Intermittent anticoagulation guided by continuous atrial fibrillation burden monitoring using dual-chamber pacemakers and implantable cardioverter-defibrillators: Results from the Tailored Anticoagulation for Non-Continuous Atrial Fibrillation (TACTIC-AF) pilot study

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BACKGROUND Chronic anticoagulation is recommended for atrial fibrillation (AF) patients with thromboembolic risk factors regardless of AF duration/frequency. Continuous rhythm assessment with pacemakers (PMs)/implantable cardioverter-defibrillators (ICDs) and use of direct-acting oral anticoagulants (DOACs) may allow anticoagulation only around AF episodes, reducing bleeding without increasing thromboembolic risk.

OBJECTIVE The purpose of this study was to evaluate the feasibility/safety of intermittent DOAC use guided by continuous remote AF monitoring via dual-chamber PMs or ICDs.

METHODS Patients with nonpermanent AF, current DOAC use, $CHADS_2$ score $\leq$3, a St. Jude Medical dual-chamber PM or ICD, and rare AF episodes were followed with biweekly and AF-alert based remote transmissions. Patients free of AF episodes lasting $\geq$6 minutes with a total AF burden $<$6 hours/day for 30 consecutive days discontinued DOAC. If AF burden surpassed these limits, DOAC was restarted and/or continued. Total days on DOAC and adverse events were assessed.

RESULTS Among 48 patients (mean age 71.3 years; 65% male; 79% paroxysmal AF; 87% $CHADS_2$ score 1–2), 14,826 days of monitoring were completed. Patients used DOACs for 3763 days, representing a 74.6% reduction in anticoagulation time compared to chronic administration. Adverse events included 2 gastrointestinal bleeds (both on DOAC), 1 fatal intracerebral bleed (off DOAC), and no thromboembolic/stroke events.

CONCLUSION Among patients with rare AF episodes and low-to-moderate stroke risk, PM/ICD-guided DOAC administration is feasible and decreased anticoagulation utilization by 75%. Few adverse events occurred, although the study was not powered to assess these outcomes. PM/ICD-guided DOAC administration may prove a viable alternative to chronic anticoagulation. Future studies are warranted.

KEYWORDS Anticoagulation; Atrial fibrillation; Cardiac implantable electronic device; Remote monitoring; Stroke; Thromboembolism

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Introduction

Atrial fibrillation (AF) affects more than 33 million people worldwide,[1] and its incidence and prevalence continue to increase.[2] Although AF is associated with cardiovascular symptoms, reduced quality of life (QOL), and symptomatic heart failure,[3] stroke and systemic thromboembolism[4] remain the most dreaded complications of AF. Anticoagulation with warfarin or other novel direct-acting oral anticoagulants

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(DOACs) significantly reduces the thromboembolic risk associated with AF,[5,6] and current practice guidelines recommend chronic anticoagulation to reduce the risk of stroke and systemic thromboembolism in patients with known risk factors regardless of AF episode duration or frequency (AF burden).[7] Recent studies, however, have demonstrated that AF burden does seem to modify thromboembolic risk,[8,9] but because AF episodes may be asymptomatic and/or too brief to be detected by standard electrocardiography, current guidelines do not account for AF burden when assessing thromboembolic risk and the benefit to using long-term oral anticoagulation.[7] This continuous anticoagulation strategy guarantees that patients will be anticoagulated should an episode of AF occur, but in patients with a very low AF burden, it also results in elevated bleeding risk without clear benefit during prolonged periods of sinus rhythm when the risk of AF-related thromboembolism is presumably low.

Recent advances in long-term cardiac rhythm monitoring technology available through pacemakers (PMs), implantable cardioverter-defibrillators (ICDs), and subcutaneous implantable loop recorders (ILRs) now allow clinicians to have near real-time access to accurate AF burden data. In addition, the recent availability of DOACs with onset of therapeutic anticoagulation in hours instead of days has allowed development of the concept of "tailored anticoagulation" (TAC), in which patients can start and stop anticoagulation based on their AF burden.[10] The feasibility and safety of TAC were recently tested in a small study of patients with ILRs,[11] but the strategy has not been evaluated in patients with PMs or ICDs. The Tailored Anticoagulation for Non-Continuous Atrial Fibrillation (TACTIC-AF) pilot study was performed to establish the feasibility of using AF burden monitoring through frequent PM or ICD remote monitoring to guide intermittent DOAC administration in patients with a low burden of AF.

Methods

Study design

TACTIC-AF (Clinicaltrials.gov Identifier NCT01650298) was an investigator-initiated, prospective, multicenter, pilot study designed to assess the feasibility of TAC with DOACs in patients with PMs or ICDs and to assess the reduction in time on anticoagulation using this approach. The study was funded by St. Jude Medical (Saint Paul, MN). Patients were enrolled in 10 U.S. centers between January 2013 and August 2015. The study protocol was approved by the institutional review boards of all participating centers, and all patients provided written informed consent before enrollment. The primary outcome was total days on anticoagulation. Secondary outcomes included adverse events and QOL. The study was designed primarily as a pilot/feasibility study and was not powered to detect thromboembolic events.

Inclusion/exclusion criteria

Patients were eligible for inclusion if they were >18 years old, had a St. Jude Medical PM or ICD with a functioning atrial lead and a generator with the ability for remote monitoring using radiofrequency transmissions, had at least 1 episode of AF documented either by electrocardiogram or intracardiac electrograms, and had a $CHADS_2$ score ≤3. Additionally, for at least 30 continuous days before enrollment, patients had to be taking an approved DOAC and had to have a "low" burden of AF, defined as <30 minutes of AF total per day (including all episodes) and no continuous episodes of AF lasting >6 minutes. Patients were excluded from the study if they had previous stroke/transient ischemic attack (TIA), permanent AF, contraindications to anticoagulation, medical condition(s) that prohibited discontinuation of anticoagulation, complex aortic atheroma, current pregnancy or plans to become pregnant, use of warfarin, or life expectancy <12 months.

Data collection/patient follow-up

Baseline patient characteristics and medical history, $CHADS_2$ score, New York Heart Association (NYHA) functional class, and assessment of QOL via the Duke Anticoagulation Satisfaction Scale (DASS)[12] were obtained at the time of enrollment. $CHADS_2$ score, NYHA functional class, and DASS were also reassessed at 6- and 12-month follow-up visits.

Study protocol

The study protocol is shown in Figure 1. Patients were initially randomized in a 1:1 ratio to TAC (anticoagulation was initiated or discontinued based on atrial tachycardia/atrial fibrillation [AT/AF] burden as assessed through frequent remote PM/ICD transmissions via St. Jude Medical Merlin.net™) or standard/continuous anticoagulation (anticoagulation was initiated/discontinued based on standard of care/guidelines). The follow-up period was 12 months. Frequent remote AT/AF monitoring was only performed in the TAC group. In the control group, remote transmissions were scheduled per each institution's device monitoring protocol. Patients in the TAC group sent in biweekly remote transmissions (1 manual and 1 automatic, usually on Monday and Thursday, respectively), automatic alert-triggered transmissions for AT/AF burden above a set threshold (see lower down in this section), and unscheduled patient-activated transmissions as needed if there was concern about symptoms or possible AT/AF. Device programming was standardized to detect AT/AF with an atrial rate >200 bpm to minimize the chance of false-positive detections. Atrial sensitivity was individualized for each patient and could be adjusted if needed. Automatic AT/AF transmissions were programmed to occur for any single AT/AF episode lasting >30 minutes and for a total AT/AF burden >6 hours over a 24-hour period. Because of technical limitations of transmitting AT/AF alerts via Merlin.net™, AT/AF episodes lasting <30 minutes could not be automatically transmitted.

To facilitate enrollment, the study protocol was amended in December 2014 to remove the control arm and continue as a single-arm prospective study. After this protocol

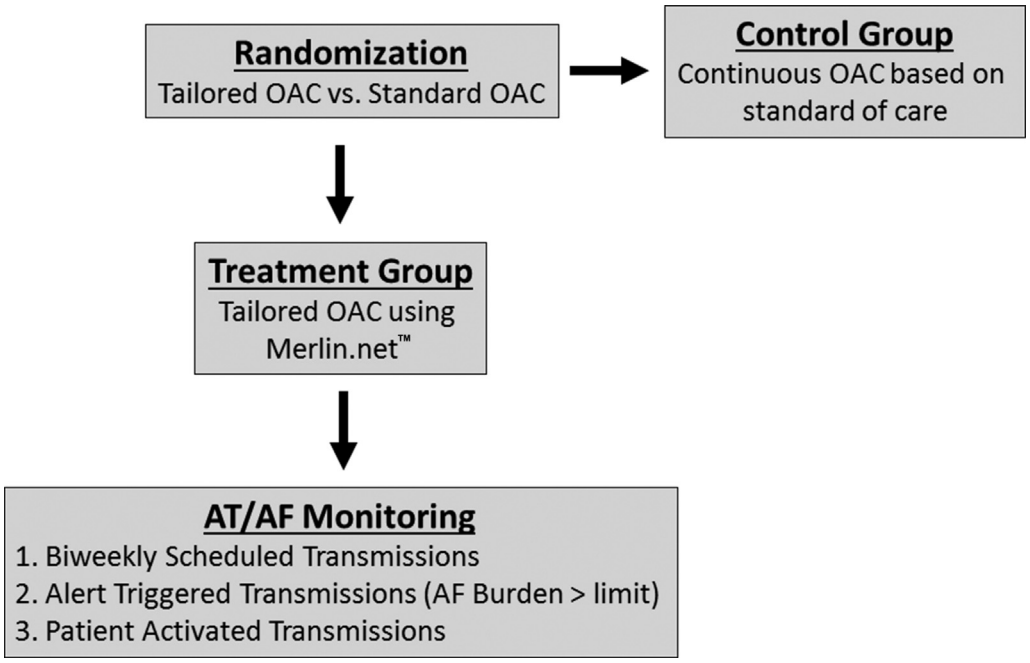

Figure 1 Tailored Anticoagulation for Non-Continuous Atrial Fibrillation (TACTIC-AF) randomization. Patients were initially randomized 1:1 to the treatment group (tailored anticoagulation) and the control group (continuous anticoagulation based on the standard of care). Because of amendment of the study protocol, the study was subsequently changed to a single-arm study in which all patients were enrolled in the tailored anticoagulation group (see text for details). AF = atrial fibrillation; AT = atrial tachycardia; OAC = oral anticoagulant.

amendment, patients who were still enrolled in the control group or patients who had completed the study in the control group were eligible to cross over to the TAC arm for an additional 9 months of follow-up as long as they met inclusion criteria.

All patients completed 30 days on anticoagulation after enrollment as part of the study protocol regardless of their AT/AF burden before study enrollment. Patients in the control group continued anticoagulation regardless of their AT/AF burden and could stop/start based on clinical indications as needed. In the TAC arm (Figure 2), patients stopped anticoagulation if they were free of a continuous episode of AT/AF lasting >6 minutes *and* if they did not have a total daily AT/AF burden >6 hours for 30 continuous days. During periods when anticoagulation was discontinued, initiation of aspirin was not required per study protocol and was left to the discretion of the treating physician. After discontinuing anticoagulation, patients would resume previously prescribed anticoagulation only if remote monitoring revealed a continuous AT/AF episode lasting >6 minutes or a total AT/AF burden >6 hours over 24 hours. In special circumstances in which patients could not make transmissions or if they would not be in daily proximity to their remote monitor (eg, during periods of travel or equipment failure), anticoagulation was temporarily resumed and then stopped once patients resumed monitoring and no AT/AF was confirmed on the next remote transmission.

Study personnel at each study center reviewed all remote transmissions for AT/AF events. Electrograms of all device-detected AT/AF events were adjudicated by study personnel to confirm true AT/AF. False AT/AF detections were not considered toward the AT/AF burden that would necessitate resuming/continuing anticoagulation. All device data and electrograms were archived on Merlin.net™.

Adverse events

All potential adverse events were reviewed by an independent clinical events committee. Bleeding and neurologic events were assessed in accordance with guidelines.[13,14] Detailed definitions can be found in the Supplemental Materials.

Results

Patient characteristics

During the study period, 61 patients enrolled. The control arm enrolled 16 patients, and the TAC arm enrolled 48 patients. Of these 48 patients, 45 were enrolled directly in the TAC arm, and 3 crossed over from the control arm to the TAC arm. Characteristics of the 48 patients enrolled in the TAC arm are listed in Table 1. The average patient age was 71.3 ± 10.2 years, 64.6% of patients were male, and 87.5% of patients had a $CHADS_2$ score of 1 (35.4%) or 2 (52.5%). Antiarrhythmic drugs were used in 45.8% of patients. Characteristics of the 16 patients who were enrolled in the control arm of the study before the study protocol was amended are also listed in Table 1.

Time on anticoagulation

Among the 48 patients in the TAC group, after a 30-day run-in period during which anticoagulation could not be stopped per study protocol, 14,826 days of monitoring were completed.

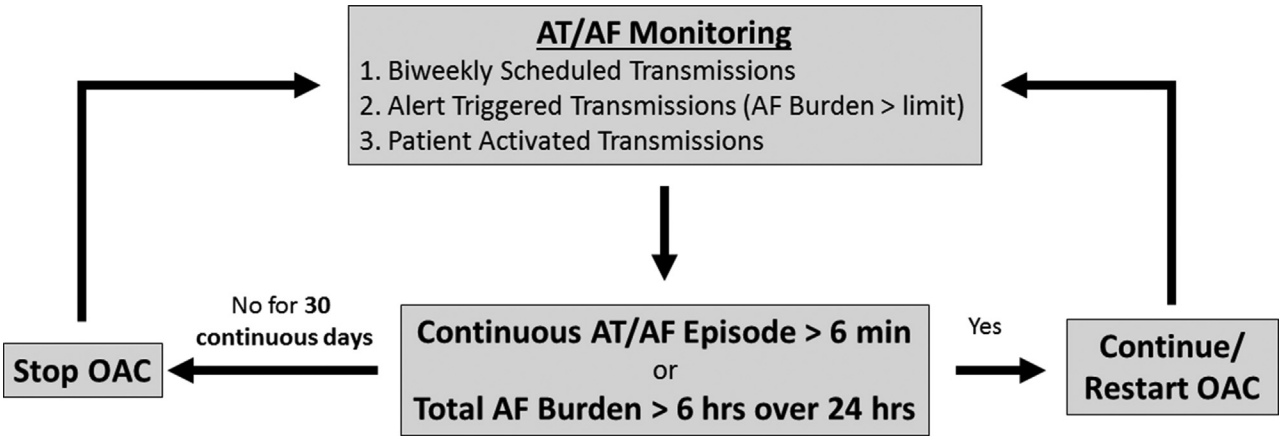

Figure 2 TACTIC-AF remote monitoring and anticoagulation protocol. Patients would stop anticoagulation if they were free of an episode of AT/AF lasting >6 minutes *and* a total daily AT/AF burden >6 hours for 30 consecutive days. Once off anticoagulation, patients would resume anticoagulation for an episode of AT/AF lasting >6 minutes *or* a total daily AT/AF burden >6 hours. Because of technical limitations of transmitting AT/AF alerts via Merlin.net™, continuous AT/AF episodes lasting <30 minutes could not be automatically transmitted and would be picked up only during biweekly scheduled transmissions or patient activated transmissions. Abbreviations as in Figure 1.

Patients were on anticoagulation for 3763 of these 14,826 days, representing a 74.6% reduction in time on anticoagulation compared to standard of care (continuous anticoagulation). Sixteen patients (33% of the study population) had no AF during the study and were never restarted on anticoagulation, whereas 6 patients (13% of the study population) had a single episode of AF during the study period that required only 30 days of anticoagulation.

The reasons for resuming anticoagulation and the number of days accounting for each reason are listed in Table 2. Unfortunately, 1777 days on anticoagulation (12.0% of study time and 47.2% of total days on anticoagulation) were inappropriate days on anticoagulation primarily because of protocol violations at 1 study site (1497 days) where the local principal investigator did not adhere to protocol-defined criteria for initiating and discontinuing anticoagulation. Baseline demographic data and the reasons for resuming anticoagulation and the number of days accounting for each reason excluding these patients are given in Supplemental Tables 1 and 2. The next most common indication for resuming anticoagulation was an AT/AF episode lasting >6 minutes (1317 days, 35.0% of total days on anticoagulation). Significantly fewer days on anticoagulation were secondary to multiple short episodes of AT/AF totaling >6 hours/day. A minority of days on anticoagulation (59 days, 0.4% of study time, and 1.6% of total days on anticoagulation) were secondary to travel and/or the inability to participate in remote transmissions. Only 1 day on anticoagulation was secondary to equipment malfunction.

Adverse events

The study was not powered to assess for adverse events, but adverse events that occurred during the study period were reviewed. The 6 adverse events that occurred in the TAC group are listed in Table 3. Importantly, 3 hemorrhagic events occurred: 2 minor hemorrhagic events (both gastrointestinal bleeds) in patients who were on anticoagulation and 1 major hemorrhagic event (fatal intracranial hemorrhage) in a patient who was not on anticoagulation at the time of the bleeding event/death. Eight potential neurologic events were reviewed, and no stroke or TIAs occurred. During the study period 2

Table 1 Baseline patient characteristics

Parameter	Tailored anticoagulation (n = 48)	Control group (n = 16)
Age (years)	71.3 ± 10.2	75.0 ± 11.1
Age ≥75 years	18 (37.5%)	8 (50.0%)
Male	31 (64.6%)	10 (62.5%)
White/Caucasian	46 (95.8%)	16 (100.0%)
Hypertension	37 (77.1%)	15 (93.8%)
Diabetes	10 (20.8%)	3 (18.8%)
Previous stroke/TIA	0 (0%)	0 (0%)
NYHA functional class		
I–II	45 (93.8%)	15 (93.8%)
III–IV	0 (0.0%)	0 (0.0%)
LVEF (%)	58.4 ± 12.5	58.5 ± 15.1
Any antiarrhythmic drug	22 (45.8%)	10 (62.5%)
Class I	5 (10.4%)	3 (18.8%)
Class III	17 (35.4%)	7 (43.8%)
AF type		
Paroxysmal	38 (79.2%)	14 (87.5%)
Persistent	10 (20.8%)	2 (12.5%)
$CHADS_2$ score		
0	2 (4.2%)	1 (6.3%)
1	17 (35.4%)	4 (25.0%)
2	25 (52.1%)	8 (50.0%)
3	4 (8.3%)	3 (16.7%)
Anticoagulant		
Rivaroxaban	28 (58.3%)	10 (62.5%)
Dabigatran	10 (20.8%)	3 (18.8%)
Apixaban	10 (20.8%)	3 (18.8%)

Results are presented as mean ± SD or n (% total).
AF = atrial fibrillation; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; TIA = transient ischemic attack.

Table 2 Reasons for resuming anticoagulation in the tailored anticoagulation patients

Reason for restarting/ continuing DOAC	Total days on DOAC	Study time on DOAC (%)	Total time on DOAC (%)
Days on DOAC after first 30 days	1777	12.0	47.2
AT/AF episode ≥6 min	1317	8.8	35.0
Total AT/AF ≥6 hr/day and AT/AF episode ≥6 min	283	1.9	7.5
Total AT/AF ≥6 hr/day	209	1.4	5.6
Perioperative management	117	0.8	3.1
Unable to transmit/travel	59	0.4	1.6
Transmitter malfunction	1	0.0	0.0
Total days on DOAC	3763	25.4	100

Total possible days on anticoagulation = 14,826.

AF = atrial fibrillation; AT = atrial tachycardia; DOAC = direct-acting oral anticoagulant.

patients died: 1 patient on anticoagulation died of pneumonia, and 1 patient off anticoagulation died of fatal intracranial hemorrhage as noted earlier. In the smaller control group, 3 adverse events occurred, including 2 minor hemorrhagic events (both episodes of epistaxis) (Table 4).

Quality of life

Results from the DASS as a QOL measure in the 45 patients who were initially enrolled in the TAC group (excluding 3 crossover patients) are given in Supplemental Tables 3A and 3B. Overall, there were no significant differences in QOL metrics during the study period. It was not possible to directly compare QOL/DASS scores between those in the TAC and control groups because of the small numbers of patients in the control group.

Discussion

TACTIC-AF was a pilot study evaluating the novel strategy of TAC using DOACs in patients with St. Jude Medical PMs or ICDs and endocardial atrial leads for AT/AF detection along with wireless remote monitoring capabilities to detect AF. The study demonstrated the feasibility of tailored DOAC administration to reduce anticoagulation utilization. TAC resulted in a 75% reduction in time on anticoagulation compared to standard of care with continuous anticoagulation regardless of AF burden, with few adverse events and no thromboembolic events. Although this pilot study was small and underpowered to detect thromboembolic events, the results are nonetheless encouraging and demonstrate that further study of TAC is warranted. TAC (and its associated reduction in time on anticoagulation) has the potential to reduce hemorrhagic events associated with anticoagulation, reduce cost, and improve QOL. Additionally, if future studies confirm the safety of TAC, successful rhythm control might allow some patients with AF, appropriate risk factors, and the ability for continuous remote monitoring via an implantable or wearable device capable of continuous rhythm monitoring to safely stop taking oral anticoagulation during prolonged periods of sinus rhythm.

Table 3 Adverse events in tailored anticoagulation patients

Adverse event	Total	On DOAC	Off DOAC
Minor hemorrhagic event	2	2*	0
Major hemorrhagic event	1	0	1†
Stroke/TIA	0	0	0
Lead insulation damage	1	1	0
Syncope	1	1	0
Death	2	1‡	1†

DOAC = direct-acting oral anticoagulant; TIA = transient ischemic attack.

*Two gastrointestinal bleeds.

†Fatal intracranial hemorrhage (single patient).

‡Fatal pneumonia.

The feasibility of TAC was also recently verified in the REACT.COM (Rhythm Evaluation for Anticoagulation with Continuous Monitoring) pilot study, which used Medtronic (Minneapolis, MN) Reveal XT® ILRs to assess AF burden in patients with a $CHADS_2$ score of 1–2 and infrequent AF episodes. The REACT.COM study protocol was slightly different (patients would stop DOAC if they remained free of continuous episodes of AT/AF lasting >1 hour for 30 continuous days, resuming DOAC if they experienced a continuous AT/AF episode lasting >1 hour) and the study population was healthier given that patients were younger (average age 67 years) and did not need to have a PM/ICD. REACT.COM demonstrated a 94% reduction in time on anticoagulation with few adverse events, no strokes, and 1 TIA in a patient with a $CHADS_2$ score of 1 who was off anticoagulation and on aspirin.[11]

TAC was also previously investigated in a population of patients with dual-chamber and biventricular ICDs in the IMPACT (Multicenter randomized study of anticoagulation guided by remote rhythm monitoring in patients with implantable cardioverter-defibrillator and CRT-D devices) randomized control trial comparing outcomes in TAC and continuous anticoagulation. In that study, different criteria (based on $CHADS_2$ score) existed to start or stop anticoagulation. The study enrolled >2700 patients before it was terminated early because of lack of benefit in the TAC arm. At the time the study was performed, however, DOACs were not widely available, and warfarin was the primary mode of anticoagulation. The lack of positive outcome in that study was likely related to inclusion of a higher-risk population, as well as a greater number of days required for warfarin to reach therapeutic anticoagulation. In addition, patients did not have to have AF to be enrolled, thus diluting the study population, which was reflected in a very low incidence of thromboembolic events (n = 69) before study termination.[15]

The AF burden that warrants anticoagulation remains controversial. In the peri-cardioversion period, data have suggested that patients with AF of <48 hours' duration can safely undergo cardioversion without excluding intracardiac thrombus,[7,16] presumably because it takes time for thrombi to form once AF initiates. In this study, all patients would be restarted on oral anticoagulation within 48 hours of detecting AF, which is within current practice guidelines.

Recent studies using cardiac implantable electronic devices such as PMs and ICDs, however, have suggested

Table 4 Adverse events in control patients

Adverse event	On DOAC
Minor hemorrhagic event*	2
Major hemorrhagic event	0
Stroke/TIA	0
LV thrombus	1
Death	0

LV = left ventricle; other abbreviations as in Table 3.
*Both minor bleeding events were epistaxis.

that significantly shorter episodes of AF may be associated with a significant increase in the risk of thromboembolism. The TRENDS (The Relationship Between Daily Atrial Tachyarrhythmia Burden From Implantable Device Diagnostics and Stroke Risk) study, which used dual-chamber PMs and ICDs, demonstrated a trend toward increased risk of thromboembolic events with AT/AF events lasting >5.5 hours (2.4% vs 1.1%; $P = .06$),[17] and the ASSERT (The Asymptomatic Atrial Fibrillation and Stroke Evaluation in Pacemaker Patients and the Atrial Fibrillation Reduction Atrial Pacing) trial, which also used dual-chamber PMs and ICDs, demonstrated that AT/AF episodes as short as 6 minutes were associated with a borderline increase in thromboembolic risk, whereas AT/AF episodes lasting >18 hours were associated with a significantly increased rate of thromboembolism (4.9% vs <1.3%).[18] For this reason, and to maximize safety, a very low burden of AF was used in the TACTIC-AF protocol to reinitiate/continue anticoagulation. Future studies will hopefully refine the AF burden that is associated with a significant risk of thromboembolism across various risk profiles. The cutoff AT/AF burden needs to maximize safety while not becoming overly burdensome or requiring patients to restart anticoagulation for trivial episodes of AT/AF. Future studies might also consider using an AT/AF cutoff that varies depending on other risk factors and comorbidities, and some patients, such as those with previous thromboembolic events or very high $CHADS_2$-VASc scores, might best be served by being on continuous anticoagulation regardless of their AF burden.

Despite widespread knowledge of the link between AF and thromboembolism, rates of anticoagulation use remain low.[19] Concerns about bleeding and the hassle associated with long-term anticoagulation monitoring are frequent reasons for not starting anticoagulation in patients who would otherwise be candidates for it. TAC has the potential to maximize the risk-to-benefit ratio associated with anticoagulation by only exposing patients with low AF burden to the increased risk of bleeding associated with anticoagulation around periods of AF when the risk of thromboembolism is elevated compared to prolonged periods of sinus rhythm. This concept is sound, as studies with continuous rhythm monitoring have found a temporal association between AF burden and stroke.[20] However, future prospective studies designed to investigate the safety of TAC will be required as the temporal association between AF episodes and stroke remains controversial, and all studies have not consistently found a temporal association between AF episodes and thromboembolic events.[21,22] For example, in the ASSERT trial, only 51% (n = 26) of patients with strokes had AF around the time of their stroke, and only 4 patients had AF within 1 month of their stroke.[22] Similar findings were observed in the TRENDS study, in which only 28% (n = 11) of patients with thromboembolic complications had an AF episode within 1 month of their thromboembolic event.[21] Patients with AF can have thromboembolic events unrelated to their arrhythmia, and whether these thromboembolic events, which are temporally distinct from episodes of AF, might also be prevented by chronic anticoagulation is unclear. TAC would not prevent thromboembolic events that occur without a temporal association to AF episodes; therefore, the safety of TAC will have to be tested in a large and adequately powered study before it can be safely adopted into clinical practice.

Use of DOACs instead of warfarin has increased dramatically over the last few years, and although these drugs have many beneficial properties (eg, fewer dietary/drug interactions and no need for long-term drug-level monitoring), they are significantly more expensive than warfarin. Thus, TAC also has the potential to reduce costs associated with AF in appropriate patients. Although a formal cost-effectiveness analysis was not performed as part of this study, TAC using DOACs and an ILR was found to be cost-saving in the REACT.COM study.[23] A formal cost analysis of the TACTIC-AF study is currently underway.

Finally, it is interesting that we did not find significant changes in QOL metrics in patients who participated in the TAC group. This may be due to the relatively small sample size and insufficient statistical power, or it may be due to the fact that although there were benefits to being off anticoagulation, these may have been offset by the need for very close remote monitoring and frequent physicians contact. In addition, some patients may have found the potential to have recurrent AF while off anticoagulation to be stressful.

Study limitations

This pilot study was designed to assess the feasibility of TAC and was not powered to assess for adverse events and other safety outcomes. Therefore, although no significant adverse thromboembolic events were observed, the results from this study do not suggest that TAC is equivalent to continuous anticoagulation (the current standard of care) in terms of safety. Additionally, because of low enrollment, the study protocol was amended to change the study from a prospective, randomized control trial to a prospective, single-arm observational study. Thus, key differences between treatment and control patients may not have been observed. Difficulty in patient recruitment and the significant amount of time on anticoagulation because of protocol violations may limit the generalizability of the results. The study was also not powered to detect small differences in QOL outcomes, so although we did not observe significant changes in QOL measures, it is possible that a larger study may have found significant differences. Finally, there were significant protocol violations at 1 study site accounting for an extra 1777

inappropriate days on anticoagulation. However, although this did increase the overall time on anticoagulation, this study still demonstrated the feasibility of TAC and provides important preliminary data for future, larger studies designed to investigate the long-term safety of TAC.

Conclusion

Among patients with rare AF episodes and a low-to-moderate thromboembolic risk as assessed by the $CHADS_2$ score, tailored DOAC administration guided by wireless PM or ICD remote monitoring is feasible, and in the current study decreased anticoagulation use by 75% with few adverse events and no thromboembolic events. Future studies evaluating TAC are warranted to determine the overall safety of this novel approach to anticoagulation for AF and before this approach can be used clinically. If future studies confirm the safety of TAC, patients may be allowed to personalize their anticoagulation care based on real-time continuous arrhythmia monitoring, just as diabetics adjust their daily insulin dosages based on blood sugar measurements.

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Appendix

Supplementary data

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.hrthm.2018.06.027.

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