Use of Dabigatran for Periprocedural Anticoagulation in Patients Undergoing Catheter Ablation for Atrial Fibrillation

Mohamed Bassiouny, MD; Walid Saliba, MD; John Rickard, MD; Mingyuan Shao, MS; Albert Sey, MD; Mariam Diab, MD; David O. Martin, MD; Ayman Hussein, MD; Maurice Khoury, MD; Bernard Abi-Saleh, MD; Samir Alam, MD; Jay Sengupta, MD; P. Peter Borek, MD; Bryan Baranowski, MD; Mark Niebauer, MD; Thomas Callahan, MD; Niraj Varma, MD; Mina Chung, MD; Patrick J. Tchou, MD; Mohamed Kanj, MD; Thomas Dresing, MD; Bruce D. Lindsay, MD; Oussama Wazni, MD

Background—Pulmonary vein isolation (PVI) for atrial fibrillation is associated with a transient increased risk of thromboembolic and hemorrhagic events. We hypothesized that dabigatran can be safely used as an alternative to continuous warfarin for the periprocedural anticoagulation in PVI.

Methods and Results—A total of 999 consecutive patients undergoing PVI were included; 376 patients were on dabigatran (150 mg), and 623 patients were on warfarin with therapeutic international normalized ratio. Dabigatran was held 1 to 2 doses before PVI and restarted at the conclusion of the procedure or as soon as patients were transferred to the nursing floor. Propensity score matching was applied to generate a cohort of 344 patients in each group with balanced baseline data. Total hemorrhagic and thromboembolic complications were similar in both groups, before (3.2% versus 3.9%; P=0.59) and after (3.2% versus 4.1%; P=0.53) matching. Major hemorrhage occurred in 1.1% versus 1.6% (P=0.48) before and 1.2% versus 1.5% (P=0.74) after matching in the dabigatran versus warfarin group, respectively. A single thromboembolic event occurred in each of the dabigatran and warfarin groups. Despite higher doses of intraprocedural heparin, the mean activated clotting time was significantly lower in patients who held dabigatran for 1 or 2 doses than those on warfarin.

Conclusions—Our study found no evidence to suggest a higher risk of thromboembolic or hemorrhagic complications with use of dabigatran for periprocedural anticoagulation in patients undergoing PVI compared with uninterrupted warfarin therapy. (Circ Arrhythm Electrophysiol. 2013;6:460-466.)

Key Words: ablation ■ anticoagulants ■ catheter ablation ■ fibrillation ■ stroke

Atrial fibrillation (AF) ablation has evolved during the past decade, providing patients with symptomatic AF an alternative to medical therapy.1,2 Thromboembolic and bleeding complications, however, represent rare but serious consequences.3 Sheaths and catheters in the left atrium (LA), atrial stunning, endothelial damage, and inflammation from ablation heighten the risk of thromboembolic complications during and early after ablation.4 Periprocedural management of anticoagulation in patients undergoing pulmonary vein isolation (PVI) is critical to limit complications.

Clinical Perspective on p 466

Warfarin has been the only effective oral anticoagulant available since 1950. Most centers prefer to discontinue warfarin before PVI and bridge anticoagulation before and after ablation.5,6 More recently, several studies have shown that PVI can be safely performed in patients with a therapeutic international normalized ratio (INR).7,8 This strategy is gaining momentum and has been endorsed in the 2012 Heart Rhythm Society (HRS)/ European Heart Rhythm Association (EHRA)/European Cardiac Arrhythmia Society (ECAS) expert consensus statement.9

Emergence of dabigatran as a safe and effective alternative to warfarin in patients with nonvalvular AF11 offers new challenges and possibilities for minimizing perioperative thromboembolism and hemorrhage. The purpose of our study was to evaluate the use of dabigatran for periprocedural anticoagulation in patients undergoing AF ablation compared with uninterrupted warfarin therapy.

Methods

The study was a review of a prospectively collected registry of patients undergoing PVI between December 2010 and July 2012 at our center. All consecutive patients referred for PVI while on dabigatran etexilate (150 mg) were included and compared with consecutive patients undergoing PVI while on uninterrupted warfarin with a therapeutic INR during the same time period. The incidence of thromboembolic and hemorrhagic complications during the initial
30 days after ablation and the intraprocedural heparin and activated clotting time (ACT) were compared between the 2 groups. The study was approved by the Cleveland Clinic Institutional Review Board, and all patients gave written informed consent before ablation.

Major hemorrhage was defined as the occurrence of tamponade or hemopericardium that required intervention or caused excessive bleeding (≥25 g/L decrease in hemoglobin or need for transfusion), hematoma requiring intervention or additional hospitalization, significant hemothysis, hemotherax, or retroperitoneal bleeding. Minor hemorrhage was defined as the occurrence of a hematoma or any bleeding that did not require intervention or prolong hospitalization. Thromboembolic complications were defined as the occurrence of ischemic stroke, transient ischemic attack, peripheral embolic events, or deep venous thrombosis.

**Ablation Protocol**

Our AF ablation approach was previously described in detail. In summary, 2 sheaths were placed in each of the femoral veins under ultrasound guidance. Intracardiac echocardiography was used in all procedures to assist with transseptal punctures, view catheters in the LA, and identify complications, including pericardial effusion. Two catheters were advanced into the LA for mapping and ablation guided by intracardiac echocardiography. All pulmonary veins were isolated using a 3.5-mm irrigated tip catheter using fluoroscopy and a 3-dimensional navigation system for guidance (CARTO, Biosense-Webster Inc or Ensite NavXTM, St. Jude Medical Inc. MN). Radiofrequency energy was limited to 35 to 40 W. Impedance and esophageal temperature were closely monitored to avoid excessive heating and tissue injury. In patients with concomitant atrial flutter, activation mapping and entrainment were performed to locate and ablate the critical isthmus.

**Periprocedural and Intraprocedural Anticoagulation**

Early in our experience, patients were instructed to hold 1 or 2 doses of dabigatran before ablation according to the preference of the electrophysiologist performing the procedure. More recently most patients are instructed to hold only 1 dose on the morning of the procedure. Patients on warfarin were instructed to continue taking the therapeutic dose. No heparin was administered to any patient in either group before ablation. Transeosophageal echocardiography was performed immediately before PVI in patients presenting in AF with compliance issues on dabigatran, or subtherapeutic INR on warfarin within 4 weeks of the procedure. For PVI, an initial unfractionated heparin bolus (80–150 U/kg) was administered before transseptal puncture. During the procedure, unfractionated heparin was continuously given to all patients via intravenous infusion. ACT was monitored every 10 to 30 minutes (Hemochron Jr. Signature+ Micro coagulation System, ITC Medical, Edison, NJ). Additional heparin boluses were given, and the infusion rate was adjusted to target an ACT of 350 to 450 seconds. After ablation, catheters were withdrawn, and heparin was stopped and partially reversed with protamine before sheaths were pulled. PVI was performed under conscious sedation with fentanyl and Midazolam in the majority of patients. This allowed for safe administration of dabigatran (150 mg) and aspirin (325 mg) in the EP laboratory at the conclusion of the procedure. Patients who underwent PVI under general anesthesia were extubated in the EP laboratory, transferred to the postanesthesia care unit, and received dabigatran before ablation according to the preference of the electrophysiologist performing the procedure. More recently most patients were advanced into the LA for mapping and ablation guided by intracardiac echocardiography. All pulmonary veins were isolated using a 3.5-mm irrigated tip catheter using fluoroscopy and a 3-dimensional navigation system for guidance (CARTO, Biosense-Webster Inc or Ensite NavXTM, St. Jude Medical Inc. MN). Radiofrequency energy was limited to 35 to 40 W. Impedance and esophageal temperature were closely monitored to avoid excessive heating and tissue injury. In patients with concomitant atrial flutter, activation mapping and entrainment were performed to locate and ablate the critical isthmus.

**Periprocedural Monitoring and Postprocedural Follow-up**

Patients were monitored for thromboembolic and hemorrhagic complications throughout the procedure, overnight, and before discharge the following day, using frequent symptom, neurological, vascular access site, and heart and peripheral pulsation evaluations. Transthoracic echocardiography and ultrasound were performed as needed. Patients on dabigatran were discharged on 150 mg twice daily. Patients on warfarin had INR checks the day of the procedure and were followed by their local doctors and Coumadin clinics to maintain therapeutic INR. Follow-up weekly telephone calls were made in the first 3 months postdischarge by dedicated AF–electrophysiology registered nurses to assess progress of recovery and symptoms. In addition, all patients were instructed to call our center for AF if any symptoms developed and to send weekly transtelephonic ECG transmissions for the first 3 months after ablation. Patients with suspected complications were asked to seek the nearest emergency department or their local physician. Documentation from these visits were obtained and added to our records. All patients had scheduled follow-up appointments with their electrophysiologist 3 months after PVI or earlier if symptoms arise to evaluate success and exclude complications.

**Statistical Analysis**

Demographic and baseline characteristics were summarized, categorical variables were compared using χ² tests, and continuous variables were compared using analysis of variance if normally distributed and using Kruskal–Wallis test if not normally distributed.

Because of significant differences in some baseline characteristics between the dabigatran and warfarin groups, propensity score matching was applied, by constructing a logistic regression model, in which the dabigatran versus warfarin treatment was regressed on baseline characteristics related to dabigatran treatment and outcome of PVI. The estimated propensity score was obtained as the predicted probability of exposure of each patient to dabigatran. Matching was based on the logit of propensity score, using calipers of width 0.2 of the SD of the logit of the propensity score. To assess bias reduction achieved by propensity matching, the absolute standardized differences of the 11 covariates included in propensity score calculation were compared before and after matching, with a value <10% indicating between-group balance (Figure 1 in the online-only Data Supplement). The matched baseline data are estimated by paired test or Wilcoxon signed-rank test for normally or non-normally distributed continuous variables, and McNemar test or the Stuart–Maxwell statistics for binary or polynomial categorical variables. Complications after matching were compared between the dabigatran and warfarin groups using the McNemar test and a special method for estimating relative risks (RR) and their 95% confidence intervals (CI), to account for the dependent nature of the matched pairs.

To evaluate intraprocedural ACT values and heparin requirements, a greedy 5 → 1 digit matching of patients on warfarin to those who held dabigatran for 1 dose and those who held it for 2 doses without replacement was, respectively, performed on a population of patients with complete ACT values up to 165 minutes, based on logistic regression models for deriving propensity scores, in which dabigatran 1 dose or 2 doses were AF-exposed. Categorical AF duration years that were related to dabigatran and ACT measures. A cohort of triple matched samples (warfarin, dabigatran 1 dose, and dabigatran 2 doses) was subsequently formed by merging these matched samples using the common warfarin patients. A random coefficient mixed model repeated measures analysis for ACT against measurement time across the treatment groups was performed in this matched cohort, and least-squares means (mean±SE) were calculated. Furthermore, a growth curve model was built, showing regression lines of the treatment groups. A time-to-event analysis was performed to examine time to first ACT>350 seconds in a cohort of triple matched samples from the 3 treatment groups constructed on the same greedy 5 → 1 digit matching method with main effects in the propensity score model being age, males, AF duration, and hypertension that were related to dabigatran and time to first ACT>350 seconds, and merged on common warfarin patients. Cumulative Kaplan–Meier estimates were plotted and compared.

Some variables that are related to the repeated measures or time-to-event were compared pairwise among the treatment groups using the Bonferroni adjustment, in the respective matched cohorts. All statistical analyses were performed using the SAS software (version 9.2, SAS Institute, Inc, Cary, NC). A 2-sided P value of 0.05 was considered statistically significant.

**Results**

**Baseline Characteristics**

A total of 999 patients undergoing PVI at our institution between December 2010 and July 2012 were included in the study, of
which 376 patients were on dabigatran, and 623 patients were on uninterrupted warfarin with a therapeutic INR. Dabigatran was started 62 days (median; interquartile range [34–120]) before PVI, and was held for 1 dose in 203 patients and for 2 doses in 173 patients before PVI. Baseline patient characteristics are summarized in Table 1. Propensity score logit matching identified 344 dabigatran (92%) and the same number of warfarin patients who were comparable with respect to age, sex, body mass index, common comorbidities, CHADS II score, prevalence of persistent AF, and aspirin intake. INR was not included in matching because it is inherently higher in the warfarin group.

Complications
Total hemorrhagic and thromboembolic complications were similar in the dabigatran and warfarin groups before (3.2% versus 3.9%; \(P=0.59\); RR [95% CI], 0.828 [0.420–1.636]) and after matching (3.2% versus 4.1%; \(P=0.53\); RR [95% CI], 0.786 [0.368–1.676]; Table 2). Thromboembolic events occurred in 1 patient in each of the warfarin and dabigatran groups. In the warfarin group, a 71-year-old male with a CHADS II score of 2 (hypertension and heart failure) developed right upper extremity weakness and expressive aphasia 1 hour after PVI secondary to a small left middle cerebral artery thromboembolic event. Transesophageal echocardiography was performed before PVI for subtherapeutic INR in the preceding week, revealing spontaneous echo contrast but no LA thrombi. He was managed conservatively, and no thrombolytic therapy was given because of therapeutic INR on the day of the procedure. The right upper extremity weakness completely resolved within few hours and minimal neurological deficits were noted on the 3 months follow-up visit. In the dabigatran group, 1 patient who held 1 dose before ablation reportedly complained of pleuritic chest pain and was diagnosed with pulmonary embolism at an outside hospital within 2 weeks of discharge. Investigations that supported this diagnosis were not available for our review. He was managed by switching to warfarin in addition to aspirin.

Major hemorrhagic complications were similar between the dabigatran and warfarin groups before (1.1% versus 1.6%; \(P=0.48\); RR [95% CI], 0.663 [0.209–2.099]) and after propensity matching (1.2% versus 1.5%; \(P=0.74\); RR [95% CI], 0.800 [0.215–2.981]). A 40-year-old male patient in the dabigatran group with CHADS II score of 2 (hypertension and diabetes mellitus) developed a small hemorrhagic stroke that presented 48 hours after PVI with severe headache, dizziness, and ear ringing without any focal deficit. Symptoms resolved by the time he was evaluated in the emergency department. Brain computed tomography showed a small right hemispheric hemorrhagic stroke. Brain MRI showed a cavernous malformation associated with a congenital venous

Table 1. Baseline Characteristics* of the Study Population Before and After Propensity Matching

<table>
<thead>
<tr>
<th>Variables</th>
<th>Before Propensity Score Matching</th>
<th>P Value</th>
<th>After Propensity Score Matching</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dabigatran (n=376)</td>
<td>Warfarin (n=623)</td>
<td></td>
<td>Dabigatran (n=344)</td>
</tr>
<tr>
<td>Age, y</td>
<td>58.6±11.0</td>
<td>62.7±9.6</td>
<td>&lt;0.001</td>
<td>60.0±10.0</td>
</tr>
<tr>
<td>Male</td>
<td>282 (75.0)</td>
<td>457 (73.4)</td>
<td>0.57</td>
<td>256 (74.4)</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>30.3±5.3</td>
<td>30.6±6.2</td>
<td>0.95</td>
<td>30.5±5.4</td>
</tr>
<tr>
<td>AF duration, y</td>
<td>3.0 (1.0–6.5)</td>
<td>4.5 (2.0–8.5)</td>
<td>&lt;0.001</td>
<td>3.0 (1.0–7.0)</td>
</tr>
<tr>
<td>Persistent AF</td>
<td>161 (42.8)</td>
<td>279 (44.9)</td>
<td>0.53</td>
<td>155 (45.1)</td>
</tr>
<tr>
<td>CAD</td>
<td>45 (12.0)</td>
<td>130 (20.9)</td>
<td>&lt;0.001</td>
<td>44 (12.8)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>40 (10.6)</td>
<td>92 (14.8)</td>
<td>0.06</td>
<td>39 (11.3)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>183 (48.7)</td>
<td>370 (59.4)</td>
<td>0.001</td>
<td>176 (51.2)</td>
</tr>
<tr>
<td>CHF</td>
<td>32 (8.5)</td>
<td>88 (14.1)</td>
<td>0.01</td>
<td>32 (9.3)</td>
</tr>
<tr>
<td>Previous stroke/TIA</td>
<td>24 (6.4)</td>
<td>52 (8.3)</td>
<td>0.26</td>
<td>23 (6.7)</td>
</tr>
<tr>
<td>CHADS2 score</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

AF indicates atrial fibrillation; BMI, body mass index; CAD, coronary artery disease; CHF, congestive heart failure; INR, international normalized ratio; LAVI, left atrium volume index; LVEF, left ventricular ejection fraction; PVI, pulmonary vein isolation; SR, sinus rhythm; TEE, transesophageal echocardiography; and TIA, transient ischemic attack.*Categorical variables are expressed as frequency (percentage), continuous variables are expressed as mean±SD if normally distributed or as median (interquartile range) if not normally distributed.
anomaly. Dabigatran was discontinued, and the patient was started on warfarin 1 week later after a repeat brain computed tomography showed no evidence of further bleeding.

Tamponade occurred in 3 patients on dabigatran and in 7 patients on warfarin before propensity matching (0.8% versus 1.1%; \( P=0.75 \); RR [95% CI], 0.710 [0.185–2.730]) and in 3 patients on dabigatran and in 3 patients on warfarin after propensity matching (0.9% versus 0.9%; \( P=1.00 \); RR, 1.000 [0.202–4.955]). In the dabigatran group, tamponade was recognized during mapping of the LA in 1 patient and after PVI completion in 2 patients. One patient held dabigatran for 1 dose and 2 patients held it for 2 doses before ablation. In all patients on dabigatran, tamponade was managed by reversing heparin with protamine and performing percutaneous pericardiocentesis in the EP laboratory. No reaccumulation was detected on follow-up transthoracic echocardiography, and no surgery or dialysis was required in any patient. In the warfarin group, 7 patients developed tamponade; 3 detected during LA mapping or ablation and 4 patients after PVI completion. Six patients were managed with heparin reversal and pericardiocentesis. One patient developed tamponade several minutes after a steam pop that occurred during ablation along the LA roof. He remained hemodynamically unstable despite heparin reversal and pericardiocentesis. Surgical exploration showed an intact LA roof and a right ventricular laceration at the site of the pericardial sheath. He stabilized after repair of the laceration, and no reaccumulation was detected on follow-up transthoracic echocardiography.

Hemoptysis occurred in 2 patients on warfarin after PVI. One patient had major bleeding that required blood and fresh frozen plasma transfusion and intubation. Chest computed tomography and bronchoscopy showed no evidence of bronchial injury, and bleeding resolved spontaneously without further interventions. The other patient had minor hemoptysis that resolved overnight without any interventions. One patient on warfarin developed epistaxis 1 month after PVI that required an ED and cauterization.

Incidence of groin hematoma was similar between the dabigatran and warfarin groups before (1.3% versus 1.6%; \( P=0.73 \); RR [95% CI], 0.828 [0.285–2.405]) and after matching (1.2% versus 2.0%; \( P=0.37 \); RR [95% CI], 0.571 [0.167–1.951]). Only 2 patients on warfarin required thrombin injections for pseudoaneurysm. No interventions were required in any of the patients on dabigatran.

One patient on dabigatran developed bleeding secondary to hemorrhoids 5 days after PVI and was managed by holding 2 doses of dabigatran and a banding procedure. Two patients on warfarin developed limited lower gastrointestinal bleeding that did not require transfusion or interruption of the oral anticoagulation.

### Intraprocedural Activated Clotting Time and Heparin Requirements

Intraprocedural ACT and heparin requirements were evaluated in a population of 184 patients (70 held 1 dose of dabigatran, 63 held 2 doses of dabigatran, and 51 on warfarin). Propensity matching of 5→1 digit identified a cohort of 42 patients with balanced baseline characteristics in each of the 3 groups. A mixed model repeated measures analysis that incorporated linear random coefficients and quadratic fixed time effects (Figure 1) revealed that ACT was significantly lower across time in patients who held dabigatran for 2 doses before the PVI procedure (least-squares mean±SE, 336.05±4.76) than those who held it for only 1 dose (351.68±5.61; \( P=0.037 \), and those on warfarin therapy (391.68±7.34; \( P<0.001 \)).

The heparin dose throughout ablation was significantly higher in patients who held dabigatran for 1 or 2 doses (mean±SD 225.2±64.37 U/kg versus 239.0±64.99 U/kg) than those on warfarin (164.9±36.06 U/kg; \( P<0.001 \)). The mean heparin dose required to achieve target ACT (≥350 seconds) was significantly higher in patients who held dabigatran for 1 or 2 doses versus those on warfarin (153.3±42.74 U/kg and 175.1±57.65 U/kg versus 103.4±23.57 U/kg, respectively; \( P<0.001 \)). All these multiple comparisons remained significant after the Bonferroni adjustment.

Time to first ACT ≥350 seconds was analyzed in 261 patients (91 in warfarin, 102 in dabigatran 1 dose, 68 in dabigatran 2 doses). Matching of 5→1 digit was used to identify a cohort of 52 patients with balanced baseline characteristics in each of the 3 groups. Kaplan–Meier curves (Figure 2) and Z statistics\(^{13}\) demonstrated that time to first ACT ≥350 seconds was significantly longer in patients who held 2 doses of dabigatran before PVI (median [interquartile range], 50 minutes [35–72.5]) than those who held 1 dose (20 [15–40]; \( Z=2.94; \ P=0.003 \)) and those who were on warfarin (20 [15–30]; \( Z=4.71; \ P<0.001 \)).
Discussion

In this study, there was no evidence of increased risk of thromboembolic or hemorrhagic complications with use of dabigatran for periprocedural anticoagulation in patients undergoing AF ablation. However, compared with patients who underwent AF ablation on uninterrupted warfarin therapy, patients who were on dabigatran had higher intraprocedural heparin requirements, lower mean ACT, and more prolonged time to reach the target ACT.

Periprocedural Safety of Dabigatran

In our study, dabigatran was held for only 1 to 2 doses before ablation and restarted immediately after sheaths were pulled or once patients were on the floor. Major hemorrhagic and thromboembolic complications were rare. In the dabigatran group, a single hemorrhagic cerebrovascular event occurred in a young patient with cerebral cavernous malformation. In contrast, a single thromboembolic stroke occurred in a patient on warfarin with long-standing persistent AF and a very large atrium with spontaneous echo contrast on transesophageal echocardiography as described in the Results section.

Tamponade occurred in 3 patients in the dabigatran group, and although the medication was held briefly before PVI, bleeding was self-limited with no need for surgical intervention or dialysis. Despite the similarity of the periprocedural anticoagulation strategies, dabigatran held 1 dose before ablation and restarted 3 hours afterward, Lakkireddy et al recently reported a higher risk of bleeding with use of dabigatran in a multicenter study involving 145 patient undergoing PVI compared with a similar number of patients on uninterrupted warfarin. In their study, the incidence of hemorrhagic and thromboembolic complications was generally high in both the dabigatran (16%) and the uninterrupted warfarin (6%) groups. Tamponade occurred in 9 patients (6%) on dabigatran and in 1 patient on warfarin (1%). Procedural techniques were operator dependent, and high radiofrequency energy outputs (up to 45

Figure 1. Mean intraprocedural activated clotting time (ACT) measurements throughout the pulmonary vein isolation procedure. Left, Mean ACT measurements across the time categorized by the 3 treatment groups. Right, Growth curves generated from the random coefficient mixed model repeated measures analysis showing predicted mean ACT measurements across the time stratified by the 3 treatment groups.

Figure 2. Kaplan–Meier estimates of the rates of first achieving activated clotting time >300 seconds after initial heparin bolus dose, stratified by the 3 treatment groups.
W) were used. It is unclear whether complications occurred predominantly in ≥1 of the 8 involved centers. In addition, a higher percentage of patients on dabigatran were older than 75 years of age compared with our patient population (7% versus 4.5%). Interestingly, they reported an alarming 31% complication rate in this age group, which is consistent with recent published data suggesting increased risk of major bleeding in patients ≥75 years old with use of dabigatran 150 mg.17 Thromboembolic complications occurred in 2% of patients on dabigatran and none in the warfarin group. Target ACT was lower (300–400 seconds), and all patients were empirically given a bolus of 10,000 U of heparin before the transseptal puncture. Intraprocedural ACT levels and heparin requirements were not reported.

Early in our study, significantly low intraprocedural ACT was noted in patients on dabigatran and, subsequently, more aggressive anticoagulation with higher initial and more frequent boluses of heparin were administered to avoid this situation as we gained experience with managing the heparin requirements in 376 consecutive ablation procedures on dabigatran. This may not have been possible in a multicenter study, in which 145 cases were distributed over 8 centers and performed simultaneously, and may have contributed to the higher complication rates in patients on dabigatran.

**Perioperative Anticoagulation Strategies**

The optimal perioperative anticoagulation strategy in patients undergoing AF ablation remains unclear. Historically, interruption of oral anticoagulation, insufficient intraprocedural anticoagulation, and use of nonirrigated catheters were associated with up to 5% risk of thromboembolic complications.18 More recently, a worldwide survey of AF ablation reported an incidence of 0.94%, 1.31%, and 1.47% of stroke/transient ischemic attack, tamponade, and pseudoaneurysm or arteriovenous fistulae, respectively.1 Interruption of warfarin and bridging with full dose enoxaparin is associated with a higher bleeding risk,6 while bridging with half dose enoxaparin is inconvenient and expensive. PVI can be safely performed on uninterrupted warfarin with therapeutic INR throughout the periprocedural period with less stroke and major hemorrhagic complications.7,8 This strategy is currently gaining wider acceptance and has been endorsed in the 2012 HRS/EHRA/ECAS expert consensus statement.10

The efficacy and rapid onset and offset of action of dabigatran make it an ideal candidate for periprocedural anticoagulation in PVI. Anticoagulant effects of dabigatran parallel its plasma concentrations. Onset of action is within 1 hour of oral administration, peak is within 2 to 3 hours, and terminal half-life is 12 to 17 hours. To minimize time spent with subtherapeutic anticoagulation, in our study, dabigatran was held for 1 to 2 doses before PVI and restarted immediately afterward. This strategy was associated with no cerebral thromboembolic complications and a similar incidence of major hemorrhagic events compared with warfarin. It is important to note that it is not the anticoagulant that causes spontaneous bleeding, but rather this is an inherent risk of the procedure. The concern is management of bleeding once it occurs, especially in the dabigatran group given the absence of a reversal agent. However, in the 3 patients in our study and in the 9 patients in the study by Lakireddy et al16 who did develop tamponade, bleeding was self-limited requiring no surgical intervention or hemodialysis for elimination of dabigatran.

**Intraprocedural Heparin Requirements and ACT Measurements**

Despite the minimal interruption of dabigatran for only 1 to 2 doses, intraprocedural heparin requirements to achieve the target ACT of 350 to 450 seconds were significantly higher compared with those on continuous warfarin group. Possible explanations of these findings include interaction between dabigatran and heparin, inadequacy of the ACT test with dabigatran use, or diminution of anticoagulation effects of dabigatran after holding 1 to 2 doses compared with continuous warfarin.

The fact that patients who held 1 dose of dabigatran before PVI had relatively less heparin requirements, earlier and more consistent achievement of target ACT, and higher mean ACT values compared with those who held dabigatran for 2 doses suggests that rapid elimination of dabigatran is the most likely explanation for the higher heparin requirements. If interactions between dabigatran and heparin or the ACT test were responsible, we would have expected higher heparin requirements and lower ACT in patients who held dabigatran for 1 dose compared with 2 doses as higher levels of the drug remain in the circulation leading to more interaction.

Our results suggest that heparin requirements are indirectly proportionate to the intensity of therapeutic oral anticoagulation at the time of PVI, with lower anticoagulation intensity after holding 1 to 2 doses of dabigatran compared with uninterrupted warfarin. Interestingly, intraprocedural heparin requirements in patients who held dabigatran for 1 to 2 doses were comparable with historical heparin needs reported in patients who underwent PVI with a subtherapeutic or normal INR after interruption of warfarin. Our current recommendation is to hold dabigatran for only 1 dose before PVI because this strategy was associated with more consistent achievement of target ACT without significant increase in hemorrhagic complications.

**Limitations**

This was not a randomized trial. A much larger randomized study would be required to detect any differences if present in thromboembolic and hemorrhagic events between patients on dabigatran and those on continuous warfarin, given the low incidence of complications with either strategy. The majority of our patients were younger than 75 years old with normal renal functions. Further studies are needed to assess safety of dabigatran for periprocedural anticoagulation in other patient populations. Unlike warfarin, it is currently impossible to confirm a patient’s compliance to dabigatran with a laboratory test. Transesophageal echocardiography was performed in patients who may have missed doses in the days to weeks before PVI. Nevertheless, in this study of our current practice, which included all patients on dabigatran, the results are encouraging and were not associated with higher complication rates.

**Conclusion**

There was no evidence of increased thromboembolic or hemorrhagic complications with use of dabigatran for periprocedural anticoagulation in patients undergoing AF ablation.
compared with uninterrupted warfarin therapy. Proper procedural techniques and vigilant monitoring of intraprocedural ACT are needed with use of dabigatran to avoid the inherent procedural risks. Larger studies are needed to confirm these findings and assess safety in subpopulations, including patients older than 75 and those with renal impairment.

Disclosures
None.

References

CLINICAL PERSPECTIVE
To our knowledge, our study is the largest to date to report on the use of dabigatran for periprocedural anticoagulation in patients undergoing periprocedural anticoagulation ablation compared with uninterrupted warfarin therapy. Warfarin has been the only effective oral anticoagulant available since 1950. Dabigatran has emerged as a safe and effective alternative to warfarin in patients with nonvalvular atrial fibrillation, offering new challenges and possibilities for minimizing perioperative thromboembolism and hemorrhage. The efficacy and rapid onset and offset of action of dabigatran make it an ideal candidate for periprocedural anticoagulation in pulmonary vein isolation. To minimize time spent with subtherapeutic anticoagulation, dabigatran 150 mg was held for only 1 or 2 doses before pulmonary vein isolation and restarted immediately afterward in the EP laboratory or as soon as the patient arrived to the nursing floor. Compared with warfarin, use of dabigatran was associated with no cerebral thromboembolic complications and a similarly low incidence of major hemorrhage that did not require surgical intervention or hemodialysis for elimination of dabigatran. Despite higher doses of intraprocedural heparin, the mean activated clotting time was significantly longer in patients who held dabigatran for 1 or 2 doses than those on warfarin. This is most likely because of lower anticoagulation intensity after holding 1 to 2 doses of dabigatran compared with uninterrupted warfarin. Proper procedural techniques and vigilant monitoring of intraprocedural activated clotting time are needed with use of dabigatran to avoid the inherent procedural risks. Our study provides valuable data to electrophysiologists given the evergrowing number of patients presenting for pulmonary vein isolation while on dabigatran.
Use of Dabigatran for Periprocedural Anticoagulation in Patients Undergoing Catheter Ablation for Atrial Fibrillation

Mohamed Bassiouney, Walid Saliba, John Rickard, Mingyuan Shao, Albert Sey, Mariam Diab, David O. Martin, Ayman Hussein, Maurice Khoury, Bernard Abi-Saleh, Samir Alam, Jay Sengupta, P. Peter Borek, Bryan Baranowski, Mark Niebauer, Thomas Callahan, Niraj Varma, Mina Chung, Patrick J. Tchou, Mohamed Kanj, Thomas Dresing, Bruce D. Lindsay and Oussama Wazni

_Circ Arrhythm Electrophysiol_. 2013;6:460-466; originally published online April 3, 2013; doi: 10.1161/CIRCEP.113.000320

_Circulation: Arrhythmia and Electrophysiology_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Copyright © 2013 American Heart Association, Inc. All rights reserved.
Print ISSN: 1941-3149. Online ISSN: 1941-3084

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circep.ahajournals.org/content/6/3/460

An erratum has been published regarding this article. Please see the attached page for:
/content/6/5/e79.full.pdf

Data Supplement (unedited) at:
http://circep.ahajournals.org/content/suppl/2013/04/03/CIRCEP.113.000320.DC1

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation: Arrhythmia and Electrophysiology_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation: Arrhythmia and Electrophysiology_ is online at:
http://circep.ahajournals.org//subscriptions/
In the article “Use of Dabigatran for Periprocedural Anticoagulation in Patients Undergoing Catheter Ablation for Atrial Fibrillation” by Bassiouny et al, which was published in the June 2013 issue (Circ Arrhythm Electrophysiol. 2013;6:460–466), corrections were needed.

In the Abstract, main text, and the Table 1 footnote, the acronym “INR” was incorrectly spelled out as “international normalization ration.” The correct expansion of “INR” is “international normalized ratio.”

The compositor apologizes for the error.

The online version of the article has been corrected.
Supplemental Figure 1. Bias reduction by propensity score matching