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Clinical outcomes of apixaban in patients with atrial fibrillation and very high thromboembolic risk (CHA_2DS_2-VASc ≥5): a retrospective cohort study

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Abstract

Background

Real-world evidence on apixaban in patients with atrial fibrillation (AF) at very high thromboembolic risk (CHA_2DS_2-VASc ≥ 5) is limited, particularly from the Middle East. We compared clinical outcomes between apixaban-treated patients with CHA_2DS_2-VASc scores ≥ 5 and 0–4, and between prescribed doses within the very high-risk group.

Methods

In this retrospective cohort study at a tertiary referral center in Makkah, Saudi Arabia, adults with AF treated with apixaban between January 2019 and December 2024 were grouped by baseline CHA_2DS_2-VASc score. Outcomes were documented thromboembolic events, bleeding of any severity, and in-hospital mortality. Odds ratios (ORs) were estimated by unadjusted and multivariable logistic regression. A sensitivity analysis excluded patients with a recorded prior stroke.

Results

Of 596 patients, 175 (29.4%) had scores ≥ 5. Thromboembolic events (31.4% vs 7.1%; adjusted OR 6.6, 95% CI 3.9–11.0) and in-hospital mortality (14.3% vs 1.7%; adjusted OR 7.7, 95% CI 3.2–18.5) were more frequent with scores ≥ 5, whereas bleeding did not differ significantly (54.9% vs 46.8%; adjusted OR 1.3, 95% CI 0.9–1.9). Of 68 patients with a recorded prior stroke, 58 also had a documented thromboembolic event; after their exclusion, thromboembolic events no longer differed (5.2% vs 5.1%), whereas bleeding (adjusted OR 3.2, 95% CI 2.0–5.1) and mortality (adjusted OR 8.7, 95% CI 3.4–22.1) were more frequent with scores ≥ 5. Among very high-risk patients, prescribed dose (2.5 mg, n = 73; 5 mg, n = 102, twice daily) was not significantly associated with any outcome.

Conclusions

A CHA_2DS_2-VASc score ≥ 5 was associated with higher in-hospital mortality among apixaban-treated patients with AF. The excess of thromboembolic events was confined to patients with a recorded prior stroke and may reflect overlap between baseline history and outcome recording. Prescribed dose was not associated with outcomes, although dose appropriateness could not be assessed. Larger studies with complete dosing criteria and event timing are needed.

Background

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, affecting approximately 2–4% of the adult population, and its prevalence is projected to at least double in the coming decades, largely

driven by population aging and the growing burden of cardiovascular comorbidities [1, 2]. AF substantially increases the risk of thromboembolic complications, particularly ischemic stroke, with untreated AF associated with approximately a five-fold higher risk of stroke [1, 3]. Patients with AF are also at increased risk for systemic embolism, heart failure exacerbation, and mortality, which emphasizes the need for early risk assessment and preventive management to reduce adverse clinical outcomes [2].

Apixaban, a direct oral factor Xa inhibitor, has become a cornerstone therapy for stroke prevention in patients with non-valvular AF [4–6]. In the ARISTOTLE trial, apixaban was superior to warfarin, with significant reductions in stroke or systemic embolism, major bleeding, and all-cause mortality [5, 7]. Consistent with these findings, a meta-analysis reported that apixaban was associated with a lower risk of stroke or systemic embolism (relative risk [RR] 0.77, 95% CI 0.64–0.93) and major bleeding (RR 0.58, 95% CI 0.52–0.65) compared with warfarin [8]. Moreover, several studies have demonstrated a favorable safety profile of apixaban compared with other direct oral anticoagulants, particularly rivaroxaban [6, 9–11].

The CHA_2DS_2-VASc score is a well-validated risk stratification tool widely used to estimate thromboembolic risk and guide anticoagulation therapy in patients with AF. Traditionally, patients were categorized into low- (score = 0), intermediate- (score = 1), and high-risk (score ≥ 2) groups based on their CHA_2DS_2-VASc score to predict thromboembolic events [12]. However, large cohort studies have demonstrated a progressive increase in thromboembolic risk with increasing CHA_2DS_2-VASc score values, with patients having scores ≥ 5 experiencing substantially higher annual stroke risk compared with lower-risk groups [12–14].

Apixaban has demonstrated a favorable safety profile in randomized trials and real-world studies involving patients with AF [4, 6, 7, 10, 11], in which the mean or median CHA_2DS_2-VASc score was typically about 3 to 4. However, these studies have primarily evaluated outcomes in the general AF population rather than focusing specifically on patients with very high thromboembolic risk. Consequently, evidence supporting apixaban therapy in patients with very high thromboembolic risk (CHA_2DS_2-VASc ≥ 5, although definitions of this category vary across studies [2, 15–17]) remains limited, particularly in real-world clinical settings where comorbidities and dose adjustments may influence treatment outcomes. Therefore, this study aims to evaluate the clinical outcomes of apixaban therapy in patients with AF by comparing thromboembolic events, bleeding, and mortality between patients with lower thromboembolic risk (CHA_2DS_2-VASc 0–4) and those with very high risk (CHA_2DS_2-VASc ≥ 5), and to explore outcomes according to prescribed apixaban dose within the very high-risk group.

Methods

Study design and setting

This retrospective cohort study was conducted at King Abdullah Medical City, a tertiary care hospital in Makkah, Saudi Arabia, and included adults with AF treated with apixaban between January 2019 and December 2024. The study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guideline. Patients were categorized as lower risk (CHA_2DS_2-VASc 0–4) or very high risk (CHA_2DS_2-VASc ≥ 5); because definitions of very high risk vary, the ≥ 5 threshold was selected in line with previous studies [2, 15–17]. Risk group was assigned according to the CHA_2DS_2-VASc score at baseline.

Study population

Adults (≥ 18 years) with AF who were prescribed apixaban during the study period were identified through the hospital electronic health record system. Patients with valvular AF (moderate-to-severe mitral stenosis or a mechanical prosthetic heart valve), incomplete medical records, or missing key variables were excluded. No a priori sample-size calculation was performed; all eligible records from the study period were included. Within the very high-risk group, outcomes were compared between patients prescribed apixaban 2.5 mg twice daily and those prescribed 5 mg twice daily.

Data collection

Data were extracted retrospectively from electronic medical records using a structured data collection form. Variables included age, sex, body weight, height, comorbidities (hypertension, diabetes mellitus, heart failure, vascular disease, and prior stroke), creatinine clearance estimated from serum creatinine, components of the CHA_2DS_2-VASc score, and prescribed apixaban dose. Dose was analyzed as prescribed (2.5 mg or 5 mg twice daily) and was not classified as appropriate or inappropriate against the labeled dose-reduction criteria (at least two of age ≥ 80 years, body weight ≤ 60 kg, or serum creatinine ≥ 1.5 mg/dL) [2, 16], because individual serum creatinine values were not part of the dataset.

Outcomes and follow-up

The outcomes were thromboembolic events, bleeding events, and all-cause in-hospital mortality, as documented in the hospital electronic medical record. Thromboembolic events comprised any documented stroke or systemic embolic event. Bleeding events comprised any documented bleeding, irrespective of severity. Mortality was defined as death documented in the hospital record during the study period; patients without a documented death were classified as alive, and deaths occurring outside the hospital were not sought. Patients were followed from apixaban initiation until the end of the study period (December 2024), and each outcome was analyzed as the proportion of patients with at least one documented event.

Statistical analysis

Normality of continuous variables was assessed with the Shapiro–Wilk test. Non-normally distributed variables were summarized as medians with interquartile ranges (IQRs) and compared with the Mann–Whitney U test. Categorical variables were summarized as counts and percentages and compared with the Pearson chi-square test, or with Fisher's exact test when an expected cell count was below five. Two exposures were examined: a CHA_2DS_2-VASc score ≥ 5 versus 0–4 in the whole cohort, and apixaban 5 mg versus 2.5 mg twice daily within the very high-risk group. The association between each exposure and each outcome was expressed as an odds ratio (OR) with a 95% confidence interval (CI), estimated by maximum-likelihood logistic regression with Wald intervals. Risk-group models were adjusted for prescribed dose and creatinine clearance, and dose models for age, weight, creatinine clearance, and prior stroke. An adjusted model was not fitted when the number of events was too small to support the covariate set. Because prior stroke contributes to the CHA_2DS_2-VASc score and could overlap with the thromboembolic outcome, a post hoc sensitivity analysis repeated the risk-group comparisons after excluding patients with a recorded prior stroke. Covariates were chosen on clinical grounds after data collection, so the analyses should be regarded as exploratory, and no correction was made for multiple comparisons. A two-sided *P* value < 0.05 was considered statistically significant. Analyses were performed in IBM SPSS Statistics for Windows, version 28.0 (IBM Corp., Armonk, NY, USA).

Ethical approval

The study was approved by the Biomedical Research Ethics Committee of Umm Al-Qura University, Makkah, Saudi Arabia (Approval No. HAPO-02-K-012-2026-05-3412). Because of the retrospective design, data were extracted from existing medical records and individual informed consent was not obtained. Patient identifiers were accessible only to the study team for record reconciliation, and data were handled in accordance with institutional policies to ensure patient confidentiality.

Results

Study population and baseline characteristics

Of the 597 patients in the extracted dataset, one record with a documented age of 16 years was excluded, leaving 596 patients for analysis: 421 (70.6%) with CHA_2DS_2-VASc scores of 0–4 and 175 (29.4%) with scores ≥5. Patients with scores ≥5 were older, more often female, weighed less, had lower creatinine clearance, and were less frequently prescribed apixaban 5 mg twice daily; as expected from the score definition, all score-defining comorbidities were more prevalent in this group (Table 1). Height and body mass index were not analyzed because the recorded values were inconsistent.

Clinical outcomes according to CHA_2DS_2-VASc risk group

Overall, 85 patients (14.3%) had a documented thromboembolic event, 293 (49.2%) had a documented bleeding event, and 32 (5.4%) died. Thromboembolic events and in-hospital mortality were significantly more frequent in patients with scores ≥5, whereas bleeding did not differ significantly between groups (Table 2). Of the 68 patients with a recorded prior stroke, 58 (85.3%) also had a documented thromboembolic event. In the sensitivity analysis excluding these patients (n=528), thromboembolic

events no longer differed between groups, whereas bleeding and in-hospital mortality were significantly more frequent with scores ≥5 (Supplementary Table S2).

Across individual scores, thromboembolic events were documented in fewer than 10% of patients at each score from 0 to 4 and increased progressively from a score of 5 upward; mortality followed a similar gradient, and bleeding was most frequent at scores 3 to 5 (Supplementary Table S1). Estimates for scores ≥7 were based on 27 patients and are imprecise.

Apixaban dose in very high-risk patients

Among the 175 patients with scores ≥5, 73 (41.7%) were prescribed apixaban 2.5 mg twice daily and 102 (58.3%) were prescribed 5 mg twice daily. Patients receiving 2.5 mg were older, weighed less, had lower creatinine clearance, and less often had a recorded prior stroke (Table 3). Prescribed dose was not significantly associated with thromboembolic events, bleeding, or mortality (Table 4). For thromboembolic events, the direction of the estimate reversed after adjustment but remained non-significant. Because only 25 deaths occurred in this subgroup, an adjusted model for mortality was not fitted.

Discussion

In this single-center cohort of apixaban-treated patients with AF, a CHA_2DS_2-VASc score ≥5 identified a group in whom thromboembolic events and in-hospital death were documented much more often than in patients with lower scores, whereas bleeding was common in both groups and prescribed dose was not clearly associated with any outcome. Thromboembolic events were recorded in 31.4% of very high-risk patients and in 7.1% of lower-risk patients (adjusted OR 6.6), and across individual scores the proportion rose sharply from a score of 6 upward. This gradient matches what was seen in the large cohort studies used to validate the CHA_2DS_2-VASc score, in which the risk of thromboembolism increased with each additional point and annual rates of roughly 5% to 23% were reported for patients with scores of 5 or more [12–14]. Those cohorts, however, consisted largely of patients who were not taking oral anticoagulants, and their estimates are annual rates, whereas ours are cumulative proportions over follow-up of variable length, so the figures cannot be compared directly. More importantly, this gradient needs to be interpreted with caution. Of the 68 patients with a recorded prior stroke, 58 also had a documented thromboembolic outcome, and when these patients were excluded the proportion with thromboembolic events was almost identical in the two risk groups (5.2% vs 5.1%). Recurrence on this scale would be far higher than the event rates reported in anticoagulated patients, both in ARISTOTLE and in a meta-analysis of more than 3.9 million patients receiving apixaban [5, 8]. A more likely explanation is that, in many records, the stroke counted as baseline history and the stroke recorded as an outcome were the same event. If so, the association between a high score and thromboembolism in our primary analysis reflects the way the two fields were recorded rather than residual risk despite anticoagulation. The alternative, that prior stroke identifies patients at particularly high risk of recurrence,

is consistent with the weight given to prior stroke in the score [12–14], but it cannot be confirmed without event dates.

Bleeding followed a different pattern. It was documented in about half of the cohort and was only modestly, and not significantly, more frequent in the very high-risk group (54.9% vs 46.8%; adjusted OR 1.3). This result appears to have been influenced by the same group of patients: those with a recorded prior stroke rarely had documented bleeding (14.7%), and after their exclusion bleeding was significantly more frequent in patients with scores ≥5 (74.1% vs 47.8%; adjusted OR 3.2). The high overall proportion is most likely a consequence of our outcome definition, which included any documented bleeding rather than adjudicated major bleeding; for the same reason, our figures should not be set against the major bleeding rates reported in ARISTOTLE [5]. The direction of the difference is nevertheless plausible. Older age, hypertension, and prior stroke, which accumulate at high CHA_2DS_2-VASc scores, are also components of the HAS-BLED bleeding score [18], and renal function was poorer in our very high-risk group. The patients at greatest risk of thromboembolism are therefore often those most exposed to hemorrhagic complications, and weighing these two risks remains one of the central difficulties of anticoagulation in this population [18, 19].

In-hospital mortality showed the same pattern as thromboembolic events: 14.3% of patients with scores ≥5 died, compared with 1.7% of those with lower scores, and the association remained after adjustment for dose and renal function (adjusted OR 7.7). Because every patient in our cohort received apixaban, this difference cannot be read as evidence for or against a treatment effect. In ARISTOTLE, apixaban reduced all-cause mortality compared with warfarin, and its benefit was consistent across levels of baseline stroke and bleeding risk [5, 7]. The excess deaths in our very high-risk group are more likely to reflect the burden of disease that accompanies a high score; older age, heart failure, and impaired renal function were all more frequent in this group and may contribute to mortality independently of thromboembolic events. Current guidelines recommend regular reassessment of patients with AF and their risk factors [2, 3], and our results suggest that patients with very high scores need particularly close follow-up.

Within the very high-risk group, prescribed dose was not significantly associated with thromboembolic events, bleeding, or mortality, but this comparison is difficult to interpret. Patients given 2.5 mg twice daily were older, lighter, and had lower creatinine clearance, which is the profile for which dose reduction is intended and also the profile of patients with a poorer prognosis. Confounding by indication is therefore likely and may explain the numerically higher mortality with 2.5 mg (19.2% vs 10.8%), for which the confidence interval was wide. The thromboembolic estimate changed direction after adjustment, largely because prior stroke was strongly associated with the outcome and was more common in the 5 mg group; this shows how sensitive a comparison of this size is to model specification, and a non-significant result cannot be taken to mean that the two doses are equivalent. These observations are consistent with the existing evidence on reduced-dose apixaban. In a subgroup analysis of ARISTOTLE, the effect of reduced-dose apixaban relative to warfarin on stroke or systemic embolism was not statistically significant, but that analysis was exploratory and the trial was not designed to compare the

two apixaban doses [5]. Observational studies have suggested that inappropriate dose reduction of direct oral anticoagulants may be associated with more strokes or systemic emboli and with higher mortality, probably reflecting both insufficient anticoagulation and the greater comorbidity of patients selected for lower doses [20, 21]. In the ORBIT-AF II registry, off-label underdosing occurred in approximately 9.4% of patients and was associated with more cardiovascular hospitalizations [22]. Whether the same applied in our cohort cannot be determined: without serum creatinine values, we could not tell whether dose reductions met labeled criteria, so appropriate dose reduction could not be separated from off-label underdosing.

For clinical practice, these findings argue for careful individual assessment rather than a change in dosing policy. In patients with very high scores, the choice of dose should take account of frailty [23], renal function [21, 24], and bleeding risk [18], in line with current guideline recommendations [2, 3]. Prospective multicenter studies that record every dose-reduction criterion and the timing of events are needed to establish whether outcomes in this population can be improved through closer attention to dosing.

This study has several limitations. First, its retrospective, single-center design limits causal inference and generalizability, and residual confounding is likely, particularly for the dose comparison. Second, event and follow-up dates were not available; outcomes are therefore reported as proportions rather than incidence rates, and the chronology of baseline prior stroke and subsequent thromboembolic events could not be independently verified. Because most patients with a recorded prior stroke also had a documented thromboembolic outcome (58 of 68), overlap between baseline history and outcome ascertainment is likely. The association between risk group and thromboembolic events disappeared when these patients were excluded, so the primary thromboembolic estimate should not be read as a measure of residual stroke risk during apixaban therapy. Third, bleeding severity was not consistently recorded, so major bleeding could not be classified according to International Society on Thrombosis and Haemostasis (ISTH) criteria, and thromboembolic events were not subclassified by type. Fourth, mortality was limited to deaths documented in the hospital record, and deaths elsewhere may have been missed. Fifth, serum creatinine values, dialysis status, interacting medications, adherence, and dose changes during follow-up were unavailable, preventing assessment of dose appropriateness. Sixth, 46 medical record numbers were repeated in the source data; each record was analyzed as a separate patient, which may introduce non-independence. Finally, the analyses were exploratory, covariates were selected post hoc, and the limited number of events, particularly deaths in the dose subgroup, reduced the precision of adjusted estimates.

Conclusions

Among apixaban-treated patients with AF, a CHA_2DS_2-VASc score ≥5 identified a subgroup with substantially higher in-hospital mortality and, after exclusion of patients with a recorded prior stroke, more frequent documented bleeding. The apparent excess of thromboembolic events was confined to patients with a recorded prior stroke and may reflect overlap between baseline history and outcome

recording; event timing should be verified before this association is interpreted. Within this very high-risk subgroup, prescribed apixaban dose was not significantly associated with outcomes, although the analysis could not assess dose appropriateness and was limited by sample size. These findings support close monitoring of patients with very high CHA_2DS_2-VASc scores and highlight the need for larger studies with complete dosing criteria and event timing.

Abbreviations

AF
atrial fibrillation
ARISTOTLE
Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation
CHA_2DS_2-VASc
congestive heart failure,hypertension,age ≥ 75 years,diabetes mellitus,prior stroke/transient ischemic attack/thromboembolism,vascular disease,age 65–74 years,sex category
CI
confidence interval
HAS-BLED
hypertension,abnormal renal/liver function,stroke,bleeding history or predisposition,labile international normalized ratio,elderly,drugs/alcohol
IQR
interquartile range
ISTH
International Society on Thrombosis and Haemostasis
OR
odds ratio
ORBIT-AF
Outcomes Registry for Better Informed Treatment of Atrial Fibrillation
RR
relative risk
STROBE
Strengthening the Reporting of Observational Studies in Epidemiology
TIA
transient ischemic attack

Declarations

Ethics approval and consent to participate

The study was approved by the Biomedical Research Ethics Committee of Umm Al-Qura University, Makkah, Saudi Arabia (Approval No. HAPO-02-K-012-2026-05-3412) and was conducted in accordance with the Declaration of Helsinki. Because of the retrospective design using existing medical records, individual informed consent was not obtained.

Consent for publication

Not applicable.

Availability of data and materials

The dataset analyzed during the current study is not publicly available because it contains information that could compromise the privacy of research participants, but it is available from the corresponding author on reasonable request.

Competing interests

The authors declare no competing interests.

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Authors' contributions

ASA: supervision, data curation, validation, writing – original draft, and writing – review and editing. AFA: conceptualization, methodology, project administration, resources, validation, visualization, writing – original draft, and writing – review and editing. SA: data collection, investigation, and writing – original draft. TNA: data collection, investigation, and writing – original draft. QHB: data collection, investigation, software, and writing – original draft. SAH: data collection, investigation, validation, and writing – original draft. FMH: methodology, validation, and writing – review and editing. SAlg: methodology, validation, and writing – review and editing. AMA: resources, validation, and writing – review and editing. EE: formal analysis, software, and writing – review and editing. MA: validation, visualization, and writing – review and editing. MAA: supervision, validation, and writing – review and editing. All authors read and approved the final manuscript.

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Tables

Table 1

Baseline characteristics according to CHA_2DS_2-VASc risk group

Characteristic	Overall (n = 596)	CHA_2DS_2-VASc 0–4 (n = 421)	CHA_2DS_2-VASc ≥ 5 (n = 175)	P
Age, years, median (IQR)	65 (58–74)	62 (53–70)	75 (67–79)	< 0.001
Female sex, n (%)	275 (46.1)	156 (37.1)	119 (68.0)	< 0.001
Weight, kg, median (IQR)	80.0 (68.0–92.0)	80.0 (70.0–95.0)	74.5 (67.0–87.5)	< 0.001
Creatinine clearance, mL/min, median (IQR)	76.3 (53.7–105.6)	83.5 (59.1–113.7)	63.3 (43.2–86.7)	< 0.001
Comorbidities, n (%)				
Hypertension	469 (78.7)	303 (72.0)	166 (94.9)	< 0.001
Diabetes mellitus	369 (61.9)	226 (53.7)	143 (81.7)	< 0.001
Prior stroke/TIA/thromboembolism	68 (11.4)	9 (2.1)	59 (33.7)	< 0.001
Vascular disease	231 (38.8)	133 (31.6)	98 (56.0)	< 0.001
Heart failure	260 (43.6)	140 (33.3)	120 (68.6)	< 0.001
Risk score and treatment				
CHA_2DS_2-VASc score, median (IQR)	4 (3–5)	3 (2–4)	5 (5–6)	< 0.001
Apixaban 5 mg twice daily, n (%)	426 (71.5)	324 (77.0)	102 (58.3)	< 0.001

Data are median (interquartile range) or n (%). P values were derived from the Mann–Whitney U test for continuous variables and the Pearson chi-square test for categorical variables. Height and body mass index are not reported because of inconsistent recorded values.

Abbreviations: CHA_2DS_2-VASc, congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, prior stroke/transient ischemic attack/thromboembolism, vascular disease, age 65–74 years, sex category; IQR, interquartile range; TIA, transient ischemic attack

Table 2

Clinical outcomes according to CHA_2DS_2-VASc risk group

Outcome	CHA_2DS_2-VASc 0–4 (n = 421)	CHA_2DS_2-VASc ≥ 5 (n = 175)	Crude OR (95% CI)	P	Adjusted OR (95% CI)[a]	P
Thromboembolic events	30 (7.1)	55 (31.4)	6.0 (3.7–9.7)	< 0.001	6.6 (3.9–11.0)	< 0.001
Bleeding events	197 (46.8)	96 (54.9)	1.4 (0.97–2.0)	0.07	1.3 (0.9–1.9)	0.11
In-hospital mortality	7 (1.7)	25 (14.3)	9.9 (4.2–23.3)	< 0.001	7.7 (3.2–18.5)	< 0.001

Data are n (%). ORs compare CHA_2DS_2-VASc ≥ 5 with 0–4 (reference). Outcomes are the number of patients with at least one documented event; bleeding includes events of any documented severity. Results after exclusion of patients with a recorded prior stroke are shown in Additional file 1: Table S2.

[a]Adjusted for prescribed apixaban dose (5 mg vs 2.5 mg twice daily) and creatinine clearance using multivariable logistic regression.

Abbreviations: CI, confidence interval; OR, odds ratio

Table 3

Baseline characteristics according to prescribed apixaban dose in patients with CHA_2DS_2-VASc ≥ 5

Characteristic	Overall (n = 175)	2.5 mg twice daily (n = 73)	5 mg twice daily (n = 102)	P
Age, years, median (IQR)	75 (67–79)	79 (72–81)	70 (65–77)	< 0.001
Female sex, n (%)	119 (68.0)	49 (67.1)	70 (68.6)	0.83
Weight, kg, median (IQR)	74.5 (67.0–87.5)	70.0 (64.0–79.0)	79.0 (68.6–91.0)	< 0.001
Creatinine clearance, mL/min, median (IQR)	63.3 (43.2–86.7)	51.6 (34.8–73.8)	71.2 (55.5–98.3)	< 0.001
Comorbidities, n (%)				
Hypertension	166 (94.9)	71 (97.3)	95 (93.1)	0.31[a]
Diabetes mellitus	143 (81.7)	58 (79.5)	85 (83.3)	0.51
Prior stroke/TIA/thromboembolism	59 (33.7)	17 (23.3)	42 (41.2)	0.01
Vascular disease	98 (56.0)	37 (50.7)	61 (59.8)	0.23
Heart failure	120 (68.6)	49 (67.1)	71 (69.6)	0.73
Risk score				
CHA_2DS_2-VASc score, median (IQR)	5 (5–6)	6 (5–6)	5 (5–6)	0.49

Data are median (interquartile range) or n (%). P values were derived from the Mann–Whitney U test for continuous variables and the Pearson chi-square test for categorical variables, except where indicated.

[a]Fisher's exact test.

Abbreviations: CHA_2DS_2-VASc, congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, prior stroke/transient ischemic attack/thromboembolism, vascular disease, age 65–74 years, sex category; IQR, interquartile range; TIA, transient ischemic attack

Table 4

Clinical outcomes according to prescribed apixaban dose in patients with CHA_2DS_2-VASc ≥ 5

Outcome	2.5 mg twice daily (n = 73)	5 mg twice daily (n = 102)	Crude OR (95% CI)	P	Adjusted OR (95% CI)[a]	P
Thromboembolic events	19 (26.0)	36 (35.3)	1.6 (0.8–3.0)	0.19	0.4 (0.1–1.4)	0.14
Bleeding events	41 (56.2)	55 (53.9)	0.9 (0.5–1.7)	0.77	1.5 (0.7–3.4)	0.35
In-hospital mortality	14 (19.2)	11 (10.8)	0.5 (0.2–1.2)	0.12	Not estimated[b]	—

Data are n (%). ORs compare 5 mg with 2.5 mg twice daily (reference). Dose appropriateness could not be assessed because serum creatinine values were not available.

[a]Adjusted for age, weight, creatinine clearance, and prior stroke using multivariable logistic regression; these estimates were sensitive to the inclusion of prior stroke and should be interpreted with caution.

[b]Not estimated because the 25 deaths were insufficient to support the covariate set.

Abbreviations: CI, confidence interval; OR, odds ratio

Supplementary Files

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- Additionalfile1.docx