

Original Article

Clinical Event Rates and Patient Satisfaction with Generic Rivaroxaban in Atrial Fibrillation: The Prospective Guardian Study

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ABSTRACT

Background The use of oral anticoagulants (OACs), especially direct oral anticoagulants (DOACs), for thromboprophylaxis in atrial fibrillation (AF) has increased over the last decade, and an increasing number of generic DOAC medications (particularly regarding rivaroxaban and apixaban) have been marketed recently. The aim of the present study was to prospectively observe clinical event rates and patient satisfaction with a generic rivaroxaban for thromboprophylaxis in patients with AF.

Methods Adult patients with AF in whom long-term OAC was indicated for thromboprophylaxis were included in this international, prospective, non-interventional, observational study with 1-year follow-up, conducted in the Republic of Serbia and Bosnia and Herzegovina. Data were collected at baseline and 3-, 6-, and 12-month follow-up visits. The primary endpoints were stroke/systemic embolism (SE), major bleeding, and all-cause mortality. Secondary endpoints included adverse events and patient satisfaction with generic rivaroxaban therapy.

Results Of 1092 patients (mean age 67.9 ± 9.8 , 42.9% female), 72 (6.6%) discontinued the treatment due to different reasons. The mean value of the CHA₂DS₂-VASC score (Congestive heart failure, Hypertension, Age ≥ 75 years, Diabetes mellitus, Stroke, Vascular disease, Age 65–74 years, Sex category) and HAS-BLED (Hypertension [uncontrolled], Abnormal renal and/or liver function, Stroke history, Bleeding history, Labile International Normalised Ratio, Elderly [>65 years], Drugs [non-steroidal anti-inflammatory drugs, aspirin]/Alcohol use [>8 drinks per week]) score was 3.15 ± 1.55 and 1.18 ± 0.92 , respectively. Overall, seven patients (0.64%) experienced a symptomatic thromboembolic event (two strokes, three transient ischaemic attack, and two SE), and major bleeding occurred in two patients (0.18%). At the 3-, 6- and 12-month follow-up visits, 1068 (97.8%), 1031 (94.4%) and 1014 participants (92.9%), respectively, were still taking generic rivaroxaban. At 3 and 12 months, 1024/1071 patients (95.6%) and 1005/1020 (98.5%), respectively, were very satisfied or satisfied with generic rivaroxaban.

Conclusions The observed clinical event rates during the use of generic rivaroxaban in AF patients were low, with very good 1-year persistence to treatment and persistently high level of patient satisfaction with generic rivaroxaban, including those previously taking another OAC. More studies with larger sample size are needed to allow additional analyses of factors associated with specific outcomes, including non-persistence to treatment with generic rivaroxaban.

Keywords atrial fibrillation, rivaroxaban, patient satisfaction, persistence to treatment

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Introduction

Atrial fibrillation (AF) poses a significant burden to patients, physicians, and health care system, owing to a significant morbidity and mortality associated with this most prevalent sustained cardiac arrhythmia among adults.^{1–3}

Thromboembolic ischaemic stroke or systemic embolism (SE) is a deleterious complication of AF, often being fatal or associated with significant permanent disability.^{4,5} Numerous advances in the detection and management of AF have been accomplished in recent years,^{2,3} including the management of stroke risk and thromboprophylaxis in patients with AF.⁵ In-line

with these improvements, substantial decline in the rates of stroke/SE and stroke fatality have been reported worldwide (for example, by 34% in the United States)⁶ as well as in Europe.⁷

Contemporary approach to effective stroke prevention in patients with AF includes concomitant cardiovascular risk factors/comorbidity management for and consideration of potential contribution of successful early rhythm control.^{8–10} Notwithstanding the advances in non-pharmacological stroke prevention treatments,¹¹ oral anticoagulant (OAC) therapy, either vitamin K antagonists (VKAs) or direct oral inhibitor anticoagulants (DOACs), remains a cornerstone of effective thromboprophylaxis in patients with AF in clinical practice worldwide.^{1–3}

While the overall use of OAC (particularly DOACs) for stroke prevention in patients with AF substantially increased during the last decade,^{12–14} the rates of OAC-related major or fatal bleeding remained broadly constant or slightly declined.^{6,7} While bleeding still remains a concern, other issues such as affordability (depending on the local reimbursement policy) and long-term adherence to treatment¹⁵ are being increasingly considered an unmet need in stroke prevention in patients with AF.

In recent years, increasing number of generic DOAC medications (particularly regarding rivaroxaban and apixaban) has been marketed. The aim of the present study was to prospectively observe clinical event rates and patient satisfaction with a generic rivaroxaban for thromboprophylaxis in patients with AF.

Methods

This international, multicentre, prospective, non-interventional, observational study with 1-year follow-up was conducted in secondary and tertiary health care centres in the Republic of Serbia and Bosnia and Herzegovina.

Inclusion and Exclusion Criteria

Adult patients (age ≥ 18 years) with confirmed diagnosis of AF in whom long-term OAC therapy was indicated for the prevention of AF-related thromboembolism were included in the study, whether being OAC-naïve (i.e., were not taking OAC before) or already treated with an OAC (except rivaroxaban) but unsatisfactorily (e.g., poorly controlled or experiencing adverse events). Concomitant treatment with aspirin and/or a P2Y₁₂ inhibitor for coronary artery disease was not an exclusion criterion. Eligible patients were included only if managed by a cardiologist. All participants provided a signed informed consent at enrolment, and the study has been approved by respective Institutional Review Board in each participating centre.

Patients were excluded if participating in other clinical study, deemed unable to follow clinical practice for any reason, had an active clinically significant bleeding or any other contraindication to OAC in line with contraindications in Summary of product characteristics of Xerdoxo (generic rivaroxaban), or had a medical condition considered to be a significant risk for major bleeding (e.g., active or recent gastrointestinal ulceration, presence of malignant neoplasms at high risk of bleeding, recent brain or spinal injury, recent brain, spinal or ophthalmic surgery, recent intracranial haemorrhage, known or suspected oesophageal varices, arteriovenous malformations, vascular aneurysms or major

intraspinal or intracerebral vascular abnormalities, hepatic disease associated with coagulopathy and clinically relevant bleeding risk, including cirrhotic patients with Child–Pugh B and C). Patients were also excluded if on concomitant treatment with any other anticoagulants, for example, unfractionated heparin (UFH), low-molecular-weight heparins, heparin derivatives (fondaparinux, etc.), OAC (warfarin, dabigatran etexilate, apixaban, etc.) except under specific circumstances of switching anticoagulant therapy or when UFH is given at doses necessary to maintain an open central venous or arterial catheter. Female participants who were breastfeeding or pregnant or who were planning pregnancy in the next 12 months were also excluded.

Data Collection

Data were collected at baseline (study enrolment) and during follow-up visits at 3, 6 and 12 months, using an electronic case report form.

At baseline, data on patient's demographics (age, sex, weight, height), smoking history and alcohol consumption, date of AF diagnosis, stroke and bleeding risk factors, medical history (comorbidities, thromboembolic events, major and non-major bleeding events), previous treatment of AF and previous concomitant treatment, initiated or continuing dose of generic rivaroxaban and continuing concomitant treatment were collected. The CHA₂DS₂–VASC score (Congestive heart failure, Hypertension, Age ≥ 75 years, Diabetes mellitus, Stroke, Vascular disease, Age 65–74 years, Sex category) was calculated for stroke risk assessment, and the HAS–BLED score (Hypertension [uncontrolled], Abnormal renal and/or liver function, Stroke history, Bleeding history, Labile International Normalised Ratio [INR], Elderly [> 65 years], Drugs [non-steroidal anti-inflammatory drugs, aspirin]/Alcohol use [> 8 drinks per week]) was calculated for the bleeding risk assessment.

During the follow-up visits, information about continuation of treatment with generic rivaroxaban, changes in concomitant treatment, and information about study primary endpoints (i.e., thromboembolic events, major and non-major bleeding events) and secondary endpoints (i.e., adverse events, patient's and investigator's general satisfaction with generic rivaroxaban therapy) were collected at each follow-up visit.

Study Medication

At baseline visit, all enrolled patients were prescribed generic rivaroxaban Xerdoxo¹⁶ (produced by Krka, d. d., Novo Mesto, Slovenia) 20 mg once daily, or 15 mg once daily when the creatinine clearance, as calculated using the Cockcroft–Gault formula, was < 50 mL/min. In patients switching from a VKA to generic rivaroxaban, VKA was first discontinued, and generic rivaroxaban was started when the INR was below 2.5. In patients switching from a twice daily DOAC to generic rivaroxaban, the latter is first administered at the time of the morning dose of previously used DOAC and continued once daily thereafter.¹⁷

Study Endpoints

Primary endpoints were thromboembolic events (stroke, transient ischaemic attack [TIA] or SE), major bleeding, clinically relevant non-major (CRNM) bleeding and mortality. According to the

International Society on Thrombosis and Haemostasis (ISTH), major bleeding was defined as clinically significant haemorrhage that is fatal, occurs in critical areas (brain, spinal cord, eye, heart, joints, retroperitoneal space or intramuscular with compartment syndrome) or causes a significant drop in haemoglobin (≥ 2 g/dL or ≥ 20 g/L) requiring transfusion of ≥ 2 units of blood,¹⁸ and CRNM bleeding as any sign or symptom of haemorrhage that does not fit the definition of a major bleeding but meets one of the following criteria: It requires medical intervention by a health care professional and leads to hospitalisation or increased level of care or prompts a face-to-face intervention.¹⁹ A detailed documentation (e.g., physician's written report, imaging and biochemistry test reports) were required for each primary outcome event.

Secondary endpoints were other adverse events observed during the study (including minor bleeds) and investigator's satisfaction with generic rivaroxaban therapy, which was assessed using a Likert scale. Patient self-reported satisfaction with generic rivaroxaban therapy was measured using a modified Treatment Satisfaction Questionnaire Version 2, section addressing global satisfaction with the medication of interest²⁰ (Supplementary Table S1).

Statistical Analyses

Summary data are presented as number and percentage for categorical variables, and mean, median, standard deviation, minimum and maximum, first and third quartile for continuous variables.

For inferential assessment of proportions, the two-sided 'equal-tails' Clopper–Pearson exact 95% confidence interval was employed. For the assessment of means and mean differences, the standard 95% confidence interval for the mean (with unknown variance) based on the limiting distribution of the standardised sample mean was employed.

The analyses were done on observed data only. No methods for the imputation of missing data were planned.

Data were analysed using SPSS 31.0.0.0. Microsoft Office Excel 365 was used for the preparation of tables.

Results

The study was conducted in 14 secondary or tertiary health care centres (4 centres in Republic of Serbia and 10 in Bosnia and Herzegovina). During the 1-year study enrolment period (from September 2022 to September 2023), a total of 1118 patients were enrolled in the study. Of those, 26 (2.3%) were excluded owing to a study protocol deviation, whereas 1092 patients (97.7%) were included in the present analysis (622 patients [57.0% from Bosnia and Herzegovina and 470 patients [43.0%] from the Republic of Serbia).

Patient Demographics and Clinical Characteristics

Study cohort data at baseline are shown in Table 1.

Most patients (821, 75.2%) were younger than 75 years, and female patients were significantly older compared with males (mean age 69.9 ± 8.8 vs. 66.5 ± 10.1 years, $p < 0.001$; Fig. 1).

Regarding cardiovascular risk factors, hyperlipidaemia and overweight/obesity were strikingly prevalent in the study cohort (notably, there were 255 [23.4%] obese patients).

Almost all patients (95.2%) had at least one comorbidity, most commonly hypertension, whereas 787 patients (72.1%) were multimorbid (Table 1).

The mean CHA₂DS₂–VASc score value was 3.15 ± 1.55 , and the mean HAS–BLED was 1.18 ± 0.92 . Fig. 2 shows the stroke and bleeding risk profile of the study cohort. Most patients were at moderate-to-high risk of stroke and low-to-moderate risk of bleeding (Table 1 and Fig. 2).

Nearly half of the study cohort (41.2%) had a first-diagnosed AF, and 60.1% of participants were OAC-naïve (Table 1). Among OAC-experienced patients, majority were taking a VKA before enrolment in the present study (Table 1).

Concomitant medication use at baseline is shown in Table 1. Beta blockers and ACEi were the most used drugs, whereas around 5% of patients were using aspirin or P2Y₁₂ inhibitor, each. Concomitant use of NSAIDs was low (0.4%).

Primary Endpoints

The rate of stroke/SE was low during the study follow-up period. Overall, seven patients (0.64%) experienced a symptomatic thromboembolic event (Table 2). Of those, two patients experienced thromboembolic ischaemic stroke (the incidence rate of 1.62 strokes per 1000 patient-years), three patients experienced a TIA, and two patients experienced an SE event. The incidence rate of symptomatic thromboembolic event per 1000 patient-years increased with increasing patient age (Table 2).

Overall, two patients (0.18%) experienced a major bleeding event during the follow-up period and were observed among patients older than 70 years. Both major bleedings were melæna. No intracranial or fatal major bleeding occurred during the study.

CRNM bleeding events were observed in a total of 14 patients (1.3%), resulting in a change of antithrombotic therapy in 8 patients (0.7%). In five patients, the drug was withdrawn, and in three patients the dose was reduced.

During the follow-up, eight patients died (0.7%). There was one death from stroke (thromboembolic event), one from arrhythmic death and six deaths from non-cardiovascular causes (e.g., malignancy, infection or other).

Secondary Endpoints

At baseline, 1092 participants (100%) were prescribed generic rivaroxaban. Most participants ($n = 910$, 83.3%) were prescribed a dose of 20 mg once daily, whereas 182 participants (16.7%) were prescribed 15 mg once daily.

At 3-, 6- and 12-month follow-up visits, 1068 (97.8%), 1031 (94.4%) and 1014 participants (92.9%), respectively, were still taking generic rivaroxaban. The proportion of patients receiving the 15 mg dose of generic rivaroxaban remained broadly constant throughout the study ($n = 180$ [16.5%] at the 3-month follow-up visit, and $n = 170$ [15.6%] at the 6- and 12-month follow-up visit, each).

Details on further OAC therapy after the baseline visit were not available for six patients (0.5%). Treatment with generic rivaroxaban was permanently discontinued in 72 patients (6.6%). The

Table 1 Study cohort data at baseline.

Variable	All, N = 1,092 (100%)	Variable	All, N = 1,092 (100%)
Demographics		AF-related features	
Age (years)	67.93 ± 9.75 (range 31–90)	First-diagnosed AF	450 (41.2)
<65	333 (30.5)	OAC-naïve patients	662 (60.6)
65–74	488 (44.7)	Prior VKA use	280 (25.6)
75–80	183 (16.8)	Prior dabigatran use	92 (8.4)
>80	88 (8.1%)	Prior apixaban use	51 (4.7)
Female sex	468 (42.9)	Prior LMWH use	7 (0.6%)
Cardiovascular risk factors		Concomitant medication	
BMI (kg/m ²)	27.68 ± 3.78 (range 18–50)	Aspirin	49 (4.5)
Overweight or obese	842 (77.1)	P2Y12 inhibitor	60 (5.5)
Smoker	191 (17.5)	Beta blocker	932 (85.3)
Previous smoker	250 (22.9)	Verapamil or diltiazem	7 (0.6)
Hyperlipidaemia	531 (48.6)	Digitalis	68 (6.2)
Comorbidity		Amiodarone	222 (20.3)
Any comorbidity	1040 (95.2)	Propafenone	59 (5.4)
Hypertension	963 (88.2)	Flecainide	70 (6.4)
Coronary artery disease	254 (23.3)	Sotalol	11 (1.0)
Diabetes mellitus	250 (22.9)	ACEi	695 (63.6)
Heart failure	281 (25.7)	ARB	159 (14.6)
Prior stroke/TIA	94 (8.6)	Sacubitril/valsartan	60 (5.5)
Renal impairment	79 (7.2)	MRA	171 (15.7)
Obstructive sleep apnoea	7 (0.6)	Diuretic	351 (32.1)
Multimorbidity	787 (72.1)	SGLT2 inhibitor	84 (7.7)
Stroke and bleeding risk		Dihydropyridine CCB	295 (27.0)
CHA ₂ DS ₂ –VASc score	3.15 ± 1.55 (range 0–9)	NSAID	4 (0.4)
HAS–BLED score	1.18 ± 0.92 (range 0–6)	PPI	42 (3.8)
		Statins	512 (46.9)

Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin receptor blocker; BMI, body mass index; CCB, calcium channel blocker; CHA₂DS₂–VASc, (Congestive heart failure, Hypertension, Age ≥75 years, Diabetes mellitus, Stroke, Vascular disease, Age 65–74 years, Sex category); HAS–BLED, (Hypertension [uncontrolled], Abnormal renal and/or liver function, Stroke history, Bleeding history, Labile International Normalised Ratio, Elderly [>65 years], Drugs [non-steroidal anti-inflammatory drugs, aspirin]/Alcohol use [>8 drinks per week]); LMWH, low-molecular-weight heparin; MRA, mineralocorticoid receptor antagonist; NSAID, non-steroidal anti-inflammatory drug; OAC, oral anticoagulant; PPI, proton pump inhibitor; TIA, transient ischaemic attack; VKA, vitamin K antagonist; SGLT2, sodium/glucose co-transporter 2.

reasons for discontinuation were death (8 patients), occurrence of contraindication to treatment (3 patients), treatment was not needed any more (4 patients), safety (15 patients) and other reasons (42 patients, among them patient's decision to stop the treatment, unaffordable price, patients were not coming to the visit, etc.).

A total of 51 patients (4.7%) experienced adverse events throughout the study. Adverse events were not related to the study medicine in 18 (1.7%) patients. Thirty-three (3.0%) patients experienced adverse reactions (drug-related adverse events), 24 patients (2.2% of the cohort, or 72.7% of patients experiencing adverse reactions) experienced one or more bleeding events. Of a total of 33 bleeding events, 9 (27.3%) were gastrointestinal bleeds (2 major bleedings – melaena; 5 CRNM bleedings – 2 haematochezia, 1 gastrointestinal haemorrhage, 1 gastric ulcer haemorrhage and 1 rectal haemorrhage; 2 minor gingival bleedings), 8 minor nose bleeds (24.2%), 4 cases of haematuria (12.1%) defined as CRNM bleedings and 12 cases (33.3%) of other CRNM or minor bleeds (e.g., pronounced bruising, prolonged bleeding at the site of skin puncture, etc.). Bleeding resulted in permanent generic rivaroxaban discontinuation in eight patients (0.7% of the cohort, or 33.3% of patients experiencing a bleeding).

Regarding the overall patient's satisfaction with generic rivaroxaban therapy, data were available for 1071 patients, 1038 patients and 1020 patients at the 3-, 6- and 12-month follow-up visit, respectively. Most patients were very satisfied or satisfied with generic rivaroxaban therapy, and patient's overall satisfaction with generic rivaroxaban therapy remained broadly comparable during the study follow-up period (**Fig. 3**).

Data regarding the physicians' overall satisfaction with generic rivaroxaban therapy was available for 1072, 1037 and 1024 patients at the 3-, 6- and 12-month follow-up visit, respectively. Most physicians were very satisfied or satisfied with generic rivaroxaban therapy, and their level of satisfaction remained broadly constant throughout the study period (**Fig. 4**).

Compared with patients using generic rivaroxaban therapy, a higher proportion of prescribing physicians were very satisfied, slightly lower proportion of physicians were satisfied, and a higher proportion of patients were neutral ($p < 0.001$), while the level of dissatisfaction with generic rivaroxaban therapy was broadly comparable between patients and physicians at each follow-up visit (**Figs. 3 and 4**).

Among patients who were using OAC therapy before the present study, patient's satisfaction with generic rivaroxaban therapy in comparison to previously used OAC agent was also evaluated. For this assessment, data were available for 391, 371 and 338 patients at the 3-, 6- and 12-month follow-up visit, respectively (**Fig. 5**).

Most patients felt that their satisfaction with OAC treatment was very much improved or improved after switching from previously used OAC agent to generic rivaroxaban therapy, and the self-reported level of satisfaction remained broadly constant throughout the study (**Fig. 5**).

Of note, within the very much improved and improved group, there was a total of 233/280 (83.2%) prior VKA users, 75/90 (83.3%) prior dabigatran users and 40/51 (78.4%) prior apixaban users ($p < 0.001$).

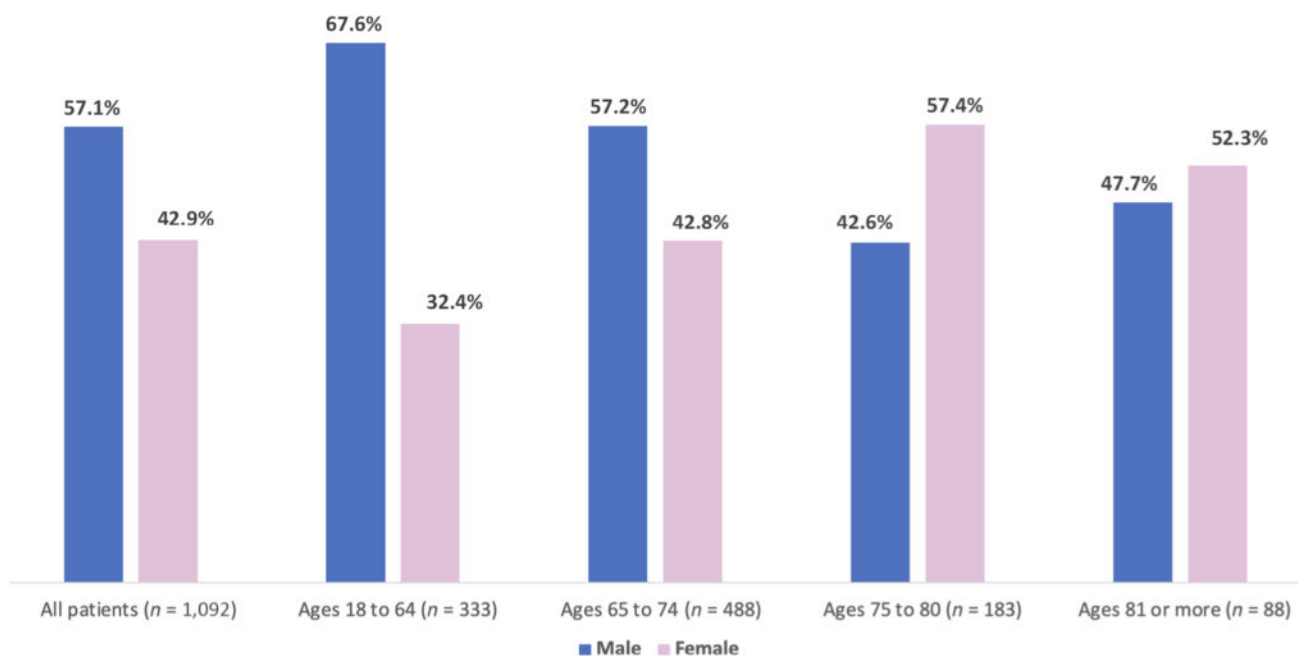
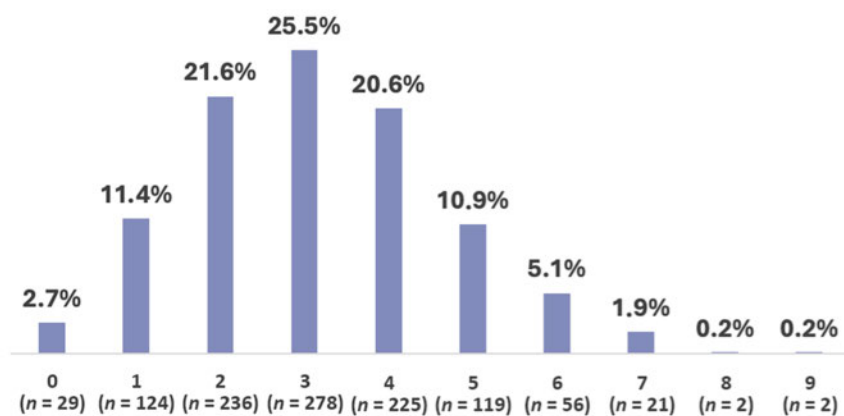


Fig. 1 Distribution of age groups by sex.

CHA₂DS₂-VASc Score



HAS-BLED Score

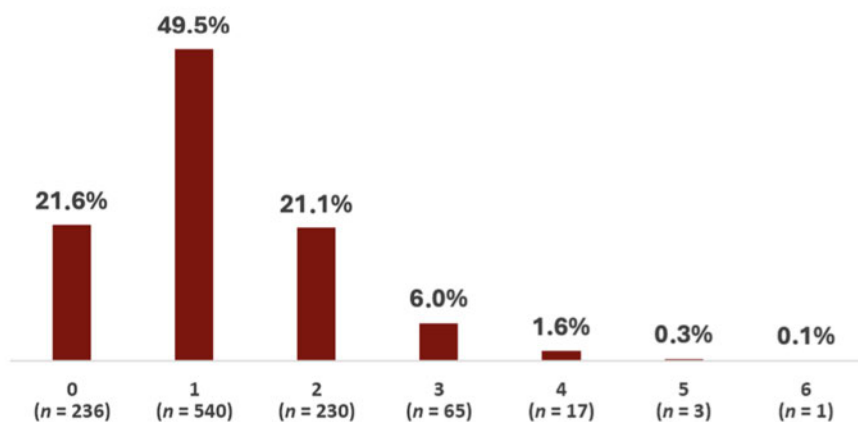


Fig. 2 Stroke and bleeding risk at baseline.

Table 2 Thromboembolic events during the study (overall and by age groups).

	Number of patients	PY	Number of patients with TE	IR per 1000 PY	95% CI
All patients	1,092	1,237.6	7	5.66	[1.8, 10.6]
Age (years)					
18–64	333	381.0	1	2.62	[0.1, 14.6]
65–74	488	552.9	2	3.62	[0.4, 13.1]
75–80	183	205.8	3	14.58	[1.2, 35.1]
≥81	88	97.9	1	10.21	[0.3, 56.9]

Abbreviations: CI, confidence interval; IR, incidence rate; PY, patient-years; TE, thromboembolic event.

Discussion

The main findings of the present international prospective, non-interventional, observational study on clinical event rates and patient satisfaction with generic rivaroxaban therapy were (1) very low stroke/SE and major bleeding rates and (2) persistently high levels of patients' satisfaction with generic rivaroxaban therapy during the 1-year follow-up. These findings are reassuring overall regarding the use of generic rivaroxaban and add information about observed event rates with generic rivaroxaban Xerdrox in clinical practice.

Baseline study cohort characteristics were mostly comparable with other contemporary 'general' AF cohorts worldwide, including, for example, a high prevalence of multimorbidity (72%),²¹ and overweight (53.7%) or obese patients (23.4%).²² As is usually observed in the Eastern European AF cohorts,^{13,23,24} patients in the present study were younger than in other regions of Europe.

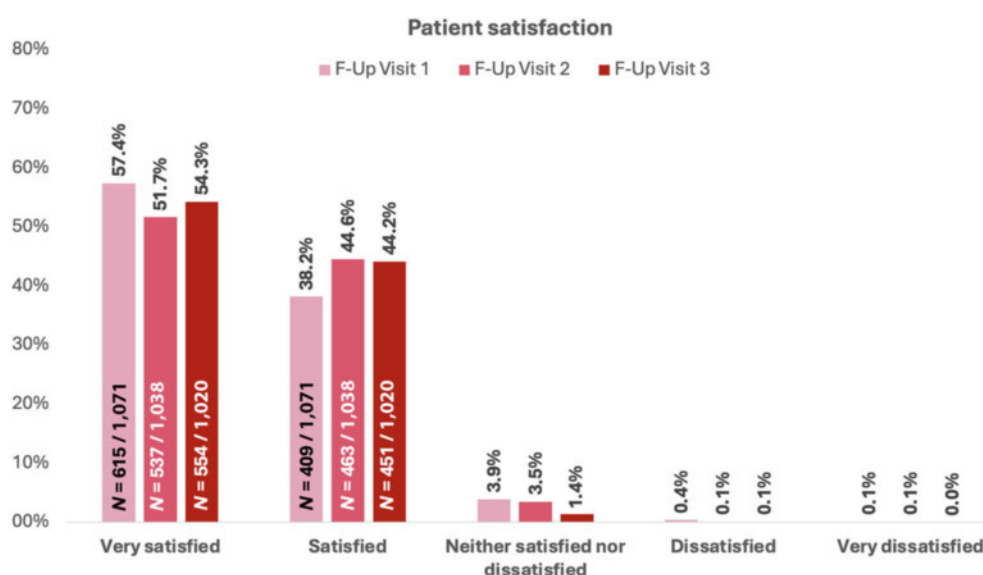
The study cohort in the present study also broadly resembles the cohort of the first prospective postapproval observational study of rivaroxaban (Xarelto) for stroke prevention in AF.²⁵ The mean CHA₂DS₂-VASC score value was comparable in the two studies (3.15 vs. 3.4), but the proportion of patients with a history of prior stroke in the present study was far lower (8.6%) than in the XANTUS study (19.0%)²⁵ or pivotal DOACs trials, where the proportion of such patients was 20.0% in the RE-LY,²⁶ 19.4% in the ARISTOTLE,²⁷ 54.9% in the ROCKET-AF²⁸ and 28.3% in the ENGAGE AF-TIMI 48 trial.²⁹

Not all stroke risk factors carry the same weight, with a history of prior stroke and advanced age being the most powerful single risk factors.^{5,30} The very low stroke/SE rate (0.57 per 100 patient-years) observed in the present study, which is substantially lower compared with stroke rates observed in the XANTUS study (1.7 per 100 patient-years),²⁵ could be at least partially attributed to different specific stroke risk factor prevalence in the two studies.

In the present study, participants were recruited from the secondary and tertiary health care centres and managed exclusively by a cardiologist. Likely more prevalent guideline-adherent overall management of AF, including the management of stroke risk factors (compared with AF management by non-cardiologists), could also contribute to very low stroke rates observed in the present study.

The prevalence of major bleeding during the present study was very low as well (0.18%), much lower than in the XANTUS study (1.9%)²⁵ or the ROCKET-AF trial (5.6%).²⁸ In contrast to the latter two studies, there were no intracranial or fatal major bleeding events in the present study. The rates of CRNM bleeding and minor bleeds (1.3% and 1.0%, respectively) were also substantially lower compared with observations in the XANTUS study.²⁵

All-cause mortality rates in the present study were very low (0.7%) and mostly driven by non-cardiovascular causes (0.5%).

**Fig. 3** Patient's overall satisfaction with generic rivaroxaban therapy. F-Up, follow-up.

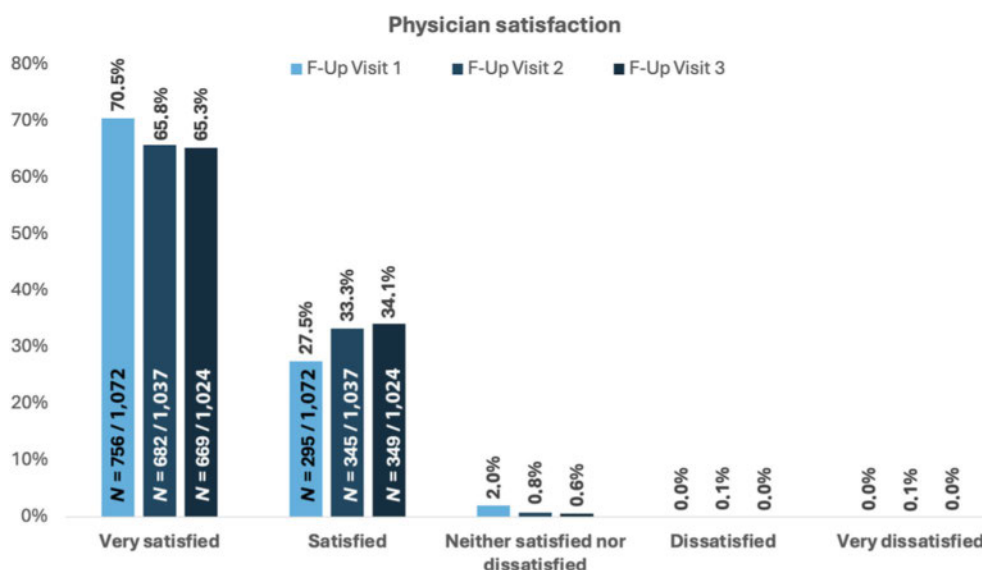


Fig. 4 Physician's overall satisfaction with generic rivaroxaban therapy. F-Up, follow-up.

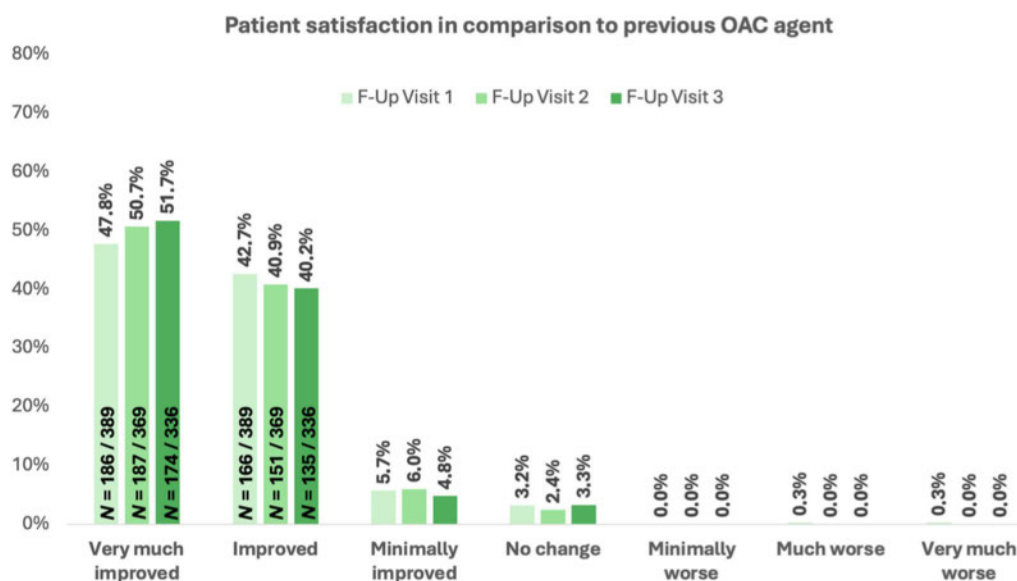


Fig. 5 Patient's overall satisfaction with generic rivaroxaban therapy in comparison to previous OAC agent. F-Up, follow-up; OAC, oral anticoagulant.

As with stroke and bleeding, mortality was substantially lower in the present study compared with XANTUS study.²⁵

In line with a large body of evidence showing that OAC therapy is effective and reasonably safe in thromboprophylaxis in AF patients,^{1–3,5} low clinical event rates were observed in the present study. However, with increasing use of OAC (especially DOACs) in AF patients,³¹ declining rates of stroke and bleeding rates remaining relatively constant,^{6,7} adherence and persistence to OAC have been increasingly recognised as a major challenge in optimal stroke prevention in patients with AF.¹⁵

In the present study, generic rivaroxaban was permanently discontinued in a total of 6.6% of patients at the end of 1-year follow-up. This is a much lower 1-year rate of discontinuation than those observed in, for example, the Dresden Registry (15%)³² or the XANTUS study (20%).²⁵ In the two recent systematic reviews addressing adherence and persistence to OAC therapy among AF patients, adherence to rivaroxaban was good (73% and 70%).^{33,34} There are multiple factors influencing non-adherence.¹⁵ In a recent study, for example, the leading causes of OAC non-prescription listed by the responsible physicians were low AF burden, patient

refusal, estimated low risk of stroke, high risk of fall and high bleeding risk.³⁵ Notably, international guidelines on the management of AF clearly specify that the anticipated risk of fall is not an independent predictor of OAC-related bleeding and the risk of falling does not outweigh the benefits of OAC in elderly patients with AF.¹

Major international guidelines also emphasise that estimated bleeding risk in itself should not preclude consideration of OAC use in AF patients, provided that modifiable bleeding risk factors are identified and addressed, and patients with non-modifiable bleeding risk factors are scheduled for more frequent clinical follow-up.^{1–3} In the present study, the risk of bleeding was estimated using the HAS-BLED score, which has been the most extensively validated bleeding risk score in AF cohorts worldwide.³⁶ Of note, the use of the recently proposed and validated DOAC score³⁷ could have been considered, since all patients in the present study were taking rivaroxaban. However, a recent comparison of the HAS-BLED and DOAC scores showed that both scores had a modest predictive ability for major bleeding events, while the DOAC score had poorer calibration for high-risk patients.³⁸

It has been reported earlier that the significance of minor bleeding events, such as nose bleeding, excessive bruising, etc., is often overestimated by patients and general practitioners, resulting in OAC discontinuation, which is an important unmet need for education of both patients and physicians.³⁹ In the present study, generic rivaroxaban was discontinued in only one participant who experienced one or more minor bleeding events.

The low drug discontinuation rate observed in the present study corresponds well with a high level of patient-reported satisfaction with generic rivaroxaban therapy (96.5% of patients were very satisfied or satisfied with generic rivaroxaban therapy at 3 months), which remained broadly constant throughout the study. The proportion of very satisfied or satisfied patients was greater than in the XANTUS study,²⁵ and the present study provided additional insight into the persistence of patient satisfaction with OAC over time. In the analysis restricted to patients previously taking another OAC, most patients (90.5%) reported that their satisfaction with OAC treatment was very much improved or improved after switching to generic rivaroxaban, and the proportion of patients with very much increased satisfaction gradually increased throughout the study. The improved satisfaction with generic rivaroxaban was slightly more prevalent among prior VKA or dabigatran users in comparison to prior apixaban users. The observed high levels of patient satisfaction with OAC therapy in the present study generally resemble findings previously reported in other studies.⁴⁰ Studies reporting patient satisfaction with OAC therapy are generally limited by a small sample size, relatively short-term observation, retrospective design, the use of satisfaction measurement tools which have not been validated, etc.⁴¹ Whereas studies comparing patient satisfaction with DOACs versus VKAs reported conflicting results,⁴¹ several studies showed that patients taking rivaroxaban were more satisfied than patients taking other OAC agents, but patient-related factors associated with those findings were not reported.^{40,42} A recent Canadian study using validated instruments for measurement of satisfaction suggested that the convenience of rivaroxaban use was a major contributor to greater satisfaction compared with

VKAs,⁴² while another registry-based study from Japan reported similar findings when rivaroxaban was compared with other DOACs in patients with AF.⁴³

The limitations of the present study include those inherent to its observational design. In addition to the patient selection bias, the single-arm, open-label study design could introduce bias related to knowledge about treatment, and the use of the questionnaires assessing physician and patient satisfaction with generic rivaroxaban could introduce additional, questionnaire-related biases. Although persistence to treatment could be indirectly assessed through treatment discontinuation rate, a formal assessment of adherence to generic rivaroxaban was not possible. The very low observed clinical event rates in the present study could, at least partly, be influenced by a possibility of event underreporting or incomplete event ascertainment. Owing to the low primary outcome events rate observed in the present study, no further analyses or adjustments for baseline characteristics were not conducted beyond description. The strengths of the present study include its prospective design, providing more complete data compared with retrospective studies, and a contemporary cohort with a meaningful sample size.

Conclusions

In the present study of generic rivaroxaban Xerdexo for stroke prevention in patients with AF in clinical practice, low clinical event rates and very good 1-year persistence to treatment with persistently high level of patient satisfaction with Xerdexo, including those previously taking another OAC agent, were observed. These reassuring observations highlight the benefits of generic option of rivaroxaban that delivers real-world evidence in patient care. More studies with larger sample size are needed to allow additional observations of generic rivaroxaban use in specific high-risk AF populations and factors associated with specific outcomes including non-persistence to treatment with generic rivaroxaban.

What is Known on This Topic?

- Similarly to recent reports, we observed low stroke and bleeding rates among unselected patients with AF taking rivaroxaban
- The 1-year persistence to rivaroxaban was very good in this study, broadly resembling earlier reports.

What this paper add?

- The low observed event rates over 1-year follow-up in this study are reassuring regarding the use of generic rivaroxaban in patients with AF in clinical practice.
 - The present study provided evidence on persistently high patients' and physicians' satisfaction with generic rivaroxaban over 1 year follow-up.
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Statements and Additional Information

Conflict of Interest The authors declare that they have no conflict of interest.

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References

- 1 Hindricks G, Potpara T, Dagres N, et al. 2020 ESC guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): the task force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC). Developed with the special contribution of the European heart rhythm association (EHRA) of the ESC. *Eur Heart J* 2021;42(05):373–498
- 2 Van Gelder IC, Rienstra M, Bunting KV, et al. 2024 ESC guidelines for the management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J* 2024;45(36):3314–3414
- 3 Joglar JA, Chung MK, Armbruster AL, et al. 2023 ACC/AHA/ACCP/HRS guideline for the diagnosis and Management of Atrial Fibrillation: a report of the American College of Cardiology/American Heart Association joint committee on clinical practice guidelines. *Circulation* 2024;149(01):e1–e156
- 4 Elsheikh S, Hill A, Irving G, Lip GYH, Abdul-Rahim AH. Atrial fibrillation and stroke: state-of-the-art and future directions. *Curr Probl Cardiol* 2024;49(1 Pt C):102181
- 5 Chao TF, Potpara TS, Lip GYH. Atrial fibrillation: stroke prevention. *Lancet Reg Health Eur* 2024;37:100797
- 6 Noubiap JJ, Tang JJ, Dewland TA, Marcus GM. Contemporary trends in incident ischaemic stroke, intracranial haemorrhage, and mortality in individuals with atrial fibrillation. *Eur Heart J Qual Care Clin Outcomes* 2025;11(03):228–238

- 7 Komen JJ, Hunt NB, Pottegård A, et al. Heterogeneity after harmonisation: a retrospective cohort study of bleeding and stroke risk after the introduction of direct oral anticoagulants in four Western European countries. *Pharmacoepidemiol Drug Saf* 2023;32(11):1223–1232
- 8 Shantsila E, Choi EK, Lane DA, Joung B, Lip GYH. Atrial fibrillation: comorbidities, lifestyle, and patient factors. *Lancet Reg Health Eur* 2024;37:100784
- 9 Eckardt L, Wolfes J, Frommeyer G. Benefits of early rhythm control of atrial fibrillation. *Trends Cardiovasc Med* 2024;34(05):288–294
- 10 Kirchhof P, Camm AJ, Goette A, et al. Early rhythm-control therapy in patients with atrial fibrillation. *N Engl J Med* 2020;383(14):1305–1316
- 11 Potpara T, Grygier M, Haesusler KG, et al. An international consensus practical guide on left atrial appendage closure for the non-implanting physician: executive summary. *Thromb Haemost* 2025;125(09):825–846
- 12 Boriani G, Proietti M, Laroche C, et al. Association between antithrombotic treatment and outcomes at 1-year follow-up in patients with atrial fibrillation: the EORP-AF general long-term registry. *Europace* 2019;21(07):1013–1022
- 13 Potpara TS, Lip GYH, Dagres N, et al. Cohort profile: the ESC EURObservational research programme atrial fibrillation III (AF III) registry. *Eur Heart J Qual Care Clin Outcomes* 2021;7(03):229–237
- 14 Kirchhof P, Ammentorp B, Darius H, et al. Management of atrial fibrillation in seven European countries after the publication of the 2010 ESC guidelines on atrial fibrillation: primary results of the PREvention of thromboembolic events–European registry in atrial fibrillation (PREFER in AF). *Europace* 2014;16(01):6–14
- 15 Potpara T, Markovic BG, Grygier M, et al. Adherence to oral thromboprophylaxis in atrial fibrillation: an overview for clinicians. *Europace* 2025;27(11):euaf250
- 16 Mangion K, Vella K, Gatt A, et al. A comparative in vitro study of the anticoagulant effect of branded versus generic rivaroxaban. *Thromb Res* 2024;235:41–51
- 17 Steffel J, Collins R, Antz M, et al. 2021 European heart rhythm association practical guide on the use of non-vitamin K antagonist Oral anticoagulants in patients with atrial fibrillation. *Europace* 2021;23(10):1612–1676
- 18 Schulman S, Kearon C, Subcommittee on Control of Anticoagulation of the Scientific and Standardization Committee of the International Society on Thrombosis and Haemostasis. Definition of major bleeding in clinical investigations of antithrombotic medicinal products in non-surgical patients. *J Thromb Haemost* 2005;3(04):692–694
- 19 Kaatz S, Ahmad D, Spyropoulos AC, Schulman S, Subcommittee on Control of Anticoagulation. Definition of clinically relevant non-major bleeding in studies of anticoagulants in atrial fibrillation and venous thromboembolic disease in non-surgical patients: communication from the SSC of the ISTH. *J Thromb Haemost* 2015;13(11):2119–2126
- 20 Atkinson MJ, Kumar R, Cappelleri JC, Hass SL. Hierarchical construct validity of the treatment satisfaction questionnaire for medication (TSQM version II) among outpatient pharmacy consumers. *Value Health* 2005;8(Suppl 1):S9–S24
- 21 Romiti GF, Proietti M, Vitolo M, et al. Clinical complexity and impact of the ABC (atrial fibrillation better care) pathway in patients with atrial fibrillation: a report from the ESC-EHRA EURObservational research programme in AF general long-term registry. *BMC Med* 2022;20(01):326
- 22 Boriani G, Laroche C, Diemberger I, et al. Overweight and obesity in patients with atrial fibrillation: sex differences in 1-year outcomes in the EORP-AF general pilot registry. *J Cardiovasc Electrophysiol* 2018;29(04):566–572
- 23 Potpara TS, Dan G-A, Trendafilova E, et al. Stroke prevention in atrial fibrillation and 'real world' adherence to guidelines in the Balkan region: the BALKAN-AF survey. *Sci Rep* 2016;6(01):20432
- 24 Lip GY, Laroche C, Boriani G, et al. Regional differences in presentation and treatment of patients with atrial fibrillation in Europe: a report from the EURObservational research programme atrial fibrillation (EORP-AF) pilot general registry. *Europace* 2015;17(02):194–206
- 25 Camm AJ, Amarencio P, Haas S, et al. XANTUS: a real-world, prospective, observational study of patients treated with rivaroxaban for stroke prevention in atrial fibrillation. *Eur Heart J* 2016;37(14):1145–1153
- 26 Connolly SJ, Ezekowitz MD, Yusuf S, et al. Dabigatran versus warfarin in patients with atrial fibrillation. *N Engl J Med* 2009;361(12):1139–1151
- 27 Granger CB, Alexander JH, McMurray JJ, et al. Apixaban versus warfarin in patients with atrial fibrillation. *N Engl J Med* 2011;365(11):981–992
- 28 Patel MR, Mahaffey KW, Garg J, et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. *N Engl J Med* 2011;365(10):883–891
- 29 Giugliano RP, Ruff CT, Braunwald E, et al. Edoxaban versus warfarin in patients with atrial fibrillation. *N Engl J Med* 2013;369(22):2093–2104
- 30 Lip GYH, Proietti M, Potpara T, et al. Atrial fibrillation and stroke prevention: 25 years of research at EP Europace journal. *Europace* 2023;25(09):euad226
- 31 Vora P, Morgan Stewart H, Russell B, Asimwe A, Brobert G. Time trends and treatment pathways in prescribing individual Oral anticoagulants in patients with Nonvalvular atrial fibrillation: an observational study of more than three million patients from Europe and the United States. *Int J Clin Pract* 2022;2022:6707985
- 32 Beyer-Westendorf J, Förster K, Ebertz F, et al. Drug persistence with rivaroxaban therapy in atrial fibrillation patients—results from the Dresden non-interventional oral anticoagulation registry. *Europace* 2015;17(04):530–538
- 33 Salmasi S, Loewen PS, Tandun R, Andrade JG, De Vera MA. Adherence to oral anticoagulants among patients with atrial fibrillation: a systematic review and meta-analysis of observational studies. *BMJ Open* 2020;10(04):e034778
- 34 Ozaki AF, Choi AS, Le QT, et al. Real-world adherence and persistence to direct oral anticoagulants in patients with atrial fibrillation: a systematic review and meta-analysis. *Circ Cardiovasc Qual Outcomes* 2020;13(03):e005969
- 35 Cannon CP, Kim JM, Lee JJ, et al. Patients and their physician's perspectives about oral anticoagulation in patients with atrial fibrillation not receiving an anticoagulant. *JAMA Netw Open* 2023;6(04):e239638
- 36 Borre ED, Goode A, Raitz G, et al. Predicting thromboembolic and bleeding event risk in patients with non-valvular atrial fibrillation: a systematic review. *Thromb Haemost* 2018;118(12):2171–2187
- 37 Aggarwal R, Ruff CT, Virdone S, et al. Development and validation of the DOAC score: a novel bleeding risk prediction tool for patients with atrial fibrillation on direct-acting oral anticoagulants. *Circulation* 2023;148(12):936–946
- 38 Mei DA, Imberti JF, Bonini N, et al. Performance of HAS-BLED and DOAC scores to predict major bleeding events in atrial fibrillation patients treated with direct oral anticoagulants: a report from a prospective European observational registry. *Eur J Intern Med* 2024;128:63–70
- 39 Cools F, Johnson D, Camm AJ, et al., GARFIELD-AF investigators. Risks associated with discontinuation of oral anticoagulation in newly diagnosed patients with atrial fibrillation: results from the GARFIELD-AF registry. *J Thromb Haemost* 2021;19(09):2322–2334
- 40 Afzal SK, Hasan SS, Babar ZU. A systematic review of patient-reported outcomes associated with the use of direct-acting oral anticoagulants. *Br J Clin Pharmacol* 2019;85(12):2652–2667
- 41 Katerenchuk V, Duarte GS, Martins E, Pereira G, et al. Satisfaction of patients with nonvitamin K anticoagulants compared to vitamin k antagonists: a systematic review and meta-analysis. *Thromb Haemost* 2021;121(03):366–382
- 42 Salmasi S, Adelakun A, Safari A, et al. Satisfaction with oral anticoagulants among patients with atrial fibrillation: a prospective observational study. *CJC Open* 2021;3(11):1347–1356
- 43 Okumura Y, Yokoyama K, Matsumoto N, et al. Patient satisfaction with direct oral anticoagulants and warfarin. *Int Heart J* 2018;59(06):1266–1274