

Comparative Safety and Effectiveness of Warfarin or Rivaroxaban Versus Apixaban in Patients With Advanced CKD and Atrial Fibrillation: Nationwide US Cohort Study

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Head-to-head data comparing the effectiveness and safety of oral anticoagulants in patients with atrial fibrillation (AF) and advanced chronic kidney disease (CKD) are lacking. We compared the safety and effectiveness of warfarin or rivaroxaban versus apixaban in patients with AF and non-dialysis-dependent CKD stage 4/5.

[Study Design](#)

Propensity score–matched cohort study.

[Setting & Participants](#)

2 nationwide US claims databases, Medicare and Optum's deidentified Clinformatics Data Mart Database, were searched for the interval from January 1, 2013, through March 31, 2022, for patients with nonvalvular AF and CKD stage 4/5 who initiated warfarin versus apixaban (matched cohort, n=12,488) and rivaroxaban versus apixaban (matched cohort, n = 5,720).

Exposures

Warfarin, rivaroxaban, or apixaban.

Outcomes

Primary outcomes included major bleeding and ischemic stroke. Secondary outcomes included all-cause mortality, major gastrointestinal bleeding, and intracranial bleeding.

Analytical Approach

Cox regression was used to estimate HRs, and 1:1 propensity-score matching was used to adjust for 80 potential confounders.

Results

Compared with apixaban, warfarin initiation was associated with a higher rate of major bleeding (HR, 1.85; 95% CI, 1.59-2.15), including major gastrointestinal bleeding (1.86; 1.53-2.25) and intracranial bleeding (2.15; 1.42-3.25). Compared with apixaban, rivaroxaban was also associated with a higher rate of major bleeding (1.69; 1.33-2.15). All-cause mortality was similar for warfarin (1.08; 0.98-1.18) and rivaroxaban (0.94; 0.81-1.10) versus apixaban. Furthermore, no statistically significant differences for ischemic stroke were observed for warfarin (1.14; 0.83-1.57) or rivaroxaban (0.71; 0.40-1.24) versus apixaban, but the CIs were wide. Similar results were observed for warfarin versus apixaban in the positive control cohort of patients with CKD stage 3, consistent with randomized trial findings.

Limitations

Few ischemic stroke events, potential residual confounding.

Conclusions

In patients with AF and advanced CKD, rivaroxaban and warfarin were associated with higher rates of major bleeding compared with apixaban, suggesting a superior safety profile for apixaban in this high-risk population.

Plain-Language Summary

Different anticoagulants have been shown to reduce the risk of stroke in patients with atrial fibrillation, such as warfarin and direct oral anticoagulants like apixaban and rivaroxaban. Unfortunately, the large-scale randomized trials that compared direct anticoagulants versus warfarin excluded patients with advanced chronic kidney disease. Therefore, the comparative safety and effectiveness of warfarin, apixaban, and rivaroxaban are uncertain in this population. In this study, we used administrative claims data from the United States to answer this question. We found that warfarin and rivaroxaban were associated with increased risks of major bleeding compared with apixaban. There were few stroke events, with no major differences among the 3

drugs in the risk of stroke. In conclusion, this study suggests that apixaban has a better safety profile than warfarin and rivaroxaban.

Graphical abstract

