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Original article

A cost-utility analysis for catheter ablation of atrial fibrillation in combination with warfarin and dabigatran based on the $CHADS_2$ score in Japan

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ABSTRACT

Background: We aimed to clarify the cost-effectiveness of an expensive combination therapy for atrial fibrillation (AF) using both catheter ablation and dabigatran compared with warfarin at each $CHADS_2$ score for patients in Japan.

Methods: A Markov model was constructed to analyze costs and quality-adjusted life years associated with AF therapeutic options with a time horizon of 10 years. The target population was 60-year-old patients with paroxysmal AF. The indication for anticoagulation was determined according to the Japanese guideline. Anticoagulation-related data were derived from the RE-LY study and the AF recurrence rate was set at 2.7% per month during the first 12 months and at 0.40% per month afterwards. Stroke risk was determined according to AF recurrence, anticoagulation, and $CHADS_2$ score. The risks for stroke recurrence and stroke death were also considered. Costs were calculated from the healthcare payer's perspective, and only direct medical costs were included.

Results: Warfarin was the most preferred option for patients with a $CHADS_2$ score of 0 from a health economics aspect. Ablation under warfarin was preferred for a $CHADS_2$ score of 1–3, while ablation under dabigatran was preferred for a $CHADS_2$ score $\geq$4. The quality of life score for AF had the largest impact on the incremental cost-effectiveness ratios in the analysis between the anticoagulation arm and the anticoagulation + ablation arm for a $CHADS_2$ score of 2. Within the range of the Japanese willingness-to-pay threshold (¥5,000,000), the ablation + warfarin arm became the best option with its probability of 81.7% for a $CHADS_2$ score of 2; the dabigatran + ablation arm was the most preferred option with its probability of 56.1% for a $CHADS_2$ score of 4.

Conclusions: Ablation under dabigatran therapy is an expensive therapeutic option, but it might benefit patients with a low quality of life and a high $CHADS_2$ score.

Introduction

Risk reduction for atrial fibrillation (AF)-related emboli and hemorrhages is important in terms of its clinical significance and from a socio-economic perspective, because the mean cost of AF-related hospitalization is increasing globally, even though the associated hospital mortality is decreasing [1]. The increased costs result from AF's not only increasing ischemic stroke-related costs by 20% [2] but also increasing hemorrhage-related costs due to

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anticoagulation therapy; in France, the estimated costs are €3,601 for gastrointestinal bleeding and €7,311 for intracranial bleeding [3]. Under these circumstances, catheter ablation for treating AF plays an important role in reducing clinical risks. In fact, the clinical risk–benefit ratio favors suspending oral anticoagulants after successful AF ablation, even in patients with a high risk of thromboembolism development [4]. From an economic standpoint, the incremental cost-effectiveness ratio (ICER) of catheter ablation compared with that for anti-arrhythmic drug use is about £7,763 for each additional quality-adjusted life year (QALY) in the United Kingdom, suggesting that catheter ablation is cost-effective for treating paroxysmal AF [5]. In the USA, catheter ablation is associated with $8,539 in higher costs, 0.033 fewer strokes, and 0.144 more QALYs over a 5-year time horizon compared with therapy with anti-arrhythmic drugs [6]. Even in persistent AF, with 49% sinus rhythm maintenance after 1.65 catheter ablation procedures, it is cost-effective in patients at risk of stroke [7]. With technical developments in catheter ablation, the indications for its use have broadened. The calculated costs for the procedure corresponded to the costs of medical therapy for 3.8–14.3 years in Japan in 2011 [8], and the procedural costs tend to continue increasing. In addition, the choice of anticoagulation therapy in Japan has also widened based on the emergence of non-vitamin K antagonist oral anticoagulants (NOACs), such as dabigatran, rivaroxaban, apixaban, and edoxaban. Their efficacies (primarily compared with that of warfarin) have been proven in large cohort studies [9]. Because of the challenges in maintaining a therapeutic range with warfarin, a hypothetical 70-year-old man is estimated to lose 7.4 days of life due to poor warfarin control and gain 4.0 days with its average control [10]. On the contrary, in exchange for their high costs, NOACs can be easily administered to patients without the necessity of regular monitoring. Thus, there is a broad consensus that NOACs are cost-effective compared with warfarin or aspirin [11,12]; however, the preferred dabigatran to use in combination with catheter ablation from an economic perspective has not been well established.

Therefore, in this study, we conducted a cost-utility analysis of anticoagulants and ablation therapy in AF treatment in Japan. We aimed to elucidate the cost-effectiveness of the expensive combination of catheter ablation under dabigatran with respect to stroke risk based on the $CHADS_2$ score [13].

Materials and methods

This study was approved by our Institutional Review Board based on the ethical guidelines of the Declaration of Helsinki. The requirement for informed consent was waived due to the nature of the study.

Decision model

Our target population was 60-year-old patients with paroxysmal AF who were not at risk of natural death, given that the mean age of patients receiving catheter ablation was reported as 62 years [14]. A Markov model was constructed to determine the expected costs of treatment and QALYs. A schematic of the model is shown in Fig. 1. The model contained the therapeutic decision for catheter ablation and five health states: normal sinus rhythm (NSR), AF, stroke, post-stroke, and death state. Patients who underwent catheter ablation [the ablation (+) arm] were initially allocated to the NSR state and were transferred to the AF state if AF recurred after ablation. All patients in the ablation (−) arm were allocated to the AF state. For both arms, patients with a $CHADS_2$ score of ≥1 were administered either dabigatran (150 mg twice daily) or therapeutic warfarin according to the Japanese guideline [15]. All patients in the ablation (+) arm took anticoagulants for 6 months

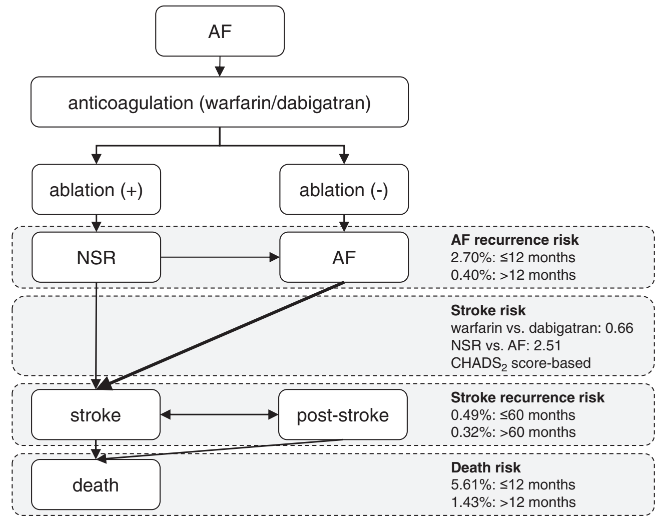

Fig. 1. Decision model. The structure of Markov state-transition model and major risks for each state are shown. Patients underwent anticoagulation with either warfarin or dabigatran and decided whether to undergo catheter ablation. Patients receiving ablation (ablation [+]) were allocated to the normal sinus rhythm (NSR) state and transferred to the atrial fibrillation (AF) state based on AF recurrence. The risk of a stroke was determined according to anticoagulation, rhythm state, and $CHADS_2$ score. Patients experiencing stroke were transferred to the post-stroke state 12 months after stroke onset. The risks for the repetitive stroke attack and death were concerned. The time horizon was set to 10 years.

periprocedurally regardless of $CHADS_2$ score. Anticoagulants were discontinued only when patients with a $CHADS_2$ score of ≤1 maintained the NSR state. Patients were transferred to the stroke state at stroke onset, to the post-stroke state 12 months after stroke onset, and to the death state on stroke-related death. One cycle of the Markov model was set to one month, reflecting the shortest period for which data were collected. In the base-case analysis, the time horizon was set to 10 years. The discount rate was set to 3% per annum for both costs and outcomes.

Transition probability

The probabilities for transitioning from one state in the model to the others were derived from epidemiological data shown in Table 1. The probability of AF recurrence after catheter ablation, which allocated patients from the NSR state to the AF state, was 2.7% per month within 12 months after catheter ablation [16] and 0.40% per month thereafter [16,17]. The probability of stroke varied based on state, medication, and $CHADS_2$ score [13] ($CHADS_2$: 0 = 0.045%/months, 1 = 0.078, 2 = 0.129, 3 = 0.224, 4 = 0.519, 5 = 0.330, 6 = 0.624). The follow-up data of NIPPON DATA 80 showed that patients with AF had a 2.51-fold greater stroke incidence compared with that for patients with NSR [18]. We therefore defined the relative risk for a stroke between the NSR state and the AF state as 2.51, since the stroke risk for patients with AF after successful ablation did not differ from that for patients without AF, regardless of $CHADS_2$ score [4,19,20]. A relative risk of 0.66 was used for the stroke risk between warfarin and 300 mg of dabigatran based on the results of the RE-LY study [21]. Since patients with a previous history of stroke were likely to have a repeat stroke, data from the Akita Stroke registry showed that the probability of stroke recurrence was 0.49% per month within the first five years after stroke onset and 0.32% per month thereafter [22]. The monthly probability of death from stroke was set at 5.61% per month during the first 12 months after stroke onset and 1.43% per month thereafter [23].