The number of patients undergoing catheter ablation for atrial fibrillation (AF) has been increasing year by year. As noted in the updated guideline (ACC/AHA/ESC) for the management of patients with AF,1 embolic stroke is one of the most serious complications of AF ablation procedures. A higher intensity of anticoagulation is required to reduce the risk of thrombus formation during ablation. The recent 2012 HRS/EHRA/ECAS expert consensus statement notes that uninterrupted warfarin is a potential alternative to bridging with low-molecular-weight heparin.2 In fact, in Japan, most of the large-volume centers adopt continuation of periprocedural warfarin in the therapeutic range. However, warfarin takes a long time to reach to its therapeutic range and there are some patients in whom it is difficult to control warfarin within the therapeutic range. Dabigatran, an oral direct thrombin inhibitor, was recently approved for the prevention of embolic stroke in patients with nonvalvular AF.3 Therefore, there has been an interest in taking advantage of dabigatran around the time of catheter ablation. Three reports that evaluated the safety of periprocedural use of dabigatran for AF ablation in comparison with warfarin have been recently published.4,4

In this issue of the Journal, Kaseno et al4 demonstrate that dabigatran at a dose of 110 mg twice daily was safe in AF ablation. In their study, 110 patients treated with dabigatran developed no symptomatic thromboembolic complications. No patients had pericardial tamponade, and minor bleeding was observed in only 5 patients. These observations suggest that dabigatran could be a safe alternative strategy. However, caution is needed when interpreting this study. First of all, as the authors acknowledge, up to 92% of the patients had a CHADS2 score of 1 or 0, indicating essentially low risk for both thromboembolic and bleeding complications. Together with the fact that the authors’ center is one of the largest-volume centers in Japan, with many experts for AF ablation, the observations cannot be wholly applicable to general AF ablation performed in medium- and low-volume centers. In addition, their study was retrospective and there was significant background inequality between the dabigatran and warfarin groups. For example, age was younger and left atrial dimension smaller in the dabigatran group. The number of patients having persistent AF was lower in the dabigatran group. Thus, their study was not one that demonstrates the superiority of dabigatran over warfarin.4

In contrast, important results from a multicenter prospective registry comparing the feasibility and safety of dabigatran with uninterrupted warfarin have been reported by Lakkireddy et al.5 In their analysis comparing 145 patients on uninterrupted warfarin with 145 patients taking dabigatran, the latter group had a significantly higher rate of major bleeding complications (9 patients, 6%), all of which were pericardial tamponade requiring drainage. Major bleeding (pericardial tamponade) was observed in only one patient (1%) in the warfarin group. The composite of bleeding and embolic complications was more frequently observed in the dabigatran group (23 patients, 16%) than in the warfarin group (9 patients, 6%, P=0.009). Based on these observations, Lakkireddy et al concluded that in patients undergoing AF ablation, continuation of dabigatran during the periprocedural period is associated with an increased risk of bleeding and a composite of bleeding or embolic complications compared with uninterrupted warfarin therapy.5

Why do these 2 studies4,4 showed distinctly different results? We should firstly review the pharmacologic characteristics of dabigatran. Dabigatran has a rapid onset of action, peaking at approximately 1 h. Its elimination half-life ranges from 12 to 14 h in patients with normal renal function. Lakkireddy et al discontinued dabigatran on the morning of the procedure.3 In other words, AF procedures were performed within approximately 1.5-fold of the elimination half-life, suggesting a significant residual pharmacodynamic effect. In this regard, Winkle et al6 recently demonstrated that periprocedural use of dabigatran caused no bleeding and thromboembolic complications until 30 days after the procedure. They discontinued dabigatran 36 h before ablation in patients whose estimated glomerular filtration rate (eGFR) was >60 ml · min⁻¹ · 1.73 m⁻². In patients whose eGFR ranged from 40 to 60 ml · min⁻¹ · 1.73 m⁻², dabigatran was stopped 48 h before ablation. In patients whose eGFR was <40 ml · min⁻¹ · 1.73 m⁻², it was stopped 60 h before ablation. Thus, when compared with the study by Lakkireddy et al,6 Winkle et al discontinued dabigatran earlier before the ablation procedure.6 The target range of the activated clotting time (ACT) during the ablation procedure is another important factor. Although Lakkireddy et al kept the ACT in the range of 300–400s,8 Winkle et al targeted an intraprocedural ACT of 225s.8 The timing of restarting dabigatran administration was also different. Lakkireddy et al resumed it within 3 h of hemostasis,5 whereas Winkle et al resumed it 22 h after the procedure.6 Taken together, it can be postulated that late discontinuation and/or early restarting of dabigatran and a higher

Can Dabigatran Be an Alternative Periprocedural Anticoagulation for Atrial Fibrillation Ablation?

Naohiko Takahashi, MD, PhD

The opinions expressed in this article are not necessarily those of the editors or of the Japanese Circulation Society.

Received June 18, 2012; accepted June 18, 2012; released online June 30, 2012

Department of Laboratory Examination and Diagnostics, Oita University Faculty of Medicine, Oita, Japan

Mailing address: Naohiko Takahashi, MD, PhD, Department of Laboratory Examination and Diagnostics, Faculty of Medicine, Oita University, 1-1 Idaigaoka, Yufu, Oita 879-5593, Japan. E-mail: takanao@oita-u.ac.jp


All rights are reserved to the Japanese Circulation Society. For permissions, please e-mail: cj@j-circ.or.jp
target range of intraprocedural ACT resulted in the increased risk of bleeding complications observed in the study by Lakkireddy et al.\(^5\)

In the report by Kaseno et al,\(^4\) the periprocedural protocol was almost equivalent to that of Lakkireddy et al (Figure). Nevertheless, no patients developed symptomatic thromboembolic or major bleeding complications, which appears worthy of praise. However, their protocol needs to become much safer by modification before applying it universally. Dabigatran is recommended to be discontinued at least 24–48 h before invasive procedures in subjects with normal renal function.\(^7\) A possible recommendation is earlier discontinuation of dabigatran (ie, at least 24 h before ablation). In any case, further studies are required to examine the optimal use of periprocedural dabigatran for AF ablation.

It should be emphasized that no evidence has been demonstrated that periprocedural dabigatran is safer than uninterrupted warfarin. Therefore, the number of patients treated with dabigatran for AF ablation should be limited and patients with obvious renal dysfunction should be excluded. Patients ≥75 years old may not be recommended. Younger patients with paroxysmal AF may be suitable. Activated partial thromboplastin time should be checked during dabigatran treatment.\(^8\) Finally, we should keep it in mind that there is not a specific acute reversal agent for dabigatran.

**Disclosure**

No conflict of interest.

---

**References**