

EDITORIAL

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Does the current apixaban dosing strategy adequately fit and ensure safety in Korean patients with atrial fibrillation?

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Atrial fibrillation (AF), the most common cardiac arrhythmia [1], is a major global public health issue owing to its strong association with increased morbidity and mortality from cardiovascular diseases, such as heart failure, embolic stroke, and acute coronary syndrome [2].

Direct oral anticoagulants (DOACs) are recommended over warfarin as first-line therapy for patients with AF [3]. Among these, apixaban has been shown to significantly reduce the risk of major bleeding compared to warfarin and is associated with lower rates of intracranial hemorrhage and gastrointestinal bleeding [3].

Routine monitoring of plasma apixaban concentration (PAC) is not typically required, but it may be helpful in specific clinical situations, such as major bleeding, overdose, emergency surgery or invasive procedures, renal or hepatic impairment, unexpected thromboembolic events, suspected drug interactions, or noncompliance [4]. Moreover, PAC levels can vary not only according to age, body weight, and renal function but also in relation to factors such as race, sex, and underlying comorbid conditions [5]. Therefore, the current Western-derived on-therapy PAC ranges may not fully capture the clinical complexity of elderly Korean patients, who often present with multimorbidity, frailty, and altered drug metabolism.

In this issue of *Blood Research*, Lee et al. [6] investigated PAC in patients with AF, with an aim of assessing

whether PAC in combination with comorbidities could offer additional value for risk stratification. They enrolled 49 Korean patients with AF who had been receiving apixaban therapy for more than one month. Apixaban-specific anti-factor Xa activity was measured within 6 h of dosing, along with routine coagulation tests (prothrombin time [PT] and activated partial thromboplastin time [aPTT]) [7]. This study evaluated the relationships between PAC and clinical variables that included age, body weight, estimated glomerular filtration rate (eGFR), presence of heart failure (HF), and bleeding events.

Among the participants, 28 received a reduced dose of apixaban (2.5 mg twice daily), while the remaining 21 received the standard dose (5.0 mg twice daily), with dosing determined by age and body weight [3]. The mean PAC was significantly lower in the reduced-dose group (137.2 ± 72.0 ng/mL) compared to the standard-dose group (191.2 ± 75.3 ng/mL) ($p=0.014$). In both groups, 85.7% of patients had PACs within the target range (24/28 in the reduced-dose group and 18/21 in the standard-dose group).

Notably, in the reduced-dose group, renal function (as indicated by serum creatinine levels and creatinine clearance) and the presence of HF were significantly associated with PAC, with HF showing a particularly strong effect. Previous studies have shown that a 2.5 mg dose yields approximately 50% lower PAC than a 5 mg dose in healthy individuals [8, 9]. However, in this study, reduced-dose patients with HF had PAC levels that reached 90% of those in the standard-dose group, whereas PAC levels were only 50% in individuals without HF.

Another important finding was that patients with reduced-dose HF experienced a higher incidence of

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bleeding than those without HF. In contrast, no significant association was observed between PAC and clinical characteristics in the standard-dose group.

The authors concluded that renal function, age, body weight, and comorbidities, especially HF, significantly affected the PAC. Patients in the reduced-dose group were generally older and had lower body weight, impaired renal function, and more comorbidities, all of which contributed to an increased risk of bleeding. These findings highlight the need to integrate renal and hepatic function assessments into dose decision-making, particularly in elderly patients with HF who may not meet traditional dose-reduction criteria yet demonstrate altered pharmacokinetics.

Importantly, this study confirmed that routine coagulation tests, such as PT and aPTT, are of limited value in monitoring apixaban levels. PAC showed weak correlations with PT and aPTT, with only modest increases in these parameters as apixaban levels increased. This underscores that PT and aPTT are not reliable indicators of apixaban exposure [7].

In conclusion, the study by Lee et al. [6] represents a key step toward future prospective research that focuses on assessing the relationship between PAC and bleeding outcomes in Korean patients with AF and their comorbidities. Therefore, it would be valuable to establish Asian-based pharmacokinetic datasets that can inform personalized dosing guidelines and complement the existing evidence derived from Western populations. A personalized approach to apixaban dosing should be considered that takes into account bleeding risk, comorbidities, and patient-specific factors. Additionally, PAC measurements using anti-Xa assays may aid clinical decision making in selected situations.

Author's contributions

B Kim wrote the main manuscript text.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Competing interests

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