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Heart Rhythm Disorders

Feasibility and Safety of Uninterrupted Rivaroxaban for Periprocedural Anticoagulation in Patients Undergoing Radiofrequency Ablation for Atrial Fibrillation

Results From a Multicenter Prospective Registry

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Objectives The purpose of this study was to evaluate the feasibility and safety of uninterrupted rivaroxaban therapy during atrial fibrillation (AF) ablation.

Background Optimal periprocedural anticoagulation strategy is essential for minimizing bleeding and thromboembolic complications during and after AF ablation. The safety and efficacy of uninterrupted rivaroxaban therapy as a periprocedural anticoagulant for AF ablation are unknown.

Methods We performed a multicenter, observational, prospective study of a registry of patients undergoing AF ablation in 8 centers in North America. Patients taking uninterrupted periprocedural rivaroxaban were matched by age, sex, and type of AF with an equal number of patients taking uninterrupted warfarin therapy who were undergoing AF ablation during the same period.

Results A total of 642 patients were included in the study, with 321 in each group. Mean age was 63 ± 10 years, with 442 (69%) males and 328 (51%) patients with paroxysmal AF equally distributed between the 2 groups. Patients in the warfarin group had a slightly higher mean HAS- BLED (hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile international normalized ratio, elderly, drugs/alcohol concomitantly) score (1.70 ± 1.0 vs. 1.47 ± 0.9, respectively; $p = 0.032$). Bleeding and embolic complications occurred in 47 (7.3%) and 2 (0.3%) patients (both had transient ischemic attacks) respectively. There were no differences in the number of major bleeding complications (5 [1.6%] vs. 7 [1.9%], respectively; $p = 0.772$), minor bleeding complications (16 [5.0%] vs. 19 [5.9%], respectively; $p = 0.602$), or embolic complications (1 [0.3%] vs. 1 [0.3%], respectively; $p = 1.0$) between the rivaroxaban and warfarin groups in the first 30 days.

Conclusions Uninterrupted rivaroxaban therapy appears to be as safe and efficacious in preventing bleeding and thromboembolic events in patients undergoing AF ablation as uninterrupted warfarin therapy. (J Am Coll Cardiol 2014;63:982–8)

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Catheter ablation has dramatically changed the management of atrial fibrillation (AF) and is currently a standard-of-care treatment option for drug-refractory symptomatic AF (1). Over the past decade, AF ablation has been increasingly performed and is one of the most commonly performed ablation procedures in many electrophysiology laboratories across the world. AF ablation is a relatively complex procedure involving multiple critical steps which can pose a potential risk for both bleeding and thromboembolic complications (2–4). With improved techniques and experience, the incidence of periprocedural complications has decreased. Nevertheless, major procedural complications, especially bleeding and thromboembolic complications, result in significant morbidity and mortality (4). Minimizing these complications with optimal periprocedural anticoagulation with an appropriate balance between bleeding and thrombosis is critical to the safety of the procedure.

There is increasing evidence for the superiority of uninterrupted warfarin therapy, with a target international normalized ratio (INR) between 2 and 3, as a periprocedural anticoagulant, compared to other interrupted anticoagulation strategies (5–9). In the last few years, increasingly more AF patients are maintained on newer anticoagulant agents, posing a management challenge for periprocedural anticoagulation when patients are scheduled for AF ablation (10). Recent studies evaluating the role of dabigatran, a new oral direct thrombin inhibitor, have yielded mixed results (11–15). Rivaroxaban, a direct factor Xa inhibitor, another new oral anticoagulant, was approved for the prevention of thromboembolism in patients with nonvalvular AF in November 2011 (16). Very limited data are available on the role of rivaroxaban as a periprocedural anticoagulant for AF ablation (17,18). Recent post hoc analysis of ROCKET AF (An Efficacy and Safety Study of Rivaroxaban With Warfarin for the Prevention of Stroke and Non-Central Nervous System Systemic Embolism in Patients With Non-Valvular Atrial Fibrillation) trial comparing the outcomes of patients who underwent electrical cardioversion, chemical cardioversion, and AF ablation in randomized groups of warfarin and rivaroxaban therapy did not find any significant differences in the bleeding or thromboembolic complication rates between the groups (18). However, only half of the patients in the rivaroxaban group who underwent AF ablation took the drug on the day of the procedure, and further details of the periprocedural anticoagulation regimen are lacking. Eitel et al. (17) reported the outcomes of AF ablation using novel anticoagulants. Patients in the rivaroxaban group received a dose of the drug on the morning prior to the procedure, and the drug was continued on the evening of the procedure. No periprocedural complications were noted in the group. However, the study was significantly limited by the sample size, with only 13 patients in the rivaroxaban group. A study systematically evaluating the role of continuous rivaroxaban as a periprocedural anticoagulant during AF ablation in comparison with continuous warfarin is lacking. We intended to evaluate the safety and feasibility of rivaroxaban as a periprocedural anticoagulant in patients undergoing AF ablation.

Abbreviations and Acronyms

ACT = activated clotting time

AF = atrial fibrillation

CFAE = complex fractionated atrial electrograms

$CHADS_2$ = congestive heart failure, hypertension, age, diabetes mellitus, and prior stroke, transient ischemic attack, or thromboembolism

CHA_2DS_2VASc = congestive heart failure, hypertension, age, diabetes mellitus, and prior stroke, transient ischemic attack, or thromboembolism, vascular disease

HAS-BLED = hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile international normalized ratio, elderly, drugs/alcohol concomitantly

INR = international normalized ratio

LA = left atrium

PV = pulmonary veins

PVAI = pulmonary vein antral isolation

TEE = transesophageal echocardiography

TIA = transient ischemic attack

UH = unfractionated heparin

Methods

We performed a multicenter, observational study from a prospectively collected registry of AF patients undergoing radiofrequency catheter ablation at 8 institutions in North America between January 2012 and March 2013. The study protocol was approved by the institutional review boards at the respective institutions. The rivaroxaban group consisted of all consecutive patients who had been taking rivaroxaban once daily for at least 30 days prior to the catheter ablation procedure. The warfarin group consisted of an equal number of patients, matched for age, sex, and type of AF, undergoing AF ablation and taking uninterrupted warfarin during the same time period. All patients who were receiving uninterrupted warfarin therapy for 30 days, regardless of the INR value at the time of the procedure, were included in the study. Only patients who underwent manual, radiofrequency catheter ablation were included in the study, and patients who underwent cryoballoon ablation or remote navigation-aided ablation were excluded from the study.

Periprocedural anticoagulation regimen. Rivaroxaban is prescribed at doses of 15 to 20 mg as a once-daily medication to be taken with the evening meal (19). Patients were asked to take their rivaroxaban dose, as scheduled, on the evening prior to the procedure. None of the patients in the rivaroxaban group was bridged with unfractionated or low-molecular-weight heparin periprocedurally. All patients in the rivaroxaban group underwent transesophageal echocardiography (TEE) on the morning of the procedure. Rivaroxaban administration was resumed on the evening of the procedure, with a minimum posthemostasis period of 3 h. Therefore, it was a completely uninterrupted rivaroxaban

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therapy regimen. In the warfarin group, AF ablation was performed without any interruption of warfarin. Outpatient monitoring of INR was performed once weekly for at least 3 weeks prior to the procedure to ensure therapeutic anticoagulation (INR between 2 and 3). Patients in the warfarin group with a therapeutic INR level did not undergo TEE. Seven patients (2%) in the uninterrupted warfarin group had an INR of <2.0 on the morning of the procedure and underwent TEE prior to the procedure; 3 of them were receiving an unfractionated heparin (UH) drip postprocedure. All 7 patients had therapeutic INR on the next morning and were discharged home without any additional anticoagulation bridge.

Ablation procedure. Patients underwent pulmonary vein antral isolation (PVAI) with a double trans-septal approach as described in detail elsewhere (20). Briefly, with the help of intracardiac echocardiography, two trans-septal accesses were obtained using standard needles and sheaths. The site, size, and number of venous sheaths and recording catheters was left to the operator's preference. A bolus of 10,000 U of UH was administered just prior to trans-septal puncture. Activated clotting time (ACT) was measured 15 min after the administration of bolus dose and after every 20 min subsequently. For the duration of the procedure when catheters were in the left atrium (LA), weight-adjusted boluses of UH were administered to keep ACT between 300 and 400 s; the LA was mapped using a circular mapping catheter (Lasso, Biosense Webster Inc., Diamond Bar, California; or Spiral, St. Jude Medical, Minneapolis, Minnesota). Electrical isolation was accomplished by ablating the antrum of pulmonary veins with 3.5-mm open irrigated tip catheter (ThermoCool, Biosense Webster Inc.). For ablating anterior segments, radiofrequency energy up to a maximum range of 40 to 45 W was used, whereas 25 to 35 W of radiofrequency output was used to ablate posterior segments. The numbers of lesions and lesion sets were determined by the operator, depending on each patient's arrhythmia substrate. Intravenous adenosine was used to confirm PV isolation in some patients.

Only PVAI was performed in patients with paroxysmal AF. The endpoint of this ablation procedure was to accomplish entry and exit blockages. In cases of persistent AF, additional substrate modification using complex fractionated electrograms (CFAEs) was also performed. CFAEs were identified with a mapping catheter on the three-dimensional map along different regions within the atria (posterior wall, left atrial septum, left atrial roof, coronary sinus, left atrial appendage base, and crista terminalis) and later ablated. In case of spontaneous intra-atrial tachycardia during the ablation procedure, it was mapped and ablated. In addition to PVAI and ablation of CFAEs, ablation of residual LA tachycardia with roof lines and a mitral isthmus line along with LA appendage and coronary sinus isolation were done in some patients at the operator's discretion. If mapping showed double potentials around the junction of superior vena cava and right atrium, then additional ablation was done in the region. Furthermore, 20 μg/min isoproterenol was given for 15 min to identify nonpulmonary vein triggers, and ablation of these triggers was performed. If PVAI and substrate modification did not achieve sinus rhythm, direct current cardioversion was performed to restore sinus rhythm.

Data collection. All participating centers had an AF registry in their respective institutions, where demographic, clinical, procedural, and complications data were collected prospectively. Another common database specific to this study was created centrally and was updated frequently by each of the participating institutions prospectively. All complications occurring within the first 30 days after the ablation procedure were included in the study database. Data for complications were collected during the hospital stay, at 1-month follow-up visits, or by 30-day telephone interview. No patients were lost to follow-up.

Safety endpoints. Pericardial effusions and hematomas were identified as bleeding complications. Transient ischemic attacks (TIA) and cerebrovascular accidents were identified as thromboembolic events after intracranial bleeding was ruled out. Major bleeding was defined as any bleeding severe enough to require blood transfusion, hematomas requiring surgical intervention, and pericardial bleeding necessitating drainage (cardiac tamponade). Small hematomas and pericardial effusion which did not require any intervention were considered minor bleeding complications. Occurrences of pericardial effusion that occurred more than 48 h postprocedure and required drainage were considered late pericardial effusion. Other complications related to the procedure but unrelated to anticoagulation were also noted.

Statistical analysis. Study populations included the "rivaroxaban" group and the "warfarin" group, each with an equal number of patients, matched by age, sex, type of AF, and the institution at which the ablation was performed. A difference of 3% in the incidence of major hemorrhage was considered clinically meaningful. With a noninferiority margin of 3%, a 2-sided type 1 error of 0.05, and 80% power, the required sample size per group was determined to be 305.

Categorical variables were compared using either the chi-square test or Fisher exact test where appropriate, and continuous variables were compared using Student *t*-test or Wilcoxon rank sum model where necessary. Baseline demographics, procedural variables, and periprocedural complications were compared between the 2 groups. Univariate analyses were performed to identify the predictors of periprocedural complications. A p value of <0.05 (2-sided) was considered statistically significant. All analyses were performed with IBM SPSS version 20.0 software (SPSS, Inc., Chicago, Illinois) for Windows (Microsoft, Redmond, Washington).

Results

Until March 2013, 321 patients underwent AF ablation on uninterrupted rivaroxaban in the participating centers. An

Table 1 Comparison of Baseline Demographics, Clinical Parameters, and Medication Use Between Patients on Rivaroxaban and Warfarin

Baseline Characteristic	Group: Rivaroxaban (N = 321)	Group: Warfarin (N = 321)	p Value
Mean age (yrs)	63 ± 10	63 ± 10	0.98
Mean body mass index (kg/m^2)	30 ± 6	30 ± 6	0.162
Male (%)	221 (69)	221 (69)	1.00
Caucasian (%)	277 (86)	292 (91)	0.06
Paroxysmal atrial fibrillation (%)	164 (51)	164 (51)	1.00
Duration of atrial fibrillation, months	42 (20–81)	48 (22–84)	0.243
Re-do procedure (%)	88 (27)	74 (23)	0.203
Heart failures (%)	30 (7)	23 (6)	0.315
Hypertension (%)	177 (55)	199 (62)	0.078
Age >75 yrs (%)	41 (13)	41 (13)	1.00
Diabetes (%)	59 (18)	64 (20)	0.616
Transient ischemic attacks or stroke (%)	34 (11)	26 (8)	0.278
Coronary artery disease (%)	60 (19)	67 (21)	0.488
Peripheral artery disease (%)	17 (5)	25 (8)	0.202
Sleep apnea (%)	74 (23)	79 (25)	0.643
Chronic obstructive pulmonary disease (%)	24 (8)	30 (9)	0.414
Chronic renal insufficiency (%)	8 (3)	9 (3)	1.00
Serum creatinine	0.845 ± 0.25	0.874 ± 0.23	0.126
$CHADS_2$ score	1.16 ± 1.0	1.18 ± 1.0	0.876
Median $CHADS_2$ score	1 (0–2)	1 (0–2)	0.737
CHA_2DS_2VASc score	2.17 ± 1.6	2.21 ± 1.5	0.781
Median CHA_2DS_2VASc score	2 (1–3)	2 (1–3)	0.808
HAS-BLED score	1.47 ± 0.9	1.70 ± 1.0	0.032
Left atrial size, cm	4.4 ± 0.8	4.3 ± 0.8	0.114
% of left ventricular ejection fraction	58 ± 8	57 ± 8	0.184
Aspirin (%)	98 (31)	84 (26)	0.220
Clopidogrel (%)	22 (7)	15 (5)	0.236
Beta blocker (%)	186 (58)	192 (60)	0.630
Calcium channel blocker (%)	90 (27)	74 (23)	0.148

Values are mean ± SD, n (%), or median (interquartile range).

$CHADS_2$ = congestive heart failure, hypertension, age, diabetes mellitus, and prior stroke, transient ischemic attack, or thromboembolism; CHA_2DS_2VASc = congestive heart failure, hypertension, age, diabetes mellitus, and prior stroke, transient ischemic attack, or thromboembolism, vascular disease; HAS-BLED = hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile international normalized ratio, elderly, drugs/alcohol concomitantly.

equal number of patients who underwent AF ablation while taking uninterrupted warfarin were matched by age, sex, and type of AF and were included in the current study of 642 patients (321 in each group).

Baseline and procedural characteristics. Mean age of the study population was 63 ± 10 years, with 442 (69%) males and 328 (51%) patients who had paroxysmal AF with no differences between the groups as shown in Table 1. There were no differences between mean body mass index, mean AF duration, proportion of re-do procedures, prevalence of advanced age (>75 years), hypertension, diabetes, prior stroke and/or TIA, coronary artery disease, sleep apnea, chronic obstructive pulmonary disease, chronic renal insufficiency, LA size and left ventricular ejection fraction between the groups. The mean $CHADS_2$ (congestive heart failure, hypertension, age, diabetes mellitus, and prior stroke, transient ischemic attack, or thromboembolism) score (1.17 ± 1.0) and mean CHA_2DS_2VASc (congestive heart failure, hypertension, age, diabetes mellitus, and prior stroke, transient ischemic attack, or thromboembolism, vascular disease) score (2.19 ± 1.6) were not different between both the groups. Patients in the rivaroxaban group had a lower HAS-BLED (hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile international normalized ratio, elderly, drugs/alcohol concomitantly) score (1.47 ± 0.9 vs. 1.70 ± 1.0, respectively; p = 0.032). There were no differences in the usage of medications, including aspirin and clopidogrel.

The dose of rivaroxaban was 20 mg/day in 315 patients and 15 mg/day in the other 6 patients. The mean time from the last dose of rivaroxaban to the start of the procedure was 16 ± 5 h. The mean time for resumption of the dose was 5.6 ± 2 h posthemostasis. The mean INR in the rivaroxaban group (available in 180 patients) was 1.41 ± 0.5 compared to a mean INR of 2.33 ± 0.4 (p < 0.001) in the warfarin group. Seven (3%) patients taking uninterrupted warfarin had an INR of <2.0 on the morning of the procedure (all, ≥1.7). There were no significant differences between the creatinine and procedural variables in either group, as shown in Tables 1 and 2, respectively. Procedure time, fluoroscopy time, and ablation time were not significantly different between the 2 groups.

Complications. A total of 47 patients (7.3%) had a bleeding complication and 2 patients (0.3%) had TIAs in the entire study population, as shown in Table 3. There were no differences in major bleeding complications (5 [1.6%] vs. 7 [2.2%], respectively; p = 0.772), minor bleeding complications (16 [5.0%] vs. 19 [5.9%], respectively; p = 0.602), or embolic complications (1 [0.3%] vs. 1 [0.3%], respectively; p = 1.00) in the rivaroxaban group compared to the warfarin group. The composite of thromboembolic and

Table 2 Comparison of Procedural Variables Between Patients on Rivaroxaban and Warfarin

Procedural Variables	Group: Rivaroxaban (N = 321)	Group: Warfarin (N = 321)	p Value
Sinus rhythm on arrival at the laboratory (%)	209 (65)	228 (71)	0.110
Ablation of CFAE/posterior wall	116 (36)	125 (39)	0.463
Additional linear lesions including right atrium (%)	101 (31)	118 (37)	0.157
Cardioversion during procedure (%)	102 (32)	90 (28)	0.300
Acute PV Isolation (%)	317 (99)	314 (99)	1.00
Procedural time, min	195 ± 62	198 ± 66	0.550
Fluoroscopy time, min	49 ± 20	51 ± 30	0.320
RF time, min	56 ± 25	58 ± 29	0.349

Values are n (%) or mean ± SD.

AF = atrial fibrillation; AFL = atrial flutter; CFAE = complex fractionated atrial electrograms; PV = pulmonary vein; RF = radiofrequency.

Table 3 Comparison of Complications between Rivaroxaban and Warfarin

Complication	Rivaroxaban (N = 321)	Warfarin (N = 321)	Total (N = 642)	p Value
Major bleeding (%)	5 (1.6)	7 (2.2)	12 (1.9)	0.772
Early cardiac tamponade (%)	2 (0.6)	4 (1.2)	6 (0.9)	
Delayed cardiac tamponade (%)	1 (0.3)	0 (0)	1 (0.2)	
≥Moderate access site hematomas (%)	2 (0.6)	3 (0.9)	5 (0.8)	
Minor bleeding complications (%)	16 (5.0)	19 (5.9)	35 (5.5)	0.602
<Moderate access site hematoma (%)	13 (4.0)	18 (5.6)	31 (4.8)	
Insignificant pericardial effusions (%)	3 (0.9)	1 (0.3)	4 (0.6)	
All bleeding complications (%)	21 (6.5)	26 (8.1)	47 (7.3)	0.449
Thromboembolic complications (stroke/TIA) (%)	1 (0.3)	1 (0.3)	2 (0.3)	1.00
TIA (%)	1 (0.3)	1 (0.3)	2 (0.3)	
Stroke	0	0	0	
Bleeding and thromboembolic complications (%)	22 (6.8)	27 (8.4)	49 (7.6)	0.457
Other complications	3 (0.9)	2 (0.6)	5 (0.8)	1.00

Values are n (%).
TIA = transient ischemic attack.

bleeding complications was not significantly different in the rivaroxaban group compared to the warfarin group (22 [6.8%] vs. 27 [8.4%], respectively; p = 0.457). Three patients in the rivaroxaban group and 4 patients in the warfarin group underwent emergent percutaneous pericardial drainage with no sequelae. None of the patients required surgical drainage. Anticoagulation reversal was attempted in 2 patients on rivaroxaban therapy (with fresh frozen plasma and activated factor VII, respectively). All 4 patients on warfarin therapy underwent emergent reversal of anticoagulation with fresh frozen plasma and vitamin K. Anticoagulation could be resumed in all patients prior to discharge. The patient in the warfarin group who had a postprocedural TIA had an INR of 1.8 on the morning of the procedure. After the procedure, the patient underwent UH anticoagulation therapy for 1 day, at which point the INR came back into the therapeutic range and the patient was discharged home with no additional anticoagulation. No patient in either group had a periprocedural stroke or death.

Discussion

Main study findings. In our multicenter, observational study, we found that uninterrupted rivaroxaban is as safe and efficacious in preventing periprocedural bleeding and thromboembolic events during AF ablation as uninterrupted warfarin therapy. This is the first study to evaluate the feasibility and safety of using continuous rivaroxaban as a periprocedural anticoagulant during AF ablation.

Thromboembolic and bleeding complications after AF ablation. Bleeding and thromboembolic events are the most common complications of AF ablation (4,21–26). Major bleeding complications are the cause of 25% of all deaths related to AF ablation. The complexity of the integral components of the procedure, including trans-septal puncture, LA cannulation by multiple large sheaths and catheters, intraprocedural anticoagulation, extensive ablation with activation of a cascade of inflammatory responses on an already diseased LA, inherently exposes the patient to an unavoidable complication risk. The evolution of the procedure over the past decade, in multiple fronts, has decreased the risk of these complications significantly (5,24,27). One such important evolutionary aspect is periprocedural anticoagulation.

Periprocedural anticoagulation. Currently, intraprocedural use of UH to keep ACTs in the range of 300 to 400 s is a routine approach in almost all centers regardless of the background anticoagulation (1). However, pre- and postprocedural anticoagulation strategies seem to be still significantly variable in different institutions (28). Several different anticoagulation protocols consisting of varied combinations of antiplatelet agents, warfarin, and unfractionated and low-molecular-weight heparin combined with TEE screening stratified by baseline risk of systemic thromboembolism and type of AF are being used and are subject to some debate (1–3,28). Operator comfort and experience seem to be the primary drivers behind the selection of periprocedural anticoagulation regimen (27).

Uninterrupted warfarin therapy with therapeutic anticoagulation has been shown to be associated with lower risk of periprocedural thromboembolic events after AF ablation and is increasingly being accepted as the preferred anticoagulation strategy (5,7,8,29). However, increasingly more patients are being treated with newer oral anticoagulants, thereby complicating the periprocedural anticoagulation management. In addition, despite being on uninterrupted warfarin therapy, some patients do have subtherapeutic INR at the time of the procedure, exposing them to a higher risk of complications. In our current study, 7 of 321 patients (2%), despite being on uninterrupted warfarin therapy and having a close outpatient follow-up, did end up having subtherapeutic INR on the morning of the procedure. Moreover, 1 of those 7 patients had a TIA after the procedure, necessitating additional anticoagulation.

Various protocols have been proposed and have experimented with dabigatran, the first of the newer oral anticoagulants for periprocedural management with mixed results (11–15). In our previous study, nearly uninterrupted anticoagulation with dabigatran (holding the morning dose), which theoretically has a better protection from periprocedural thromboembolism, was associated with both increased bleeding and thromboembolic events, especially in the nonparoxysmal AF (11). Other observational studies with a more interrupted approach showed equivalent bleeding and embolic events compared to therapeutic warfarin

(13,15,30,31). The bleeding risk in our previous study was likely related to the overlapping pharmacodynamic effect of UH and dabigatran (32). The higher incidence of thromboembolic events in our study was seen exclusively in nonparoxysmal AF patients (3 of 43 [8%]) and was probably related to a difference in the patient profile and the ablation approach. As of now, there is no consensus regarding the management of patients taking dabigatran who are referred for AF ablation (28).

An ideal periprocedural anticoagulant for AF ablation, in addition to being associated with minimal bleeding and thromboembolic events, should be the same anticoagulant the patient had been taking prior to the procedure, without interrupting the patient's dosing schedule. Rivaroxaban, the second of the US Food and Drug Administration-approved newer non-vitamin K antagonist anticoagulants, at a dose of 15 to 20 mg once daily, has been shown to be noninferior to warfarin in preventing thromboembolic events in patients with nonvalvular AF and was approved for use in the United States in November of 2011 (16). Rivaroxaban is an oral, direct inhibitor of factor Xa that is rapidly absorbed and has a time to peak plasma concentration of <4 h and a half-life ranging from 7 to 13 h, depending on the age of the patient (33,34). By inhibiting the formation of thrombin, it blocks both intrinsic and extrinsic pathways and is known to be associated with elevated INR (35). The mean INR in our rivaroxaban group was also slightly high, as seen in prior studies (36). As a once-a-day dosing medication, rivaroxaban can be used in the AF ablation periprocedural setting without interrupting the patient's regular dosing schedule. It is a potentially attractive alternative to warfarin if consistently shown to be safe in this setting.

Piccini et al. (18) recently reported a post hoc analysis of ROCKET AF trial results, comparing the outcomes of patients who underwent electrical cardioversion, chemical cardioversion, and AF ablation in randomized groups receiving warfarin or rivaroxaban therapy. The study lacked the critical details of peri-AF ablation anticoagulation management to draw any meaningful conclusions about the relative efficacy of either of the agents in AF ablation. Almost all the comparative analyses were made after pooling patients undergoing chemical cardioversion, electrical cardioversion, and AF ablation. Although the study compared the outcomes between the groups, only 49% of the patients in the rivaroxaban group were taking the drug on the day of the procedure. In addition, few patients underwent bridging with low- molecular-weight heparin. Eitel et al. (17) reported outcomes of using novel oral anticoagulants in the periprocedural setting of AF ablation. Of the 259 patients included in the study, 13 were receiving rivaroxaban both before and after the procedure, and an additional 3 patients were started on rivaroxaban after the procedure. The patients underwent some interruption of rivaroxaban, resulting in a change in the dosing time from morning (prior to the day of the procedure) to an evening dosing time (postprocedure). None of the 16 patients had any bleeding or thromboembolic complications. A randomized controlled trial comparing uninterrupted warfarin with uninterrupted rivaroxaban therapy for AF ablation (VENTURE-AF [Study Exploring Two Treatment Strategies in Patients With Atrial Fibrillation Who Undergo Catheter Ablation Therapy] trial) in patients with patients with atrial fibrillation is underway and hopefully will give us more insights into the role of this newer agent in this important setting of AF ablation (37). In our current study, approximately half of the patients had nonparoxysmal AF, and many of them underwent additional ablation lesions. Despite such additional ablation, unlike our prior experience with dabigatran, we did not notice any increased incidence of thromboembolic complications, which is very reassuring.

As with dabigatran, rivaroxaban also does not have a specific antidote at this time. Concerns about management of life-threatening hemorrhagic complications, especially in the periprocedural setting, do exist. Prothrombin complex concentrate can reverse some of the anticoagulant action of rivaroxaban in healthy volunteers (38). However, its role in clinical hemorrhagic settings has not been systematically evaluated. In our study, 3 patients taking rivaroxaban required pericardiocentesis, with no significant issues with excessive bleeding. Specific antidotes to these newer anticoagulants are eagerly awaited, especially for use in the periprocedural settings.

Study limitations. Our study has the inherent limitations of a multicenter observational study. The procedural techniques were operator-dependent, which could potentially confound the results, even though all our centers predominantly practice a similar protocol. We report only 30-day follow-up outcomes, and longer term outcomes may not be the same. However, most of the periprocedural complications occurred during this time frame. The $CHADS_2$ and CHA_2DS_2Vasc scores of the patients in our study were more reflective of real-world experience, and we cannot extrapolate to very-high stroke risk patients. Nevertheless, lack of data on the feasibility and safety of uninterrupted rivaroxaban therapy during AF ablation procedure makes our study very important to the current electrophysiology practice, especially with increasing use of rivaroxaban in clinical practice.

Conclusions

In our multicenter experience, uninterrupted rivaroxaban appears to be a feasible and safe alternative to uninterrupted warfarin therapy in patients undergoing AF ablation. Future larger and randomized trials are needed to confirm our findings.

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Key Words: periprocedural anticoagulation ■ radiofrequency ablation ■ rivaroxaban ■ warfarin.