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Original Article

# Nationwide survey of catheter ablation for atrial fibrillation: The Japanese catheter ablation registry of atrial fibrillation (J-CARAF)–A report on periprocedural oral anticoagulants

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ABSTRACT

*Background:* Catheter ablation has become an established therapy for the treatment of atrial fibrillation (AF). To obtain a perspective on the current status of this therapy in Japan, the Japanese Heart Rhythm Society (JHRS) conducted a nationwide survey, the Japanese Catheter Ablation Registry of Atrial Fibrillation (J-CARAF). In this study, we focused on whether periprocedural use of novel oral anticoagulants (NOACs) was related with excessive thromboembolic or bleeding complications.

*Methods:* Using an online questionnaire, JHRS requested electrophysiology centers in Japan to register the data of patients who underwent AF ablations in September 2011, March 2012, and September 2012. We compared the clinical profiles and ablation data, including the incidence of complications among patients in whom warfarin, a NOAC or neither was used as a periprocedural anticoagulant.

*Results:* A total of 179 centers submitted data relating to 3373 patients (62.2 ± 10.6 years). Paroxysmal atrial fibrillation (PAF) was observed in 64.4% of patients. Warfarin, as a periprocedural oral anticoagulant, was used by 53.6% (1808/3373) of patients. A NOAC was given to 541 subjects (dabigatran: 504 [16.1%], rivaroxaban: 37 [1.1%]). In the remaining 1024 patients (30.4%), no periprocedural oral anticoagulants (OACs) were used. The proportion of PAF in warfarin-treated patients (61.1%) was significantly lower than that in NOAC-treated patients (70.1%, $p < 0.01$) or in patients not treated with an OAC (67.4%, $p < 0.01$). Patients treated with uninterrupted warfarin therapy were associated with significantly higher CHA2DS2-VASc scores. A total of 158 complications occurred in 151 subjects (4.5%). The incidence of complications in NOAC-treated patients (14/541 [2.6%]) was lower than that in patients receiving uninterrupted warfarin therapy (4.8%, $p < 0.05$). The incidence of pericardial effusion in NOAC-treated patients (0.7%) was lower than in warfarin-treated patients (2.6%, $p < 0.05$). The difference in the periprocedural anticoagulant strategy was not related to the frequency of other bleeding events. Cerebral infarction occurred in one patient from each patient group.

*Conclusions:* Our results suggest that NOACs are safe for use as substitutes for warfarin without causing excessive increases in the rates of thromboembolic or bleeding complications.



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## 1. Introduction

Catheter ablation has become a potent and feasible therapy for atrial fibrillation (AF). Many clinical studies [1–3] have confirmed the safety, mid-term and long-term effectiveness, and cost-effectiveness of this procedure. However, as technological and technical innovations are continuously being introduced into practice, constant effort is necessary to confirm whether catheter ablation, now carried out worldwide, is performed in accordance with international standards [4]. The Japanese Heart Rhythm Society (JHRS) conducted a nationwide registry of patients who underwent catheter ablation for AF: the Japanese Catheter Ablation Registry of Atrial Fibrillation (J-CARAF) [5,6].

Many studies have supported the view that uninterrupted warfarin therapy is superior to interrupted anticoagulation therapy with respect to intra- and post-procedural thromboembolic and bleeding events [7–10]. Additionally, several recent studies have suggested that novel oral anticoagulants (NOACs) could be used a substitute for warfarin to maintain anticoagulant management during AF ablation [11–15]. In this study, we focused on the use of NOACs and warfarin. The aim of this analysis was to assess the safety and feasibility of the use of NOACs as a periprocedural anticoagulant.

## 2. Methods

The method of this survey has been reported previously [5]. In short, the survey was performed retrospectively using an online questionnaire. JHRS members were notified by e-mail, and data relating to patient background, methods of pulmonary vein isolation and related techniques, complications, and pre- and post-procedural pharmacological treatments were collected for AF ablation sessions performed in September 2011, May 2012, and September 2012. Patient data included age, gender, previous AF ablation, AF type (paroxysmal [PAF], persistent, or long-standing [LS] persistent), thromboembolism risk factors, and echocardiographic parameters. When warfarin or a NOAC was intentionally continued on the day of, or until the day before, the index AF ablation was performed, warfarin or a NOAC was considered to have been used periprocedurally.

We preliminarily compared clinical outcomes between patients treated with dabigatran or rivaroxaban and found no apparent differences in the incidence or type of complications. Because the number of subjects treated with rivaroxaban included in this study was small, we collectively analyzed the data from patients treated with any NOAC.

The continuous variables with a normal distribution were expressed as mean ± SD. Comparison of the continuous variables among three study groups was performed by one-way analysis of variance with a post hoc Bonferroni test. Categorical variables were compared using Tukey's test. A $p < 0.05$ was considered statistically significant.

## 3. Results

### 3.1. General observations

In total, 235 institutes responded to the survey, and 179 of these reported data from 3373 AF ablation sessions. The average patient age was 62.2 ± 10.6 years, and 76.1% (2587) were male. Of all sessions, 77.4% were first AF ablation sessions. Patients with PAF constituted 64.4% ($n=2173$), while persistent and LS-persistent AF constituted 21.7% and 13.8% ($n=733$ and 467) of all patients, respectively.

### 3.2. Periprocedural anticoagulant strategies

As a periprocedural OAC, warfarin was given to 53.6% of patients (1808/3373). Dabigatran and rivaroxaban were used in 504 (14.9%) and 37 subjects (1.1%), respectively. In total, 541 patients (16.0%) took a NOAC until the day before AF ablation or until a time that physicians considered appropriate. In the remaining 1024 patients (30.4%), an OAC was fully discontinued before AF ablation or was not given at all.

### 3.3. Comparison of patient profiles

As shown in Table 1, the proportion of PAF in those treated with warfarin (61.1%) was significantly smaller than in those treated with NOAC (70.1%, $p < 0.01$) or in those receiving no OAC treatment (67.4%, $p < 0.01$). Lone AF was less frequent in patients receiving uninterrupted warfarin treatment (20.2%) than in those taking a NOAC (25.3%) or no OAC (26.1%). The CHA2DS2-VASc score was significantly greater in warfarin-treated patients ($p < 0.0001$) than in patients treated with a NOAC or no OAC.

### 3.4. Outcome events

A total of 158 complications occurred in 151 subjects (4.5%). The number of each type of event is shown in Table 2. As shown in Fig. 1, the incidence of complications in NOAC-treated patients (2.6%, 14/541) was lower than that in the uninterrupted warfarin group (4.8%, $p < 0.05$). Pericardial effusion occurred in 75 of 151 subjects (2.2% of 3373). Incidence of pericardial effusion in NOAC-treated patients (0.7%, Fig. 1) was lower than that in warfarin-treated patients (2.6%, $p < 0.05$). Other bleeding events, namely hemothorax, hematoma at the puncture site, and retroperitoneal hematoma, were seen in 12 (1.2% of 1024), 15 (0.8% of 1808), and 3 (0.6% of 541) patients from each study group, respectively. There was no significant difference in the incidence of bleeding events.

**Table 1**
Comparison of clinical profiles and ablation data among the patients the three study groups.

| No. | No OAC | Warfarin | NOAC | *p* Value | | |
|---|---|---|---|---|---|---|
| | 1024 | 1808 | 541 | No OAC vs. warfarin | Warfarin vs. NOAC | No OAC vs. NOAC |
| Age/year | 61.6 ± 11.0 | 63.0 ± 10.2 | 60.4 ± 10.8 | < 0.001 | < 0.0001 | |
| PAF | 690 (67.4%) | 1104 (61.1%) | 379 (70.1%) | < 0.01 | < 0.01 | |
| Lone AF | 267 (26.1%) | 366 (20.2%) | 137 (25.3%) | < 0.01 | < 0.05 | |
| CHA2DS2-VASc score | 1.63 ± 1.41 | 1.87 ± 1.47 | 1.51 ± 1.32 | < 0.0001 | < 0.0001 | |
| LVEF/% | 64.5 ± 9.7 | 62.9 ± 10.2 | 65.0 ± 8.8 | < 0.0001 | < 0.0001 | |
| LAD/mm | 40.6 ± 7.6 | 40.6 ± 6.5 | 39.7 ± 6.3 | | < 0.01 | < 0.05 |
| 1st ablation | 771 (75.3%) | 1386 (76.7%) | 453 (83.7%) | | < 0.01 | < 0.01 |
| Procedure time/h | 3.68 ± 1.43 | 3.49 ± 1.20 | 3.27 ± 1.24 | < 0.001 | < 0.001 | < 0.0001 |

OAC: oral anticoagulant, NOAC: novel oral anticoagulant, LVEF: left ventricular ejection fraction, and LAD: left atrial diameter

**Table 2**
Number of complications in three patient groups.

| No. of patients | No OAC<br>102 | Warfarin<br>1808 | NOAC<br>541 | Total<br>3373 |
|---|---|---|---|---|
| PE (no drainage) | 11 | 18 | 3 | 32 |
| PE (drainage) | 13 | 29 | 1* | 43 |
| Transient AVB | 0 | 3 | 1 | 4 |
| AVB+temporary pacing | 0 | 0 | 0 | 0 |
| AVB+permanent pacemaker | 0 | 0 | 0 | 0 |
| Sinus arrest | 5 | 5 | 1 | 11 |
| TIA | 1 | 0 | 0 | 1 |
| Cerebral infarction | 1 | 1 | 1 | 3 |
| Asymptomatic cerebral infarction (MRI) | 1 | 4 | 1 | 6 |
| Pneumothorax | 0 | 1 | 0 | 1 |
| Hemothorax | 0 | 1 | 0 | 1 |
| Prolonged phrenic nerve paresthesia | 1 | 3 | 1 | 5 |
| Air embolism | 2 | 3 | 0 | 5 |
| Pulmonary vein stenosis | 0 | 0 | 0 | 0 |
| Arteriovenous fistula | 1 | 0 | 2 | 3 |
| Hematoma at the puncture site | 12 | 14 | 3 | 29 |
| Retroperitoneal hematoma | 0 | 0 | 0 | 0 |
| Pseudoaneurysm | 1 | 3 | 0 | 4 |
| Atrioesophageal fistula | 0 | 1 | 0 | 1 |
| Gastroparesis | 3 | 4 | 1 | 8 |
| Others | 0 | 1 | 0 | 1 |
| Death | 0 | 0 | 0 | 0 |
| Total/no. of incidents | 52 | 91 | 15* | 158 |
| No. of patients | 50 (4.9%) | 87 (4.8%) | 14 (2.6%) | 151 (4.5%) |

* $p < 0.05$ vs. warfarin, OAC: oral anticoagulant, NOAC: novel oral anticoagulant, AVB: atrioventricular block, PE: pericardial effusion, and TIA: transient ischemic attack.

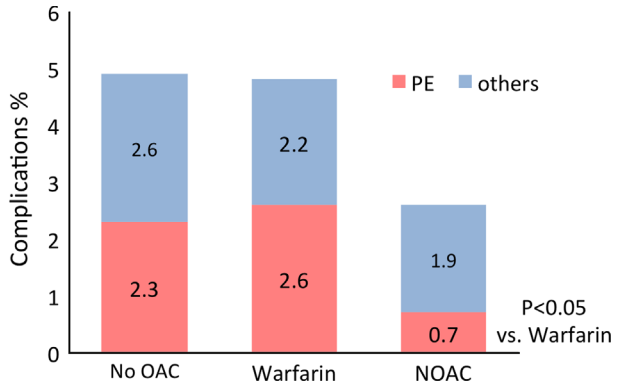


**Fig. 1.** Comparison of the incidence of complications. Overall complications were less frequent in patients treated with NOAC than in patients receiving uninterrupted warfarin treatment ($p < 0.05$). Incidence of pericardial effusion (PE) was also lower in patients treated with NOAC than in patients taking warfarin.

Cerebral infarction occurred in only one patient from each study group. One patient in the no OAC group presented TIA. Thus, the incidence of ischemic stroke was invariably low for any type of periprocedural anticoagulant strategy.

## 4. Discussion

### 4.1. Findings

The major findings of the present study are: (1) approximately 70% of AF ablation sessions were performed with periprocedural OAC treatment, (2) an NOAC was used in 25% of patients who had undergone AF ablation with periprocedural OAC treatment, (3) the uninterrupted warfarin group was characterized by a lower proportion of PAF, lone AF, and longer procedure times, and (4) the incidence of acute complications in NOAC-treated patients was lower than that in the uninterrupted warfarin patients.

### 4.2. Earlier studies

In an earlier non-randomized study [16], the perioperative use of dabigatran was related with a higher risk of bleeding or thromboembolic events than the uninterrupted use of warfarin. This study suggested that the timing of discontinuation or re-administration of dabigatran and interaction with heparin might be related with excessive or insufficient anticoagulant effects. In another randomized study by Kim et al. [12], dabigatran discontinued for 24 h before AF ablation was as safe and effective in avoiding adverse events during and after AF ablation as uninterrupted warfarin treatment. A recent meta-analysis [11] that analyzed 3841 cases from 11 studies revealed that cardiac tamponade in 1.4% of patients treated with dabigatran and in 1.1% of patients treated with warfarin ($p$=not significant). Thromboembolic events occurred in 0.6% of dabigatran-treated patients and 0.1% of warfarin-treated patients ($p$=0.12).

### 4.3. Interpretation of the present results

In the present study, thromboembolic or hemorrhagic events did not show any apparent increase in NOAC-treated patients. Overall complications and pericardial effusion were significantly less frequent in NOAC-treated patients than uninterrupted warfarin-treated patients. Although not statistically significant, hematoma at the site of puncture was relatively less frequent in patients treated with a NOAC. Each NOAC has a shorter half-life than warfarin. Therefore, the anticoagulant action of the NOACs may have all but disappeared during the procedure. The few pericardial effusion and bleeding complications may be attributable in part to this assumption.

Furthermore, differences in clinical profiles between patient groups may explain the apparent disparity of complications between the groups. Higher CHA2DS2-VASc scores, a smaller proportion of lone AF and PAF, and prolonged procedure times might indicate that warfarin was used preferentially in patients with more complex and complicated profiles. Taking the diverse

clinical features among the patient groups into consideration, it cannot be concluded that less frequent complications suggest an advantage of NOACs over warfarin as a periprocedural anticoagulant therapy. Instead, it seems rational to consider that NOACs are safe substitutes for warfarin.

### 4.4. Limitations

The present data were retrospectively collected from a large number of centers. We therefore assumed that the results could offer a broad perspective of anticoagulant management immediately before and during AF ablation. On the other hand, because thrombotic and bleeding events involve multiple factors, such as the combined use of antiplatelet and heparin therapies, it is not easy to compare the merits and demerits of different anticoagulant strategies in a non-randomized retrospective study. The prevalence of asymptomatic cerebral infarction might have been underestimated by the fact that only a limited proportion of patients were examined by MRI. Moreover, the diagnosis of complications was entrusted to each physician. Special care must be taken to interpret the present results, which might have been biased by the limitations inherent in observational studies.

In addition, detailed data of when an anticoagulant was given and for how long it remained in each patient were not included in the analysis. The potential of the present study to compare the usefulness of each anticoagulant is inevitably limited.

## 5. Conclusions

NOACs have come to be used as a feasible periprocedural anticoagulant for AF ablation. Our results suggest that NOACs are safe substitutes for warfarin without an excessive increase in either thromboembolic or bleeding complications.

## Conflict of interest

All authors have no conflicts of interest to declare.

## Acknowledgment

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