

ABSTRACTS

Anticoagulant Medications for Patients With Atrial Fibrillation and Advanced Renal Disease: A Propensity-Matched Real-World Analysis of Apixaban vs Rivaroxaban

Muhammad Asim Agha, MD¹, Muhammad Sajawal, MBBS, MD¹, Hira Batool, MBBS², Muhammad Ammar Agha, MBBS³, Hadia Batool, MBBS⁴, Aqsa Agha, MBBS⁵, Muhammad Ibrahim Khan, MD⁶, Miriam Michael, MD, FACP¹

¹ Internal Medicine, Howard University Hospital, ² Internal Medicine, Sahiwal Medical College, ³ Sindh Institute of Urology and Transplantation, ⁴ Internal Medicine, Combined Military Hospital, ⁵ Shaikh Zayed Medical College and Hospital, ⁶ Internal Medicine, Mayo Clinic

Keywords: Atrial fibrillation, Chronic kidney disease, Apixaban, Rivaroxaban, Gastrointestinal bleeding, direct oral anticoagulants, comparative effectiveness
<https://doi.org/10.52504/001c.167471>

Georgetown Medical Review

Vol. 10, Issue 1, 2026

Background

Advanced chronic kidney disease (CKD) complicates anticoagulant treatment because thromboembolic and bleeding risks compete. We compared treatment outcomes for apixaban and rivaroxaban in adults with atrial fibrillation (AF) and stage 4/5 CKD.

Methods

Deidentified TriNetX records for patients treated with apixaban (n=49,698) and rivaroxaban (n=2660) underwent 1:1 propensity score matching (demographics, medications, procedures, laboratory values); 2533 matched pairs were identified (absolute standardized mean difference <0.10, indicating adequate balance). The smaller rivaroxaban cohort constrained matching; findings apply only to the matched population. Outcomes were assessed at 1, 3, and 5 years. Myocardial infarction (MI) findings were exploratory. P values were not adjusted for multiplicity.

Results

Gastrointestinal bleeding was lower for apixaban vs rivaroxaban (5-year: 9.3% vs 10.9%; relative risk [RR], 0.86; 95% CI, 0.71-1.02; P=.09). Cerebrovascular events were significantly higher for apixaban vs rivaroxaban at 3 years only (9.8% vs 7.9%; RR, 1.24; 95% CI, 1.01-1.53; P=.04); this association may reflect chance. Cerebral infarction was significantly higher for apixaban vs rivaroxaban at 1 year (3.0% vs 1.8%; RR, 1.61; 95% CI, 1.09-2.37; P=.02) and attenuated at 3 and 5 years. Rates of MI were nominally higher in the apixaban group. Five-year mortality risk was significantly lower for apixaban vs rivaroxaban (33.3% vs 36.1%; RR, 0.92; 95% CI, 0.86-0.10; P=.04) but differences in time-to-event survival were not significant.

Conclusion

Apixaban did not have greater bleeding risk than rivaroxaban and may be associated with lower gastrointestinal bleeding, a finding that requires further study. Isolated cerebrovascular, MI, and mortality findings require cautious interpretation. A mortality advantage for either drug was not established.

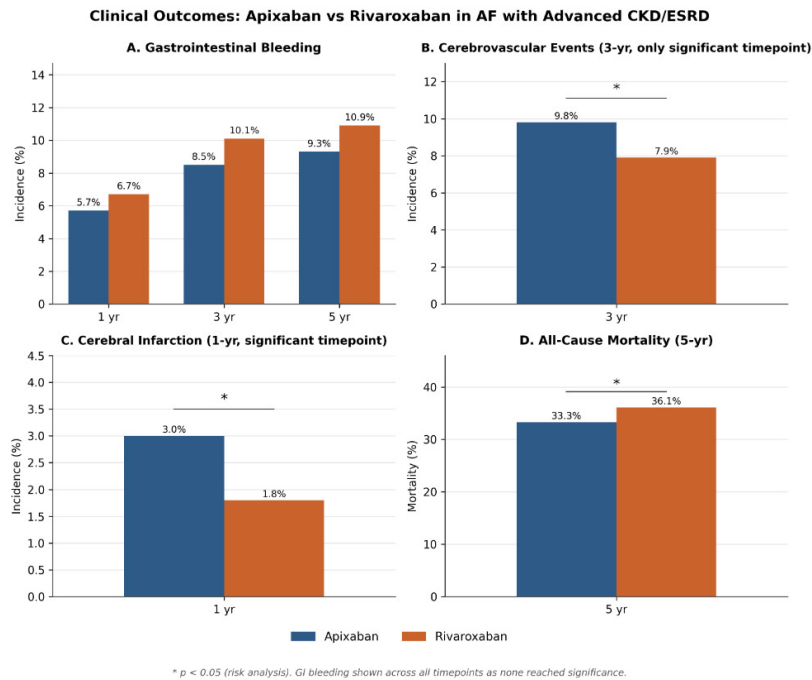


Figure 1. Selected clinical outcomes in propensity-matched adults with atrial fibrillation (AF) and advanced chronic kidney disease (CKD) or end-stage renal disease (ESRD) treated with apixaban vs rivaroxaban. Bars show cumulative incidence at the specified follow-up time. Asterisks denote statistically significant outcomes ($P < .05$) in risk analyses; multiplicity was not adjusted. Gastrointestinal bleeding is shown across all timepoints as none reached significance. The nominal 5-year mortality risk difference was not corroborated by the time-to-event analysis.

Peer Review

Abstract:

Major comments:

- Line 41: More than 95% of patients in the original apixaban group were dropped to reach the 2,533 pairs. Provide more insight on how you ensured that the matched sample was representative of the original treated population.
- Line 42: The massive difference in the size of the cohorts may prevent any of the conclusions listed about each cohort to have any true relevance because of the removal of essentially 45,000 participants. While somewhat addressed in the conclusion, further information at minimum on what assumptions and characteristics were used to drive the propensity score matching would help to address this issue.
- Lines 53-54: Please provide insight on why cerebrovascular events were significant at the 3-year timepoint but not at the 1- or 5-year timepoints. Please clarify whether the analysis adjusted for multiple comparisons, being sure to specify

which test was performed. If not, be sure to describe your results more cautiously, noting that some findings may be due to chance rather than a true treatment difference.

- Lines 46-47 & 56-57: In your Methods section, you describe that MI is assessed as an exploratory endpoint, but your Results section states “MI was consistently higher with apixaban across follow-up” with the same weight as your primary bleeding and stroke findings. I would recommend phrasing this more cautiously with an emphasis on its exploratory status.
- Lines 57-58: Please explain why the 5-year mortality risk was significantly lower with apixaban but the time-to-event analysis shows no significant survival difference. Which result should be relied on? I would recommend explaining why the findings diverge. Were there any patients differentially excluded due to loss to follow-up? Assuming a Cox model was used, is the proportional hazards assumption of RR remaining constant over time violated with a shifting trend in mortality difference?

Minor comments

- Line 60: I would not use the phrase “trended towards” as this implies that conclusions can be made from this data, which is not true. Instead, I might use the wording here: “In this propensity-matched cohort, apixaban was not associated with significantly greater bleeding risk than rivaroxaban. Additionally, there may be a signal that apixaban is associated with lower gastrointestinal bleeding, which is worthy of further investigation.”

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Funding

None to report

Conflict-of-interest statement

The authors have no relevant financial or nonfinancial interests to disclose.

IRB approval/exemption

Data were obtained by executing prespecified queries within TriNetX. The platform returned deidentified, aggregate data, and no directly identifiable patient information was accessed. As such, it was granted exemption by the Western Institutional Review Board, and no additional institutional review board approval or informed consent was required.

Corresponding Author

Muhammad Sajawal

Howard University Hospital

Email: Sajawalmalik.md@gmail.com

2041 Georgia Ave NW, Washington, DC 20060 202 262 4649

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Submitted: July 14, 2026 EDT. Accepted: August 10, 2026 EDT. Published: August 20, 2026 EDT.