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RESEARCH

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Reactive atrial-based anti-tachycardia pacing algorithm in cardiovascular implantable electronic devices is safe and feasible without increase in thromboembolic events in patients with a left atrial appendage closure device

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Abstract

Background Reactive atrial-based anti-tachycardia pacing (rATP) in CIED (cardiovascular implantable electronic devices) is effective in atrial fibrillation (AF) suppression. Uninterrupted systemic anticoagulation is recommended when this algorithm is activated to avoid stroke, however, the use of a rATP algorithm in patients with a left atrial appendage (LAA) closure device has not been studied. We assessed the safety and feasibility of rATP algorithm to suppress AF in patients with a LAA closure device over an extended period.

Methods Data from 55 consecutive patients who underwent a Watchman® implant at a tertiary care hospital between September 1, 2015, and January 30, 2020, who also had an in situ Medtronic® CIED (45 with and 10 without rATP capability) were retrospectively reviewed.

Results The 55-patient cohort was 60% male, 77 ± 8 years old, CHA_2DS_2-VASc score 5 (4–6), HAS-BLED score 3 (3–4), LVEF 53 ± 14%, LA size 4.4 ± 0.7 cm and ventricular pacing burden of 73 (1.4–98.3)%. The CIEDs (20 ICDs and 35 pacemakers) antedated Watchman® implants by 915 ± 725 days. Post-implant, all patients discontinued anticoagulation. Twenty patients in the rhythm-control group with *active* rATP algorithm displayed no increase in yearly AF burden and were less likely to develop permanent/long-standing persistent AF ($p = 0.002$) when compared to 35 patients in the rate-control group with CIEDs *inactive/incapable of* rATP over a ≤ 5-year follow-up. The longest AF episode in the rhythm-control group lasted 204 (19–2520) h. There was no increase in stroke/thromboembolism and a significant reduction in major bleeding noted over ≤ 5 years pre- versus post-implant in the whole cohort ($p = 0.005$).

Conclusion rATP algorithm use is safe and feasible in patients with a Watchman® device. Patients should be forewarned of a surge in post-Watchman® implant AF burden.

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Keywords Atrial, Anti-tachycardia pacing, Left atrial appendage closure, Atrial fibrillation, Cardiovascular implantable electronic device, Thromboembolism

Background

AF suppression algorithms in CIEDs (cardiovascular implantable electronic devices) are designed to reduce AF burden. The proprietary Medtronic® reactive atrial-based anti-tachycardia pacing (rATP) algorithm works by initiating bursts of atrial overdrive pacing to abort AF when it spontaneously converts to atrial flutter/tachycardia [1]. This algorithm is effective in AF suppression [1, 2]. Uninterrupted ongoing systemic anticoagulation is recommended when this algorithm is activated to avoid stroke and systemic thromboembolism, analogous to the anticoagulation guideline for patients undergoing elective electrical cardioversion [3]. However, the use of rATP algorithm in patients with a left atrial appendage (LAA) closure device, Watchman® (Boston Scientific®, Marlborough, MA, USA) without ongoing uninterrupted anticoagulation has not been previously studied.

Furthermore, previous data show an increase in AF incidence, post-Watchman® device implant when performed in conjunction with AF ablation, which is thought to be transient [4]. However, the longitudinal AF burden over an extended period of time post-Watchman® implant in patients who undergo rhythm *versus* rate-control strategies for AF management remains unknown. The surge in AF burden post-procedure has important clinical implications when counseling patients with symptomatic AF undergoing a Watchman® implant.

The aim of our study was twofold: (1) to assess the safety and feasibility of rATP algorithm in Medtronic® CIEDs to suppress AF in patients with a Watchman® device, (2) to assess pre- and post-Watchman® device implant AF burden in patients with in situ CIEDs over ≤ 5-year period.

Methods

This was a retrospective, single-center, chart review study. Consecutive patients, undergoing a Watchman® implant at a tertiary care hospital (Riverside Methodist Hospital, Columbus, Ohio, USA) between September 1, 2015, and January 30, 2020, who met the following inclusion criteria were selected for the study:

Inclusion criteria

1. Patient age of ≥ 18 years at the time of Watchman® implant.
2. Patient had an in situ Medtronic® CIED with accurate AF detection capability.
3. Patient was entirely followed through the hospital's electronic medical and CIED records (Epic Systems Corporation®, Madison, Wisconsin, USA and Paceart Optima System®, Medtronic®, Minneapolis, Minnesota, USA, respectively).
4. Patient electronic medical and CIED records were available for data extraction for up to 5 years both pre- and post-Watchman® implant.

Patient electronic medical and CIED records were reviewed retrospectively for patient demographics, medical history (including history of stroke/thromboembolism and major bleeding), echocardiography data (LV ejection fraction and LA dimension), Watchman® data (device size, and follow-up device leak and device-related thrombus), CIED data (type of CIED, indication for implant, baseline ventricular pacing burden, AF burden defined as the percentage of total time spent in AF, AF episode duration, total and successful rATP attempts), anticoagulation and anti-arrhythmic medication use, and any additional procedures (AF ablation and cardioversion) performed during the study period.

Standard definitions of paroxysmal, persistent, long-standing persistent, and permanent AF were used in the study [5]. Major bleeding was defined as bleeding that was fatal or caused a drop in hemoglobin level of at least 2 g/deciliter or that required transfusion of at least 2 units of packed blood cells, or hemorrhage into a critical anatomical site (e.g., intracranial, gastrointestinal).

We used standard definitions of rhythm and rate-control strategies for treatment of AF [5]. In rhythm-control strategy, every effort was made using various modalities including anti-arrhythmic medications, cardioversions, AF ablation and use of atrial reactive-ATP algorithm to maintain sinus rhythm. On the other hand, in rate-control strategy, patients were kept in AF with their heart rates below 80–110/min [5].

All the study patients were indicated for long-term anticoagulation on the basis of CHA_2DS_2-VASc score of ≥ 2 in males and ≥ 3 in females and history of atrial fibrillation. However, none of the study patients could take systemic anticoagulation (direct anticoagulants or warfarin) on a long-term basis because of absolute contraindications (history of significant gastrointestinal, urological, nasal or intracranial bleeding or history of frequent falls). Additionally, none of the study patients were

taking systemic anticoagulation for any other indications like DVT, pulmonary embolism or mechanical cardiac valves.

Statistics

Mean and standard deviation (standard error of mean where noted) for normally distributed continuous variables, or median and 25th and 75th percentile for variables not normally distributed was computed. For categorical variables, proportion and frequency count were calculated. Group comparisons of continuous variables were made using Student's t-test (for normally distributed variables) and non-parametric *t*-test or Mann–Whitney *U* test (for variables not distributed normally). Categorical variables were compared using Fisher's exact or Chi-square test. Multiple continuous independent variables were compared using ANOVA or Kruskal–Wallis test for normally and not normally distributed variables, respectively. Multiple continuous repeated variables not normally distributed were compared using Friedman test. Paired continuous variables pre- and post-intervention were compared with either paired t-test or Wilcoxon signed-rank test for normally or not-normally distributed data, respectively. Kaplan–Meier analysis with Mantel-Cox (Log-Rank) test was utilized to analyze probability of AF progression to permanent/long-standing persistent AF in the rhythm *versus* rate-control strategy subgroups. A 2-tailed statistical test was considered significant if the p value was < 0.05.

We used GraphPad statistical software Prism 9 Version 9.5.1 for statistical analysis of the data.

Results

A total of 413 patients underwent Watchman implant between September 1, 2015, and January 30, 2020. Fifty-five patients met the inclusion criteria for the study. The 55-patient cohort comprised of 60% males, age 77 ± 8 years with a CHA_2DS_2-VASc score of 5 (4–6) and HAS-BLED score of 3 (3–4). The total cohort LVEF was 53 ± 14%, LA dimension was 4.4 ± 0.7 cm and ventricular pacing burden was 73 (1.4–98.3)%. The CIED implants (20 ICDs and 35 pacemakers) antedated Watchman® implants by 915 ± 725 days. Only 45 CIEDs were capable of performing rATP algorithm with only 20/45 (44%) in whom the algorithm was active during the study period.

Table 1 depicts patient characteristics dichotomized based on rhythm and rate-control strategies. Patients in the rate-control subgroup were older with asymptomatic AF, less likely to be treated with anti-arrhythmic medications, had CIEDs with *inactive/incapable* rATP algorithm and higher ventricular pacing burden, and also underwent fewer elective cardioversions and atrial fibrillation/flutter ablations.

No longitudinal increase in AF burden or incidence of thromboembolism post-Watchman® device implant in patients with rhythm-control strategy

In the rhythm-control group, there was no significant increase in the yearly AF burden (% of total time spent in AF) post-Watchman® implant (Fig. 1, panel A). Furthermore, patients in the rate-control group were significantly more likely to develop permanent/long-standing persistent AF over the study period when compared to patients in the rhythm-control group (Fig. 2). This was despite no significant difference in baseline pre-implant 1-year AF burden ($p = 0.2$) between the two groups (Fig. 1).

In the rhythm-control group, the rATP algorithm was active on the day of the Watchman® implant in 75% (15/20) of the patients (the rest were activated during follow-up period) and was effective in aborting AF in 40% (8/20) of these patients over 895 ± 498 days. In this patient cohort 107 (0–2306) rATP attempts per patient were made by the in situ CIEDs to abort AF episodes during a period of 895 ± 498 days. However, only 20 ± 8 per hundred AF episodes per patient were successfully terminated with rATP attempts.

Post-Watchman® implant all patients in the rhythm-control group had paroxysmal or persistent AF with the longest AF episode lasting 204 (19–2520) h. There was no increase in thromboembolic events pre- *versus* post-Watchman® implant over a 5-year period in this group, with 35% (7/20) patients requiring intermittent use of systemic anticoagulation post-Watchman® implant for 40 ± 28 days over a total of 895 ± 498 days.

AF burden increases post-Watchman® implant in patients with rate-control strategy without increase in thromboembolism

In patients with rate-control strategy, the AF burden significantly increased post-Watchman® implant when compared to baseline prior to the implant (Fig. 1, panel B and Fig. 2).

Post-Watchman® implant 17 out of 35 patients in the rate-control group developed permanent/long-standing persistent AF over the next 5 years compared to none in the rhythm-control group ($p = 0.0001$). The longest AF episode in the rate-control group lasted 18,250 (643–31,755) h which was significantly longer than in the rhythm-control group ($p = 0.0014$). Despite the above, there was no increase in thromboembolic events pre-versus post-Watchman® implant over a 5-year period in the rate-control group, with 11% (4/35) patients requiring intermittent use of systemic anticoagulation post Watchman® implant for 359 ± 203 days over a total of 1011 ± 618 days.

Table 1 Clinical characteristics of the study patients dichotomized based on rhythm and rate-control strategy

Patient characteristics	Rhythm-control strategy ($n=20$)	Rate-control strategy ($n=35$)	*p*-value
Demographics			
Age (years)	74 ± 7.2	79 ± 7.4	0.01
Male gender (*n*)	14 (70%)	19 (54%)	ns
White race (*n*)	16 (80%)	34 (97%)	ns
Died during 5-years post-Watchman® implant (*n*)	9 (45%)	17 (49%)	ns
Medical history			
Hypertension (*n*)	20 (100%)	35 (100%)	ns
Diabetes mellitus (*n*)	9 (45%)	9 (26%)	ns
Chronic kidney disease (*n*)	5 (25%)	17 (49%)	ns
Peripheral arterial disease (*n*)	7 (35%)	14 (40%)	ns
Coronary artery disease (*n*)	7 (35%)	21 (60%)	ns
Obstructive sleep apnea (*n*)	6 (30%)	13 (37%)	ns
Chronic obstructive pulmonary disease (*n*)	6 (30%)	5 (14%)	ns
Major bleeding (5-yrs pre-Watchman® implant) (*n*)	13 (65%)	16 (46%)	ns
Stroke/Thrombo-embolism (5-yrs pre-Watchman® implant) (*n*)	3 (15%)	4 (11%)	ns
CHA_2DS_2-VASc score	5 ± 1.5	5.4 ± 1.4	ns
HAS-BLED score	3.2 ± 1.3	3.3 ± 1.1	ns
Baseline echocardiography			
Left ventricular ejection fraction (%)	54 ± 15	52 ± 13	ns
LA size (cm)	4.3 ± 0.7	4.5 ± 0.8	ns
Medication use (5-yrs post-Watchman® implant)			
Anti-arrhythmic use (*n*)	13 (65%)	9 (26%)	0.009
Length of anti-arrhythmic use (days)	920 (478–1268)	605 (346–1120)	ns
Anti-coagulant use (*n*)	7 (35%)	4 (11%)	ns
Length of anti-coagulant use (days)	30 (28–42)	398 (149–529)	0.01
Watchman® Data			
Implanted Watchman® size (mm)	27.6 ± 3.6	28.7 ± 3.3	ns
Patients with no peri-device leak (*n*)	20 (100%)	4 (89%)	ns
Patients with device-related thrombus (*n*)	0 (0%)	1 (3%)	ns
CIED data			
Pacemaker in situ (*n*)	14 (70%)	22 (63%)	ns
Baseline ventricular pacing burden (%)	20.75 (0.1–96.5)	75.38 (5–99)	0.04
Active rATP algorithm® (*n*)	20 (100%)	0 (0%)	< 0.001
Procedures (5-yrs post-Watchman® implant)			
Atrial fibrillation/flutter ablation (*n*)	6 (30%)	1 (3%)	0.007
Elective cardioversion (*n*)	8 (40%)	2 (6%)	0.002

cm, centimeters; mm, millimeters; The HAS-BLED acronym stands for Hypertension, Abnormal liver/renal function, Stroke history, Bleeding history or predisposition, Labile INR, Elderly, Drug/alcohol usage; The CHA_2DS_2-VASc acronym stands for congestive heart failure, hypertension, age ≥ 75 (doubled), diabetes, stroke (doubled), vascular disease, age 65 to 74 years and sex category (female); rATP, reactive anti-tachycardia pacing

In our study group, using a Multivariable Cox Proportional Hazards Model, we found, increasing age (HR 1.096, 95% CI 1.016–1.182; $p=0.01$) and history of chronic kidney disease (HR 2.858, 95% CI 1.103–7.409; $p=0.03$) predictive of development of permanent/long-standing persistent AF.

Major bleeding is reduced post Watchman® implant in the absence of uninterrupted systemic anticoagulation

Post-Watchman® implant all the patients discontinued systemic anticoagulation since follow-up LAA imaging in 6 weeks after the implant showed no peri-device leak in 53 out of 55 patients. Only 2 patients showed peri-device

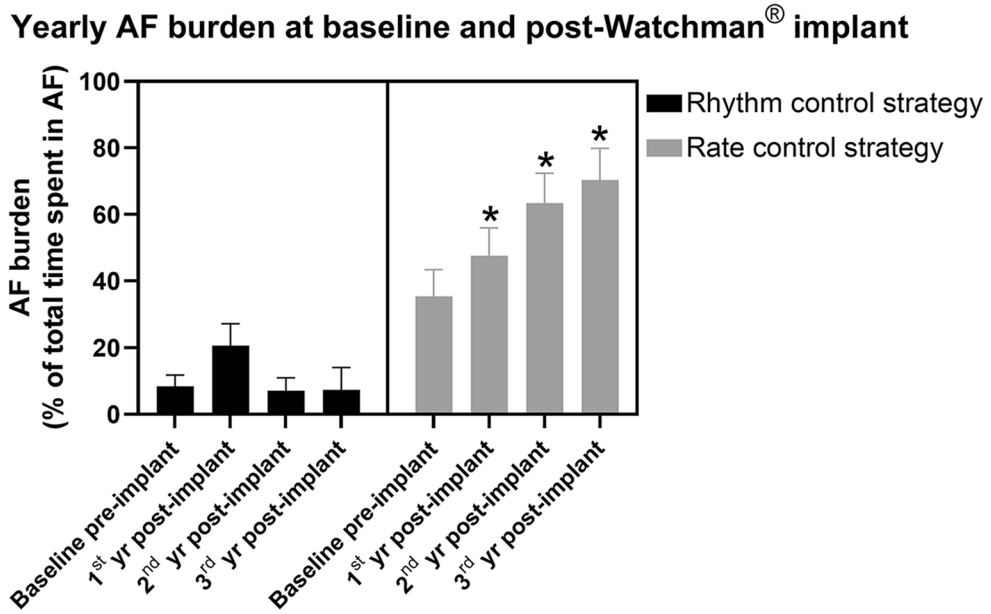

Fig. 1 A bar-graph depicting mean ± SEM AF burden (% of total time spent in AF) over 1-year timeframe, at baseline before the Watchman® implant and yearly thereafter over the next 3 years divided into rhythm-control (panel A) and rate-control (panel B) subgroups. Baseline AF burden pre-implant was not significantly different between the 2 groups ($p = 0.2$). However, note that the AF burden does not significantly increase in the rhythm-control group ($p > 0.5$) but does increase for the rate-control group (*$p < 0.05$ when compared to their respective baseline). SEM: standard error of mean

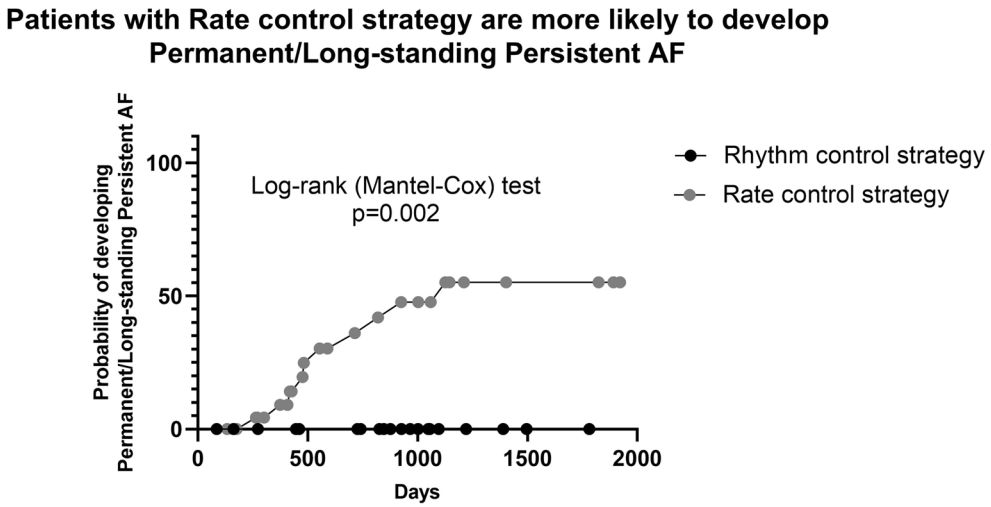

Fig. 2 A Kaplan–Meier curve depicting the probability of developing permanent/long-standing persistent AF over the study period for rate and rhythm-control subgroups. Unequivocally, patients in the rhythm-control subgroup displayed significantly reduced probability of developing permanent/long-standing persistent AF over the study period of ~ 5 years

leak of < 5 mm, which was still considered a success as per guidelines and the anticoagulation was stopped. Thereafter, only intermittent anticoagulation was instituted for some of the patients during the study period.

Despite intermittent use of systemic anticoagulation mostly around elective cardioversions, AF ablation, or rare instances of Watchman® related thrombus, there was a significant reduction in major bleeding (as defined in the methods section) over 5-years post-Watchman® implant compared to 5-years pre-implant in the whole 55-patient cohort (53% vs. 25%; $p = 0.006$; Fig. 3).

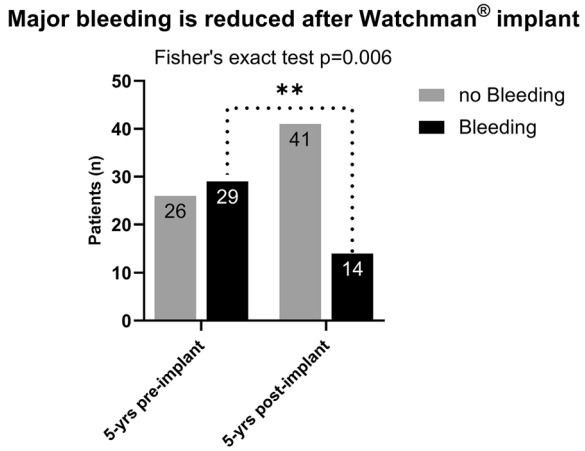

Fig. 3 A bar-graph depicting comparison of the number of study patients who had major bleeding pre- and post-Watchman® implant over 5 years, respectively. Note the significant reduction (** p = 0.006) of the number of patients who experienced major bleeding post-Watchman® implant due to cessation of systemic anticoagulation

Discussion

The salient findings from our study are, (1) the use of reactive atrial-based anti-tachycardia pacing algorithm in Medtronic® CIEDs is safe and feasible in patients with a Watchman® device without ongoing uninterrupted systemic anticoagulation. (2) Both rate and rhythm-control strategies can be pursued post-Watchman® device implant. Unless actively curtailed, there seems to be a longitudinal increase in AF burden post-Watchman® device implant. However, despite increase in AF burden, patients still derive benefit with reduction in major bleeding and no increase in thromboembolism post-Watchman® implant.

rATP is a proprietary AF suppression algorithm in Medtronic® CIEDs designed to overdrive pace in the atrium during spontaneous conversion of AF to atrial flutter or atrial tachycardia in an attempt to restore sinus rhythm [1]. It is known to slow progression of AF to persistent/permanent AF, which was also observed in our study [1, 2]. Due to the interventional nature of this algorithm designed to restore sinus rhythm after potentially long periods of AF, uninterrupted systemic anticoagulation is recommended when using it to prevent stroke/thromboembolism, akin to usage in patients undergoing elective electrical cardioversion [3]. There are no current guidelines regarding use of systemic anticoagulation in patients with an implanted LAA occlusion device like Watchman® who undergo elective cardioversion. However, preliminary data suggest that patients with a successfully implanted Watchman® device who do not harbor a device related thrombus can undergo cardioversion with or without post-procedure systemic anticoagulation without increase in post-cardioversion (< 6 weeks) thromboembolism [6]. To the best of our knowledge, the current study is the first to demonstrate the safety and feasibility of using rATP algorithm to suppress AF in patients with a Watchman® device without any identifiable adverse consequences.

A previous study showed an uptake in AF burden during the blanking period after AF ablation in patients undergoing LAA closure device at the same time [4]. The patient population in our study was older and had more co-morbidities than in this previous study [4]. Additionally, our study patients did not systematically undergo AF ablation (which is known to reduce AF burden) during the Watchman® implant. These factors likely increased the longitudinal AF burden in the rate-control group. The patients in the rhythm-control group displayed no significant increase in longitudinal AF burden post-Watchman® implant. However, these patients were younger with symptomatic AF, more likely to be treated with anti-arrhythmic medications, had *active* rATP algorithm and lower ventricular pacing burden, and underwent more elective cardioversions and atrial fibrillation/flutter ablations. Collectively, all these factors curtailed the increase in AF burden post-Watchman® implant in rhythm-control group. Both rate and rhythm control remain valid strategies for AF treatment. However, the increase in AF burden post-Watchman® implant has several clinical implications, including increase in resource utilization and its associated cost to reduce AF burden especially in patients with symptomatic AF as noted in the rhythm-control group. On the other hand, by choosing a rate-control strategy in asymptomatic patients, we risk heart failure, a long-term consequence of AF.

We want to emphasize that our data does not prove that the increase in AF burden post-Watchman® procedure is caused by the implant, although this is an intriguing hypothesis. This has been suggested [4] to be caused by a mechanical irritant effect of the device and is supported by the temporal increase in AF burden post-Watchman® implant in a previous study [4]. Our study has similar findings, including a non-significant increase in AF burden noted in the first year post-Watchman® implant in the *active* rATP subgroup (Fig. 1, panel A). Further studies are needed to clarify this relationship.

Limitations

Being a retrospective chart review study there are inherent study limitations, including selection and recall bias, and use of clinical data for research purposes. Additionally, our study may potentially have inadequate number of subjects to show statistical significance for outcomes with a small effect, such as the increase in AF burden in the

first year post-Watchman® implant in the rhythm-control group. This was a single center study and its results may not be applicable to a broader general population.

Conclusion

The reactive atrial-based anti-tachycardia pacing algorithm in Medtronic® CIEDs is safe and feasible in reducing AF burden in patients with a Watchman® device without ongoing anticoagulation. Its usage does not increase the thromboembolic risk over an extended period of follow-up. Additionally, clinicians should be aware of an increase in AF burden post-Watchman® implant, for which symptomatic patients should be forewarned.

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Each author contributed significantly to data collection and completion of the manuscript.

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Availability of data materials
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Declarations

Ethics approval and consent to participate
This study protocol was approved by OhioHealth IRB.

Consent for publication
Completed.

Competing interests
There are no competing interests.

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