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Can Differences in Non-Vitamin K Antagonist Oral Anticoagulant Preferences Result in Varying Clinical Outcomes in Patients with Atrial Fibrillation?

LETTER TO THE EDITOR

To the Editor,

We read with great interest an article by Ünlü et al[1] published in your esteemed journal. The study provides valuable, real-world insights into the use of non-vitamin K antagonist oral anticoagulants (NOACs) in Türkiye. Of particular note is the groundbreaking discovery that reduced-dose rivaroxaban usage was linked to the composite endpoint of stroke, myocardial infarction, and all-cause mortality, which merits further analysis and discussion. As this topic continues to be a highly relevant and debated issue in the field of cardiology, we would like to share our thoughts on the matter.

Although the efficacy–safety superiority between the NOACs currently in use (apixaban, dabigatran, edoxaban, rivaroxaban) remains a mystery due to the lack of randomized controlled trials, some results obtained from observational studies may still be decisive for practitioners' daily practice. Ünlü et al[1] conducted a multivariate analysis of their study, which included 1807 patients with non-valvular atrial fibrillation (AF) and a prospective follow-up of 12 months. They found that a reduced dose of rivaroxaban (15 mg single dose daily) was predictive for the primary endpoint.[1] However, we believe there is a dilemma at this point. Given the importance of appropriate/inappropriate dosing, which the authors also emphasize in the "Limitations" section, we would like to further clarify this issue. The appropriate dose for the appropriate patient is the most critical point in the profit–loss line for the use of NOACs. Otherwise, the risk of patients experiencing events affecting clinical outcomes due to either systemic thromboembolism or bleeding risk increases predictably. To ensure optimal treatment outcomes, it is crucial to individualize the approach for all NOACs and select the appropriate dosage based on the patient's specific risk factors and comorbidities. While the analysis conducted by Ünlü et al[1] suggests that reduced-dose rivaroxaban may be linked to unfavorable primary outcomes, the study's limitation to specify the appropriate dosage rate for each NOAC group introduces an element of uncertainty. Essentially, was there a higher number of patients in the rivaroxaban group who received reduced-dose rivaroxaban when they should have received a higher dosage compared to other NOAC groups? If inappropriate usage of rivaroxaban was indeed more prevalent in this group, it would once again underscore the importance of administering the appropriate dosages. However, if the rate of appropriate/inappropriate dosing is comparable across all NOAC groups and reduced-dose rivaroxaban still yields unfavorable outcomes, it could spark a new debate in clinical practice. Upon examination of the supplementary table in the study,[1] in the clinical event group, the glomerular filtration rate (GFR) for the reduced dose was 69.5 ± 20.4 mL/min/1.73 m^2, while the standard dose had a GFR of 73 ± 23.5 mL/min/1.73 m^2 ($P = .318$). Interestingly, the groupings according to GFR level (0-30, 30-60, 60-90, >90) did not differ ($P = .338$) between the rivaroxaban reduced-dose and standard-dose arms. On the other hand, there was a significant difference ($P < .001$) in GFR between reduced-dose and standard-dose

Bülent Özlek

Department of Cardiology, Faculty of Medicine, Muğla Sıtkı Koçman University, Muğla, Türkiye

Corresponding author:
Bülent Özlek
✉ bulent_ozlek@hotmail.com

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NOACs in the group of patients without clinical events. While this finding is not unique among other NOACs, it is crucial to note that GFR level is the sole criterion for dose reduction in rivaroxaban treatment. This raises the possibility that the rate of inappropriate dosing was higher in the rivaroxaban group and that cardiologists may have preferred reduced-dose rivaroxaban in patients with a GFR of 50 mL/min/1.73 m^2 and above, perhaps out of concern for bleeding risk.

Another recent study on the subject, which utilized a valuable methodology, compared the effectiveness of apixaban, dabigatran, and rivaroxaban. The study analyzed 56 553 non-valvular AF patients who were receiving NOAC therapy and found that the rate of inappropriate dosing was similar across all 3 NOAC groups. Interestingly, after almost 6 years of follow-up, the rivaroxaban group had lower rates of mortality, ischemic stroke, and intracranial hemorrhage ($P < .05$) compared to apixaban. Additionally, the apixaban group had lower rates of gastrointestinal bleeding ($P < .05$) compared to rivaroxaban.[2]

REFERENCES

1. Ünlü S, Altay S, Gedikli Ö, et al. Real-world data on the incidence of stroke, myocardial infarction, and mortality among nonvalvular atrial fibrillation patients in Türkiye: new oral anticoagulants-TURKey study. *Anatol J Cardiol*. 2024;28(1):19-28. [CrossRef]
2. Talmor-Barkan Y, Yacovzada NS, Rossman H, et al. Head-to-head efficacy and safety of Rivaroxaban, apixaban, and dabigatran in an observational nationwide targeted trial. *Eur Heart J Cardiovasc Pharmacother*. 2022;9(1):26-37. [CrossRef]