

Editorial



Benefit, Risk and Cost in Oral Anticoagulation for Stroke Prevention: Is It the Third Factor?

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Conflict of Interest

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► See the article "Cost-Effectiveness of Rivaroxaban Compared to Warfarin for Stroke Prevention in Atrial Fibrillation" in volume 49 on page 252.

Phase III trials-based data demonstrated that the relative efficacy and safety of non-vitamin K antagonist oral anticoagulants (NOACs) for stroke prevention was consistent across a wide range of patients with atrial fibrillation (AF).¹⁾ Thus, NOACs are an alternative to warfarin for preventing thromboembolism in patients with AF, and has been widely prescribed.²⁾ In Korea, although reimbursement has been covered by the medical insurance system since 2015 for patients with CHA₂DS₂-VASc scores ≥ 2 , the cost still may have an impact on clinical practice as well as patients' preferences. Therefore, it is necessary to understand the pharmacoeconomical evidence, in order to improve our healthcare system beyond patient outcomes.

Cost-effectiveness analysis is used to compare 2 or more medicines that are not exactly equivalent in terms of dose or therapeutic effect, and can reveal the trade-offs involved in choosing among alternative interventions.^{3,4)} There are many publications about the cost-effectiveness of NOACs vs. warfarin for stroke prevention in patients with AF. Shah et al.⁵⁾ reported that all the NOACs compared were more effective than adjusted-dose warfarin. Their model showed that apixaban was the most effective anticoagulant in a general AF population, and it had an incremental cost-effectiveness ratio of less than \$50,000 per quality-adjusted life years (QALYs). For those with higher stroke risk (CHADS₂ ≥ 3), dabigatran was the most cost-effective treatment option.⁵⁾ Harrington et al.⁶⁾ demonstrated that in patients with nonvalvular AF and an increased risk of stroke, apixaban 5 mg, dabigatran 150 mg, and rivaroxaban 20 mg were all cost-effective alternatives to warfarin. The cost-effectiveness of NOACs was dependent on therapy pricing in the United States, and neurological events associated with rivaroxaban 20 mg. Lee et al.⁷⁾ showed that rivaroxaban therapy may be a cost-effective alternative to adjusted-dose warfarin for stroke prevention in AF using the Markov model. However, this data was assessed in a U.S. cohort of AF patients who were 65 years old and at high-risk for stroke.

Kim et al.⁸⁾ showed that rivaroxaban may be a cost-effective alternative to warfarin in Korean patients with AF. Patients with rivaroxaban required an additional cost of \$3,735, but gained an additional 0.4 QALYs over a lifetime, resulting in an incremental cost-effectiveness ratio of \$9,707 per QALY. The probability of rivaroxaban remained cost-effective at willingness-to-pay thresholds of \$9,707 per QALY, in a Monte Carlo simulation.⁸⁾

This study has several limitations: 1) The use of NOACs including rivaroxaban was extremely low, and 2) the events were analyzed using 2012–2014 data from the Health Insurance Review and Assessment Service (HIRA) of the Republic of Korea, which do not fully reflect the efficacy and safety of the current real world. HIRA data could not provide HAS-BLED bleeding risk scores because essential factors such as abnormal liver function, abnormal renal function, and labile International Normalized Ratios were not included in the HIRA dataset. In addition, time in therapeutic range for patients who took warfarin could not be assessed.

Adherence, which was not evaluated in this study, is also an important issue in patients using oral anticoagulants. Recently, Desteghe et al.⁹⁾ found that telemonitoring resulted in high NOAC adherence due to the knowledge they were being watched, showing that telemonitoring will only be cost-effective when higher risk, lower adherent patient groups are targeted, and when technology is cheaper. Nonetheless, this is the first study to demonstrate that rivaroxaban is cost-effective in Korean AF patients.

Among Asians there are emerging issues in the current NOAC era, including low dose/underdose, comorbidities (older age, chronic kidney disease, and concomitant use of antiplatelet agents), and bleeding.¹⁰⁾ Cost-effectiveness analysis to address these medical problems is warranted to guide physicians' best practices, leading not only to a decreased socio-economic burden, but also to an improved healthcare system. Further cost-effective analyses focusing on safety (e.g. bleeding events) related to NOACs need to be performed, to more accurately take into account the risk-benefit balance for stroke prevention in patients with AF. In the NOAC era, more and more physicians need to consider cost-effectiveness as an important factor when choosing oral anticoagulants for stroke prevention in patients with AF.

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