

PUBLICATIONS

AGE-RELATED DIFFERENCES OF PEAK AND TROUGH PLASMA CONCENTRATIONS OF RIVAROXABAN IN UZBEK POPULATION WITH ATRIAL FIBRILLATION

Sh.Sh. Xolmurodov, N.U. Zakirov, A.A. Tolibov, X.I. Uralov, M.S.Mahmudov

*Republican Specialized Scientific and Practical Medical Center of Cardiology,
Tashkent, Uzbekistan*

The natural age-related decline in glomerular filtration rate may slow the clearance of partially renally excreted drugs such as rivaroxaban and increase plasma concentrations. Age 75 years is a formal clinical threshold with a distinct place in the CHA₂DS₂-VASc score (≥ 75 years — 2 points) and is frequently used in research to examine rivaroxaban pharmacokinetics. However, it has not been confirmed that the standard dose-reduction algorithm (from 20 to 15 mg based on renal function) fully compensates for age-related differences.

To evaluate the age dependence of trough and peak plasma concentrations of rivaroxaban, measured using the anti-Xa activity assay, in patients with atrial fibrillation (AF) receiving rivaroxaban.

The study included 66 hospitalized AF patients receiving rivaroxaban 15 mg or 20 mg daily at the Republican Specialized Scientific and Practical Medical Center of Cardiology: an age 39-75 years group ($n=54$, mean age 64.8 ± 7.0 years) and an age ≥ 75 years group ($n=12$, mean age 78.6 ± 2.0 years). Blood samples were drawn after at least 5-7 days of regular therapy: trough — at 24th hour after the dose was taken ($n=66$ samples), peak — 2-4 hours after the next dose ($n=66$ samples). Plasma concentration was measured using the anti-Xa activity assay (ACL TOP 350 CTS, Werfen analyzer). Continuous variables were presented as median (interquartile range) and groups were compared using the Mann-Whitney U test ($p < 0.05$ was considered statistically significant).

In patients aged ≥ 75 years, median trough concentration was significantly higher than in the 39-75 years group (78.50 vs 26.75 ng/mL, $p=0.031$), despite the reduced dose being used considerably more often in the ≥ 75 years group (median 17.5 vs 20.0 mg/day, $p < 0.0001$). This occurred alongside markedly lower creatinine clearance (median 50.5 vs 78.5 mL/min, $p < 0.0001$), indicating that dose reduction did not fully compensate for the decline in renal function. Peak concentration showed a trend in the same direction (306.80 vs 236.95 ng/mL) but did not reach statistical significance ($p=0.098$). CHA₂DS₂-VASc ($p=0.0001$) and HAS-BLED ($p=0.021$) scores were, as expected, higher in the ≥ 75 years group. In an exploratory sex-stratified analysis, the age-related association with trough level was observed mainly in women ($n=29$ vs $n=8$, $p=0.0065$), while no such association was found in men ($n=25$ vs $n=4$, $p=0.784$); however, the sample size in the male ≥ 75 years subgroup ($n=4$) was insufficient for statistical inference, so this finding is reported only as a preliminary observation.

In patients older than 75 years, trough plasma rivaroxaban concentration was significantly higher, indicating that the existing dose-reduction algorithm does not fully eliminate this difference. This finding supports the clinical relevance of anti-Xa monitoring in this age group. The additional sex-related difference observed is preliminary in nature and, given the small sample size, should be interpreted with caution and confirmed in a larger cohort.