

Comparative 30-Day and 1-Year Outcomes of Rivaroxaban vs Apixaban in Atrial Fibrillation Patients Undergoing Bioprosthetic Aortic Valve Replacement

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Introduction

- Atrial fibrillation (AF) after bioprosthetic aortic valve replacement (BAVR) requires long-term anticoagulation, yet the optimal agent remains unclear. Direct oral anticoagulants (DOACs) increasingly replace warfarin for AF, but evidence specific to bioprosthetic valves is limited and heterogeneous.
- Prior meta-analyses and cohort studies show DOACs provide similar or improved stroke/systemic embolism protection with less major bleeding than warfarin in AF with bioprosthetic valves [1–5]. Emerging head-to-head data suggest apixaban is associated with lower major and intracranial bleeding and comparable or superior effectiveness relative to rivaroxaban in AF and valvular heart disease populations [6–7], including a major bleeding hazard ratio of 0.51 for apixaban vs rivaroxaban [6].
- However, direct comparisons of apixaban vs rivaroxaban in BAVR are scarce. Many existing studies combine aortic and mitral bioprostheses, rely on claims data lacking valve-level detail, or are underpowered for drug-specific analysis [1–7].
- Pharmacokinetic differences may explain observed safety variations: apixaban has twice-daily dosing, stable plasma levels, food-independent absorption, and lower renal elimination (~27%), whereas rivaroxaban has once-daily peaks, food-dependent absorption, greater renal elimination (~33%), and more CYP3A4 sensitivity [7–9]. These properties likely contribute to apixaban's lower bleeding risk seen in large real-world studies.

Methods

- Retrospective cohort study using the TriNetX Global Collaborative Network, a federated EHR database spanning 151 healthcare organizations. Adults with AF and bioprosthetic aortic valve replacement (BAVR) were identified using CPT/ICD-10-PCS/SNOMED codes; AF required ICD-10 I48.91 before or at valve replacement
- Exclusions included mechanical valves, postoperative warfarin use, and missing key demographic or medication-timing variables. Exposure was defined as initiation of apixaban or rivaroxaban within 30 days of BAVR.
- Patients were stratified by age <80 vs ≥80 years, with the ≥80 group serving as the primary analytic cohort. Before matching, 1,946 rivaroxaban and 9,743 apixaban users met criteria; after 1:1 propensity score matching on 29 clinical covariates including comorbidities such as BMI and history of diabetes and stroke, 2,226 patients ≥80 years remained.
- Outcomes were assessed at 30 days and 1 year, including all-cause mortality, stroke/TIA, intracranial hemorrhage, gastrointestinal bleeding, other major bleeding, myocardial infarction, venous thromboembolism, heart failure, acute kidney injury, advanced CKD, and pericardial complications. Patients with prior events were excluded from that specific analysis.
- Analyses used TriNetX's association tool to generate risk difference, risk ratio, and odds ratio estimates with 95% confidence intervals. Primary comparisons focused on the ≥80 matched cohort, with <80 and all-ages analyses also performed. Summary tables and figures were generated in RStudio and Microsoft Excel.

Results

Characteristic Name	Rivaroxaban: n (%)	Apixaban: n (%)	p-Value
Essential (primary) hypertension	920 (82.7%)	921 (82.8%)	0.96
Type 2 diabetes mellitus	405 (36.4%)	376 (33.8%)	0.20
Long term aspirin use	288 (25.9%)	300 (27.0%)	0.56
Acute myocardial infarction	183 (16.4%)	166 (14.9%)	0.32
Cerebral infarction	106 (9.5%)	97 (8.7%)	0.51
Gastrointestinal hemorrhage	70 (6.3%)	77 (6.9%)	0.55
Acute embolism and DVT	46 (4.1%)	38 (3.4%)	0.37
Pulmonary embolism	41 (3.7%)	36 (3.2%)	0.56
BMI (kg/m ² ± SD)	28.82 ± 5.95	28.6 ± 5.99	0.46
Age (years ± SD)	82.07 ± 4.71	82.11 ± 4.66	0.83

Table 1: Cohort Characteristics

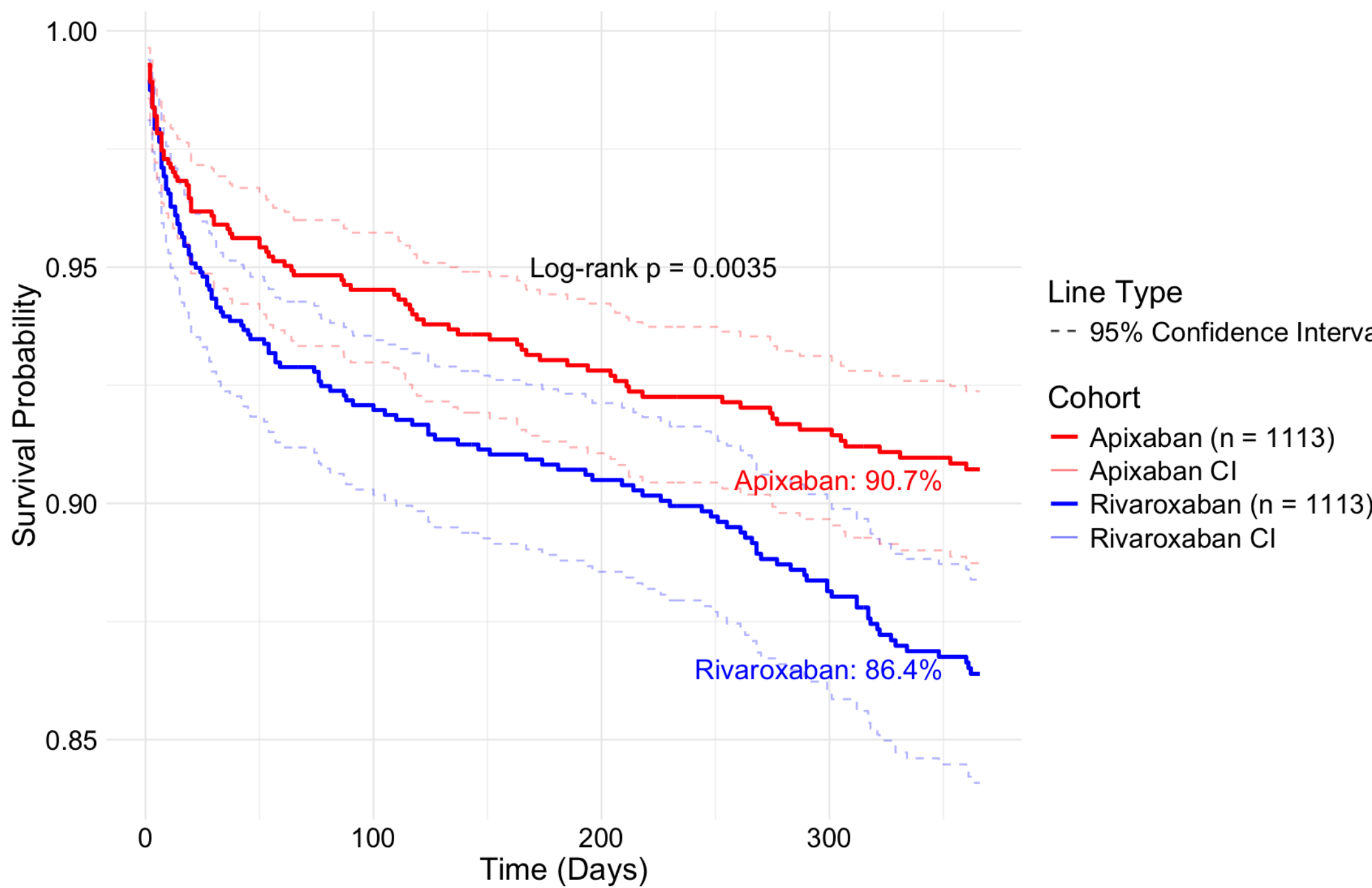


Figure 1: Major Bleeding Risk in Adults > 80 Years: Kaplan-Meier Comparison of Rivaroxaban vs Apixaban between groups

- In the full all-ages cohort (n = 3,772), rivaroxaban remained associated with higher thrombosis (OR 1.60, p = 0.0021) and GI bleeding (OR 1.44, p = 0.0161) versus apixaban.
- Among patients <80 years, no significant differences were observed for thrombotic or bleeding outcomes (all p > 0.05), indicating that rivaroxaban's excess risk is concentrated in the very elderly.
- Midpoint survival analysis for bleeding events showed:
 - Rivaroxaban: midpoint 93.2%, reached ~Day 53
 - Apixaban: midpoint 95.35%, reached ~Day 53

- Among 2,226 adults ≥80 years after bioprosthetic AVR (1,113 rivaroxaban; 1,113 apixaban; mean age 82.1 ± 4.7 years), rivaroxaban was associated with higher risks of death, thrombosis, and major bleeding compared with apixaban (Table 1, Figure 2)
 - Death: OR 1.36, p = 0.034
 - Thrombosis: OR 1.56, p = 0.037
 - Major bleeding: OR 1.53, p = 0.0027

- Other 30-day outcomes (stroke, MI, HF, intracranial hemorrhage) did not differ significantly between groups (all p > 0.05).
- Kaplan–Meier curves showed a significant difference in overall event-free survival between cohorts, with apixaban demonstrating consistently higher survival probabilities throughout 12 months (log-rank p = 0.0035, Figure 1).
- At 1 year, apixaban maintained a higher survival estimate (90.7%) compared with rivaroxaban (86.4%), with non-overlapping confidence intervals across much of the follow-up period.

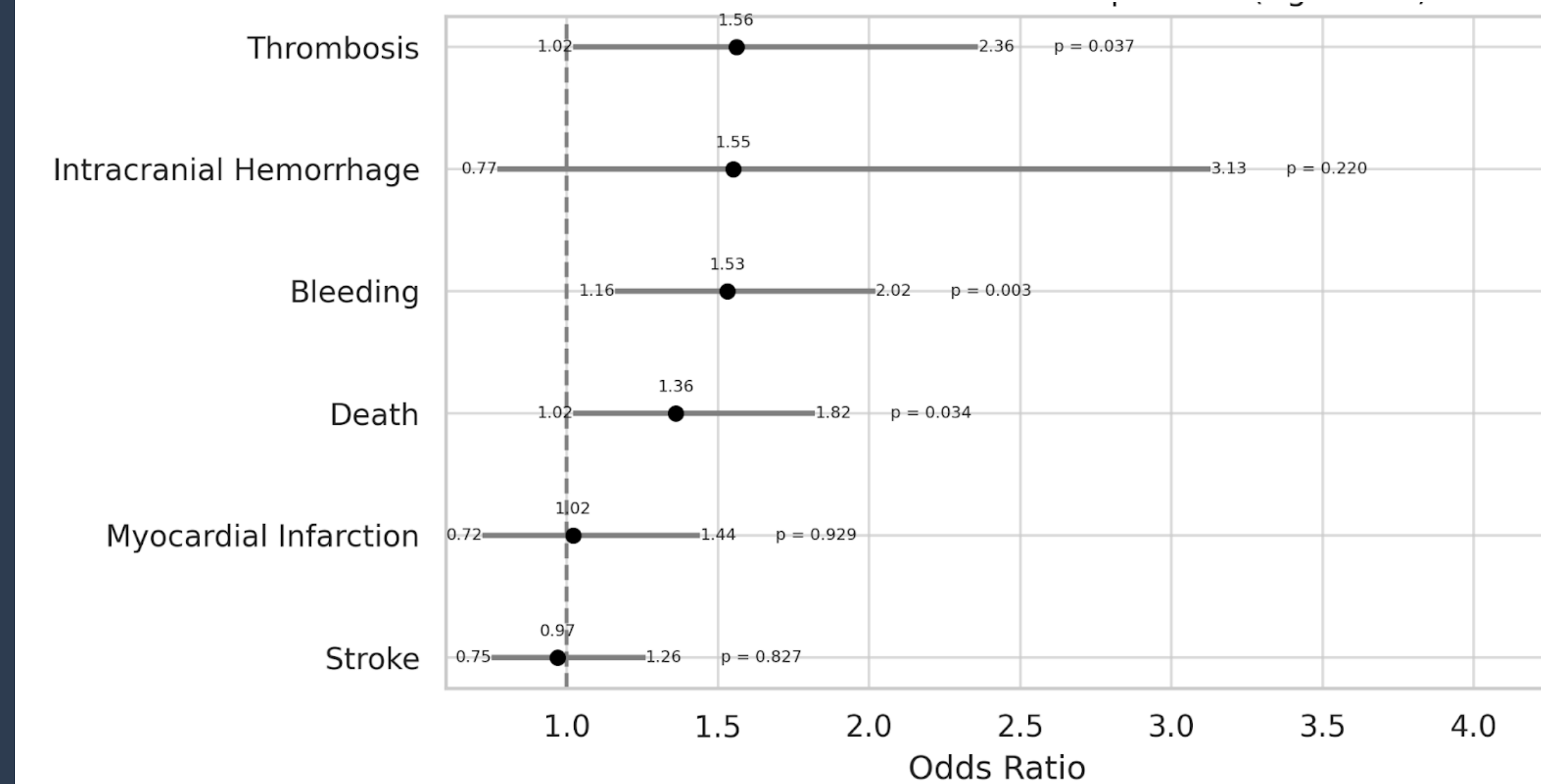


Figure 2: Odds Ratios for Rivaroxaban versus Apixaban (Age ≥80)

Discussion

- In this 365-day cohort of AF patients after bioprosthetic AVR, rivaroxaban was associated with higher 1-year risks of major bleeding, thrombosis, and mortality, with the strongest effects in adults ≥80 years [10–12]. Early (30-day) outcomes were similar, suggesting a cumulative hazard rather than perioperative differences [10–12].
- These results mirror large observational studies showing lower major and GI bleeding with apixaban, including Dawwas et al. (HR 0.51) [11]. The age-specific pattern is pharmacologically plausible given apixaban's more stable PK profile—twice-daily dosing, lower peak-to-trough variability, food-independent absorption, and lower renal elimination—compared with rivaroxaban's greater variability and food dependence [7, 13–14].
- Among patients <80 years, outcomes did not differ, indicating that anticoagulant choice becomes increasingly important with advanced age and comorbidity [12]. Across all ages, rates of stroke, MI, and intracranial hemorrhage were similar, consistent with evidence that both DOACs provide comparable thromboembolic protection [10, 13–14].
- Midpoint survival analysis showed similar timing of bleeding events (~Day 53), but apixaban maintained a higher midpoint survival (95.35% vs 93.2%), indicating rivaroxaban causes more total bleeding rather than earlier bleeding.

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