months after randomization, when patients assigned to device therapy could discontinue adjunctive anticoagulation and dual antiplatelet therapy. LAA closure decreased bleeding beyond the procedural period in older and younger patients, those with high and low HAS-BLED scores, and in males and females. Society guidelines recommend that antithrombotic therapy should be individualized on the basis of shared decision-making after discussion of the absolute and relative risks of stroke and bleeding (Class I, Level of Evidence: C) (25). The effect of LAA closure on long-term bleeding should be integrated into this discussion when selecting a management strategy for stroke prevention in AF patients.

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PERSPECTIVES

WHAT IS KNOWN? LAA closure with the WATCHMAN device followed by discontinuation of long-term OAC is an effective alternative to long-term warfarin anticoagulation for the prevention of stroke, systemic embolism, and cardiovascular death in AF patients at moderate-to-high thromboembolic risk.

WHAT IS NEW? Although there was no difference in the overall rate of major bleeding over 3 years of follow-up in patients assigned to LAA closure compared with extended warfarin therapy, LAA closure significantly reduced bleeding beyond the immediate periprocedural period, and particularly beyond 6 months, when patients assigned to device therapy could discontinue adjunctive anticoagulation and dual antiplatelet therapy. This bleeding benefit continued to accrue over time, and was consistent across baseline bleeding risk strata.

WHAT IS NEXT? Whether a shorter period of post-procedural warfarin or dual antiplatelet therapy could reduce nonprocedural bleeding and improve the post-procedural risk profile of LAA closure deserves further evaluation.

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