Current Optimal Anticoagulation Regimen of Rivaroxaban in Atrial Fibrillation Catheter Ablation

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Atrial fibrillation (AF) is one of the major arrhythmias encountered in clinical practice. The prevalence of AF has increased along with the super-aging of society in Japan. It is anticipated that the number of people with AF will increase to more than 1,000,000 in 2030 in Japan. AF per se is not a fatal arrhythmia, but it can lead to severe complications such as systemic thromboembolisms and strokes, especially in patients with high CHADS2 scores. Anticoagulation therapy with warfarin has been used for the prevention of thromboembolisms in AF for more than 50 years. However, warfarin increases the bleeding risk, and requires frequent blood sampling to adjust the international normalized ratio of the prothrombin time. In addition, multiple drug and food interactions are also a major concern for warfarin use. Therefore, warfarin therapy seems to be complicated for some patients with AF and even for the physicians. The Fushimi registry, which was started in March 2011, revealed that the rate of prescription of anticoagulants (mostly warfarin) has been approximately 50%. In other words, half of the patients with AF do not receive anticoagulation therapy.

Four direct oral anticoagulants (DOAC) have been developed that inhibit thrombin or activated factor X (factor Xa). These drugs have a rapid onset and offset of action, no effect of vitamin K intake on their activity, and fewer drug interactions. The safety and efficacy of DOACs compared with warfarin has been confirmed in 4 large-scale clinical trials. DOACs have been widely prescribed for patients with nonvalvular AF (NVAF) in Japanese clinical practice.

Catheter ablation in patients with paroxysmal AF has become established with the development of the technology and improvement in the techniques. The number of catheter ablation procedures for AF has been increasing and spreading throughout the world. Preoperative anticoagulation therapy for at least 3 weeks and during the postoperative period for at least 2 months is recommended to prevent thromboembolism. Based on a previous observational study that evaluated the efficacy and safety of periprocedural anticoagulation therapy with DOACs

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

Received September 27, 2016; accepted September 28, 2016; released online October 8, 2016
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Figure. Suggested safety and reliable route of rivaroxaban for successful catheter ablation of atrial fibrillation.
as compared with warfarin, the use of DOACs for perioperative anticoagulation therapy in patients with AF has become prevalent in Japan. Indeed, the 4th survey of the Japanese Catheter Ablation Registry of AF (J-CARAF) revealed that among the anticoagulation therapies prescribed, 61.1% were DOACs and 37.5% were warfarin. VENTURE AF was the first prospective randomized trial designed to clarify the efficacy and safety of uninterrupted rivaroxaban and warfarin in patients with NVAF who underwent catheter ablation. There were no major bleeding events in the rivaroxaban group (0/123) and in 1 (1/121) in the warfarin group. As a result of the VENTURE AF trial, uninterrupted rivaroxaban is feasible for patients with AF who undergo catheter ablation. However, the patients in the rivaroxaban group were prescribed rivaroxaban at a dose of 20mg, which differs from the standard dose in Japan. The efficacy and safety of rivaroxaban during the perioperative period of catheter ablation might differ between Caucasians and East Asians. Further, catheter ablation of AF is an invasive procedure and might potentially cause severe complications. It is important to verify the evidence of the efficacy, safety, and risk of DOACs in patients with AF who are undergoing catheter ablation in Japan.

In this issue of the Journal, Okumura et al. investigate the efficacy and safety of rivaroxaban in Japanese patients with AF during the catheter ablation perioperative period. Their study prospectively registered NVAF patients scheduled for catheter ablation and who were receiving rivaroxaban (JACRE-R) or warfarin (JACRE-W) during the perioperative period and a follow-up evaluation was performed. The total population in the JACRE-R and JACRE-W cohorts was 1,118 and 204, respectively. The JACRE-R cohort had a very low incidence of the primary outcome (0.6%), including 2 cases of thromboembolism and 5 major bleeding incidents. They found that the incidence was significantly lower in the rivaroxaban group than in the warfarin group (0/123) and in 1 (1/121) in the warfarin group. As a result of the VENTURE AF trial, uninterrupted rivaroxaban is feasible for patients with AF who undergo catheter ablation. However, the patients in the rivaroxaban group were prescribed rivaroxaban at a dose of 20mg, which differs from the standard dose in Japan. The efficacy and safety of rivaroxaban during the perioperative period of catheter ablation might differ between Caucasians and East Asians. Further, catheter ablation of AF is an invasive procedure and might potentially cause severe complications. It is important to verify the evidence of the efficacy, safety, and risk of DOACs in patients with AF who are undergoing catheter ablation in Japan.

The JACRE cohort revealed that, in total, 41.9% of the patients received rivaroxaban on the day of the catheter ablation procedure, but among them only 10% (43/469) were uninterrupted administered rivaroxaban before the catheter ablation. Recently, uninterrupted dabigatran and apixaban during AF ablation procedures have been reported to show similar safety and efficacy as compared with uninterrupted warfarin by a retrospective analysis from a single center study. The occurrence of major bleeding complications during catheter ablation (i.e., cardiac tamponade) is unavoidable, even in experienced high-volume centers. The event rate of cardiac tamponade and pericardial effusions is very low, but uninterrupted DOACs might make bleeding uncontrollable because of the unavailability of neutralizing drugs. The majority of patients in the JACRE-R cohort were prescribed rivaroxaban in the morning of the day before and after the catheter ablation and it was interrupted in the morning of the day of the catheter ablation. Therefore, rivaroxaban just withheld on the morning of the catheter ablation session to avoid bleeding complications during the procedure is currently feasible and safe in Japan (Figure). We must keep in mind that AF ablation must ensure “safety first”.

It has been reported that andexanet alfa is effective for treating acute major bleeding associated with factor Xa inhibitors, including rivaroxaban and apixaban. A bolus and infusion of andexanet immediately reduces both the unbound fraction of the plasma level of the factor Xa inhibitor and anti-factor Xa activity without any serious adverse effects. Although andexanet alfa is currently unavailable in Japan, an antibody for factor Xa anticoagulants might affect the anticoagulation therapy regimen during the ablation procedure in patients with NVAF in the near future.

Acknowledgments
We thank Mr John Martin for his linguistic assistance.

References