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Original article

Evaluation of safety and efficacy of periprocedural use of rivaroxaban and apixaban in catheter ablation for atrial fibrillation

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ABSTRACT

Background: We previously reported that dabigatran increased the risk of microthromboembolism and hemopericardium compared with warfarin. The safety of non-vitamin-K-antagonist oral anticoagulants (NOACs) in the periprocedural use of atrial fibrillation (AF) ablation is controversial. This study aimed to compare the incidence of asymptomatic cerebral microthromboembolism and hemopericardium in AF ablation among periprocedural use of rivaroxaban, apixaban, and warfarin.

Methods and Results: This study was a prospective, randomized registry. Patients taking NOACs upon visiting our hospital were randomly assigned into 2 groups; rivaroxaban and apixaban. Warfarin was continued in patients taking warfarin. Asymptomatic cerebral microthromboembolism was evaluated by magnetic resonance imaging on the day after the ablation procedure. In 176 consecutive patients (101 paroxysmal, and 75 persistent AF), rivaroxaban was used in 55, apixaban in 51, and warfarin in 70. There were no symptomatic cerebral infarctions in this study. Asymptomatic cerebral microthromboembolism was detected in 32 (18.4%) patients; nine (16.4%) with rivaroxaban, 10 (20%, $p = 0.80$; vs. rivaroxaban) with apixaban, and 13 (18.8%, $p = 0.81$; vs. rivaroxaban) with warfarin. Hemopericardium occurred in 5 (2.8%) patients; 2 with rivaroxaban, 1 with apixaban ($p = 1.0$; vs. rivaroxaban), and 2 with warfarin ($p = 1.0$; vs. rivaroxaban). In multivariate analysis, concomitant coronary angiography ($p < 0.05$, odds ratio 5.73) was a predictor of cerebral thromboembolism.

Conclusions: The incidence of asymptomatic cerebral microthromboembolism and hemopericardium in AF ablation is similar among the periprocedural use of rivaroxaban, apixaban, and warfarin.

Introduction

The prevalence of atrial fibrillation (AF) increases with advanced age and is associated with higher mortality and morbidity [1–5]. Thromboembolic events coexisting with AF are commonly related to congestive heart failure, hypertension, advanced age, diabetes mellitus, a history of stroke or transient ischemic attack, vascular disease, and female sex [6–8]. Warfarin is an essential agent in the prevention of thromboembolic events for patients with AF [9–11]. More recently, the safety and efficacy of non-vitamin-K-antagonist oral anticoagulants (NOACs), such as dabigatran, rivaroxaban, and apixaban, have been reported in clinical use [12–14].

Catheter ablation is an effective approach for the management of AF [15–21]. Pulmonary vein isolation (PVI) is the most common curative therapy for AF [22,23], but the outcome of PVI alone for patients with persistent AF is suboptimal [24–26]. Nademanee et al. described a different approach for AF ablation. This strategy involved identifying the target "substrate" site using electro-anatomical mapping on complex fractionated atrial electrograms (CFAEs) [21,27,28]. PVI is not required with this approach, and AF ablation guided solely by CFAE (CFAE ablation) results in a high rate of success in maintaining sinus rhythm in patients with paroxysmal and persistent AF. Results of the study by Nademanee et al. are similar to those in our previous studies [29,30], but not by others [20,31]. Therefore, the role of CFAE ablation in treating AF patients remains controversial.

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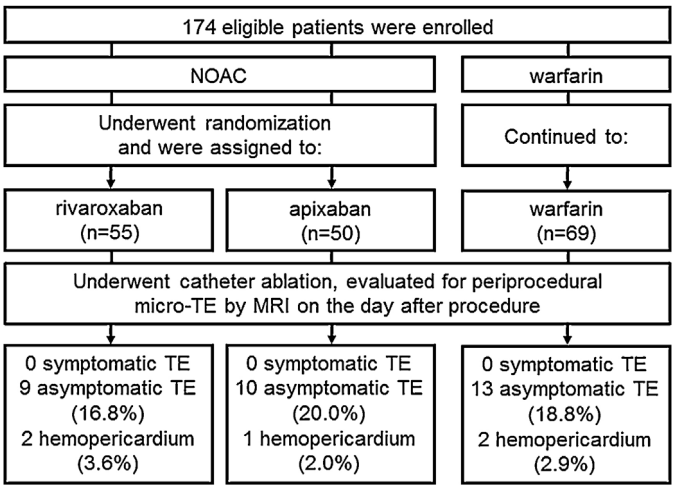

Fig. 1. Study design. A flow diagram shows enrollment to evaluation of periprocedural microthromboembolism by MRI on the day after procedure.
NOAC, non-vitamin-K-antagonist oral anticoagulant; TE, thromboembolism; MRI, magnetic resonance imaging.

Cerebral thromboembolism after PVI occurs in 2% to 14% of patients [32–36]. We reported that the incidence of asymptomatic cerebral microthromboembolism after AF ablation solely guided by CFAE was 7.0% in 2011 [37]. Several studies have shown that uninterrupted periprocedural use of warfarin decreases cerebral thromboembolic events in catheter ablation for AF without increasing the risk of hemorrhagic complications [11,38–41].

From 2011, dabigatran was available for preventing thromboembolic events for patients with AF in Japan. We reported that asymptomatic microthromboembolism occurred in 10.0% of the warfarin group and 26.7% of the dabigatran group, and the incidence of hemopericardium treated with pericardiocentesis was 2.5% in the warfarin group and 11.1% in the dabigatran group [42]. Dabigatran increases the risk of microthromboembolism and hemopericardium compared with warfarin. However, there is controversy about the safety of NOACs in the periprocedural use of AF ablation [43–45].

Therefore we compared the incidence of hemopericardium and asymptomatic cerebral microthromboembolism after AF ablation among periprocedural use of warfarin, rivaroxaban, and apixaban using cerebral magnetic resonance imaging (MRI), including diffusion-weighted and T2-weighted MRI (DW- and T2W-MRI).

Methods

Data sources

This prospective, randomized study was performed from March 2013 to December 2014 in Kagoshima University Hospital. All of the patients provided written informed consent for the procedure, and the institutional ethics committee of Kagoshima University Hospital approved the study protocol.

Study population

This study included 176 consecutive patients (101 with paroxysmal AF and 75 with persistent AF, including 21 with long-standing persistent AF) who underwent AF ablation guided by CFAE with ($n = 104$) or without ($n = 72$) PVI. Patients taking NOACs upon visiting our hospital were randomly assigned into two groups: rivaroxaban ($n = 55$) and apixaban ($n = 51$) (Fig. 1). This randomization was stratified by type of AF and sex using the table of random numbers. Warfarin was continued in patients who were taking warfarin ($n = 70$). Rivaroxaban was administered in the evening and continued, and apixaban was interrupted only on the morning of the procedure. Two patients with paroxysmal AF (1 patient with apixaban, 1 with warfarin) who did not undergo MRI because of the patients' condition were excluded. The other patients underwent evaluation for cerebral microthromboembolism on the day after the ablation procedure using MRI. An example of CFAE is shown in Fig. 2a and CARTO maps of CFAE ablation with PVI are shown in Fig. 2b and without PVI in Fig. 2c.

Ablation procedure

All of the patients underwent a blood examination, chest X-ray, electrocardiography, brachial-ankle pulse wave velocity, and transthoracic and transesophageal echocardiography prior to AF ablation. We confirmed that there was no thrombus in the left atrium (LA) and LA appendage in the day or 1 day before the procedure by transesophageal echocardiography.

We decided on the AF ablation strategy as follows. We performed a double-blind study to compare AF ablation guided

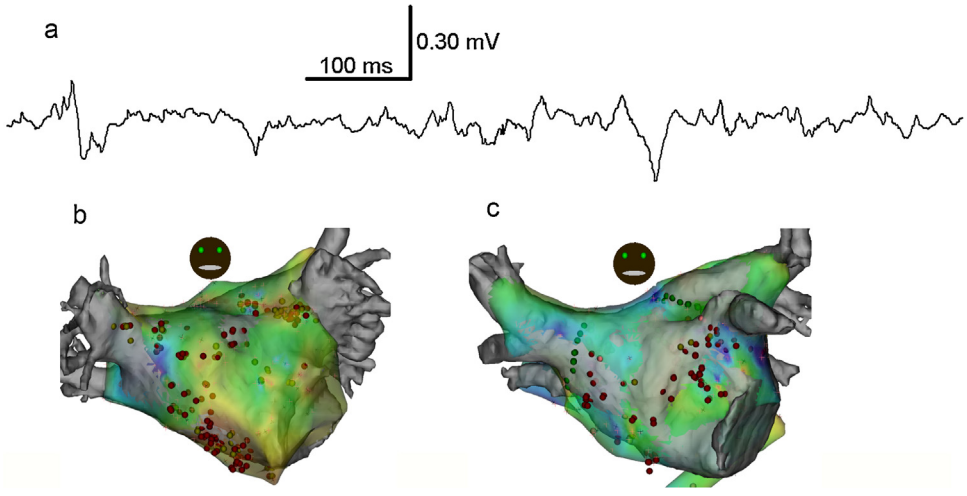

Fig. 2. Examples of CFAE and CARTO maps of 2 cases. (a) Example of CFAE. (b) Ablation guided by CFAE without pulmonary vein isolation (PVI). (c) CFAE ablation combined with PVI in the session.
CFAE, complex fractionated atrial electrograms.

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