

## PECULIARITIES OF USE OF ANTITHROMBOTIC DRUGS WARFARIN AND XARELTO IN PATIENTS WITH CORONARY HEART DISEASE

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**Abstract:** Objective: The study investigates the characteristics of the utilization of antithrombotic medications warfarin and Xarelto among patients diagnosed with coronary heart disease.

Methods: This research was conducted over a span of 1.5 years, from 2020 to 2022, at the Department of Cardiology within the Multidisciplinary Medical Center of the Bukhara region. Within this study, a total of 76 patients (42 men and 34 women) aged between 60 and 74 years were assessed, with men comprising 55.3% and women 44.7%. The cohort encompassed 44 patients (36 men and 8 women) diagnosed with ischemic heart disease necessitating myocardial revascularization, among whom 33 exhibited persistent atrial fibrillations, with 11 presenting long-term persistent forms of the condition.

**Results:** The observational study conducted on a restricted patient sample utilizing NOACs (New Oral Anticoagulants) as part of antithrombotic treatment post-coronary artery bypass grafting, individuals exhibited a decreased occurrence of thromboembolic complications (TEC) and hemorrhagic complications in contrast to those administered warfarin. However, due to the limited sample size, no statistically significant variances between the groups were discerned. Undoubtedly, clinical trials involving a larger patient cohort in this domain hold promise.

**Conclusion:** In hospitalized patients with coronary artery disease complicated by atrial fibrillation, it was observed that in 16% of cases, the dosage of a new oral anticoagulant prescribed exceeded the therapeutic dose. Comparative studies between NOACs, specifically rivaroxaban, and warfarin indicated that patients receiving warfarin spent only 64% of their time within the therapeutic range of INR (2-3). These trials underscored that NOACs are equally efficacious as warfarin in preventing thromboembolic complications, with a superior safety profile and enhanced ease of administration.

**Key words:** atrial fibrillation, anticoagulant therapy, thromboembolic complications, bleeding, international normalized ratio.

**Introduction:** In recent decades, coronary heart disease (CHD) has consistently remained a prominent focus in treatment strategies.

As per the WHO, over 17 million individuals succumb to cardiovascular diseases annually across the globe, with coronary artery disease alone accounting for more than 7 million of these deaths.

Mortality from CHD among individuals under 65 has decreased by 50%, attributed to more aggressive treatment approaches for acute myocardial infarction such as thrombolysis and early revascularization. However, overall CHD mortality rates have remained steady due to the aging population, where mortality

naturally rises despite advancements in medication usage. Among men under 65, CHD mortality is three times higher than in women, but after the age of 65, mortality rates become similar in both genders, and after 80, it becomes twice as high in women compared to men. It's noteworthy that only 40-50% of individuals with angina are aware of their condition. The pathogenesis of most cardiovascular diseases (CVDs) involves acute or chronic myocardial ischemia, resulting in compromised heart muscle function, fatal arrhythmias, severe hypoxia, and metabolic imbalances. The quest for novel treatments and prevention methods for ischemic CVDs remains a global cardiology priority, yet mortality rates in this domain persist at elevated levels. The primary nosological entity of ischemic CVDs is CHD, particularly myocardial infarction (MI), alongside rhythm and conduction disturbances, and heart failure.

Atrial fibrillation (AF) is closely related to coronary artery disease, and the mechanism of pathogenetic influence on the development of AF is due, among other things, to ischemia of atrial cardiomyocytes [2]. The Framingham study revealed an rise in the CHD in patients with AF [4].

Atrial fibrillation is heart rhythm disorder. Its prevalence doubles with each decade of life, from 0.5% at the age of 50-59 to 9% at the age of 80-89. AF is a complication of a large number of cardiovascular diseases, in particular, coronary heart disease (CHD), arterial hypertension, congenital and acquired heart defects, cardiomyopathy, myocarditis. Whereas, the most common pathology leading to the development of atrial fibrillation is coronary artery disease.

The case of atrial fibrillation is approximately 3% in adults aged 20 years and older [1], with a higher prevalence in the elderly [2], as well as in the presence of associated conditions, including hypertension disease (HD), chronic heart failure (CHF), coronary artery disease (CHD). The prevalence of AF among patients referred for CABG surgery is 6.1%, which in absolute terms is estimated at tens of thousands of patients [1]. After direct myocardial revascularization, AF may manifest in certain patients, either as a new occurrence or diagnosed earlier, prior to surgical intervention. Anticoagulant therapy is indicated for individuals with a risk score of > 2 points in men and > 3 points in women [3]. An important consideration in treating patients with AF post-CABG is the administration of antiplatelet agent's alongside anticoagulant therapy. Balancing the need to prevent thrombosis with the hemorrhagic complexity can pose challenges. Shunt condition in the early postoperative phase is a critical determinant of CABG outcomes. Research has demonstrated that 3 to 12% of venous shunts become occluded within the first month after CABG [4, 5]. Acute heart failure resulting from acute shunt thrombosis serves as a primary cause of mortality in patients with initially severe coronary artery lesions [4, 5].

Considering the absence of evidence indicating a survival or feasibility benefit of DAPT in patients with CHD, it is not advised to administer DAPT in the postoperative period to mitigate the risk of vascular graft occlusion [3].

The integration of direct oral anticoagulants (NOACs) into routine clinical practice for thromboembolic prophylaxis in people with nonvalvular AF presents new opportunities for safely managing individuals receiving both antiplatelet and anticoagulant therapy following myocardial revascularization [1, 2]. In the European Society of Cardiology's recommendations for antithrombotic therapy aimed at preventing thromboembolic complications in AF patients' post-CABG, experts advocate for the use of NOACs. Additionally, in patients with AF characterized by a low risk of bleeding, a history of myocardial infarction (MI), and a high risk of reoccur ischemic case, consideration may be given to adjunctive acetylsalicylic acid therapy at a dosage of 75–100 mg/day alongside long-term anticoagulant therapy [3]. It's noteworthy that several international studies, including PIONEER AF, REDUAL PCI, and AUGUSTUS, have been published, demonstrating the safety and efficacy of NOACs when incorporated into DAPT or triple antithrombotic treatment for people with AF and CHD who have undergone PCI [2, 3].

Despite the availability of various diagnostic methods for early detection of coronary heart disease (such as angiography, computed tomography, myocardial scintigraphy with contrast agents) and the utilization of modern treatment modalities (including balloon angioplasty, coronary artery stenting, aorto- and mammary coronary artery bypass grafting (CABG, MCABG), and access to a contemporary array of medications), there is optimism for reducing mortality and complications associated with cardiovascular conditions.

Given the multifaceted nature of ischemic cardiovascular disease occurrence and progression, there is considerable interest in addressing this issue through antithrombotic therapy for both treatment and prevention. Therefore, the issue of preventing and treating thrombosis remains pertinent in modern medicine, and pharmaceutical interventions targeting the hemostasis system represent a viable approach to mitigating thromboembolic complications associated with cardiovascular diseases.

**Objective:** The study investigates the characteristics of the utilization of antithrombotic medications warfarin and Xarelto among patients diagnosed with CHD.

**Material and methods of research:** This study spanned 1.5 years (from 2020 to 2022) and was conducted in the cardiology department of the Multidisciplinary Medical Center (MMC) of the Bukhara region. A total of 76 patients (42 men and 34 women) aged 60 to 74 years (comprising 55.3% men and 44.7% women) underwent examination. Among them, 44 patients (36 men and 8 women) with CHD and indications for myocardial revascularization, including 33 with persistent and 11 with long-term persistent forms of atrial fibrillation (AF), participated in the study. The median age was  $63.5 \pm 7.8$  years. Initial evaluations included clinical examinations, standard laboratory tests, 12-lead electrocardiography (ECG), echocardiography, and coronary angiography. The efficacy endpoint was defined as the cumulative incidence of cardiovascular complications (CVS), encompassing cardiovascular death, ischemic stroke, systemic embolism, and ACS.

Statistical data indicates that the AF is approximately 3% among individuals aged 60 years and more, particularly in the presence of associated CVD such as CHD, AH, and CHF. Additionally, non-cardiac conditions including obesity, DM, and CKD are also linked to the case of AF in this age group.

**Results and discussion:** A total of 76 patients (42 men and 34 women) aged 60 to 74 years (55.3% men; 44.7% women) underwent examination. Among them, 44 patients (36 men and 8 women) with CHD and indications for myocardial revascularization, comprising 33 with persistent and 11 with long-term persistent forms of atrial fibrillation (AF), were in the study. The median age was  $63.5 \pm 7.8$  years. The clinical and anamnestic characteristics of the patients are detailed in Table 1. The study adhered to the standards of Good Clinical Practice.

**Table 1 Clinical and anamnestic characteristics of patients**

Indicators	Values
Age, years, $M \pm SD$	$63.5 \pm 7.8$
Persistent form of AF, n (%)	33 (75)
Long-term persistent form of AF, n (%)	11 (25)
CHA2DS2-VASc, Points, $M \pm SD$	$3.8 \pm 1.1$
HAS-BLED, points, $M \pm SD$	$2.1 \pm 0.7$
Left ventricular ejection fraction, %, $M \pm SD$	$59 \pm 6.5$
Left atrium size, mm, $M \pm SD$	$43.7 \pm 3.5$
Prior history: PICS/PCI, n (%)	23/10 (52/22)

CHF FC according to NYHA I/II/III/IV, n (%)	8/28/8/0 (18/64/18/0)
Syntax Coronary Lesion Volume, Scores, M $\pm$ SD	27.1 $\pm$ 3.5
Euroscore, баллы, M $\pm$ SD	2.1 $\pm$ 1.0

Note: AF – atrial fibrillation, CHD – coronary artery disease, PICS – post-infarction cardiosclerosis, PCI – percutaneous coronary intervention, CHF – chronic heart failure, FC – functional class.

**Study inclusion criteria:** The inclusion criteria for the study were coronary heart disease (CHD) with documented persistent or long-term persistent atrial fibrillation (AF), indications for direct revascularization, and patient consent to participate in the study.

**Exclusion criteria:** The exclusion criteria for direct revascularization included contraindications such as patient refusal for the operation, left ventricular (LV) aneurysm, valvular lesions, LV ejection fraction less than 40%, acute coronary syndrome, presence of a thrombosis in the LP, contraindications to taking anticoagulants, and severe psychiatric disorders that could impact the administration regimen and dosage of anticoagulant therapy.

All patients received antiarrhythmic therapy during the pre-hospital stage. Given the presence of structural heart pathology, the majority of patients predominantly took class III antiarrhythmic drugs, specifically amiodarone (n = 39; 89%) and sotalolol (n = 5; 11%). However, despite the antiarrhythmic therapy, paroxysms of atrial fibrillation persisted in all patients. Upon admission to the hospital, patients presented with complaints of rapid irregular heartbeat (n = 40; 93%), pressing pain behind the sternum (n = 44; 100%), dyspnea of an inspiratory nature (n = 42; 96%), and cough (n = 4; 9%). Among the patients, there were (n = 3; 7%) who did not experience subjective arrhythmias, and atrial fibrillation (AF) was detected incidentally during routine electrocardiogram (ECG) recording. For an objective evaluation and systematic analysis of patients' complaints, a point arrhythmia symptom according to the European Heart Rhythm Association scale was utilized, with the average score on this scale being  $2.3 \pm 0.5$ . Coronary angiography performed prior to revascularization revealed that the average number of affected arteries was  $2.7 \pm 0.6$ . The mean score on the Syntax scale was  $27.1 \pm 3.5$ , with a duration of arrhythmological history before the intervention being  $3.1 \pm 2.1$  years, and the duration of coronary heart disease (CHD) experience being  $8.4 \pm 1.3$  years. Of the total patients, 23 (52%) had previously experienced acute myocardial infarction (AMI), with 22 patients having a history PCI. Patients with clinically significant congestive heart failure (CHF) of functional class II and higher predominated (82%). All patients underwent direct myocardial revascularization, including ligation of the LAA to prevent blood clots. The CHA<sub>2</sub>DS<sub>2</sub>-VASc scale was employed to stratify AF, with a mean score of  $3.8 \pm 1.1$ . Additionally, the HAS-BLED score was utilized to assess bleeding risk, with a mean score of  $2.1 \pm 0.7$ .

Thus, person with a risk of thromboembolic complications (TEC) exceeding the potential risk of bleeding predominated. These patients exhibited preserved or moderately reduced left ventricular (LV) ejection fraction ( $59 \pm 6.5\%$ ) and a mean left atrial appendage (LAA) size of  $43.7 \pm 3.5$  mm, as determined by echocardiography. No intracardiac thrombosis was detected in patients at the time of enrollment in the study. Follow-up examinations were conducted at 12- and 24-months post-discharge from the hospital. Of the discharged patients, 40 (91%) attended follow-up visits. During these visits, heart rhythm was assessed using electrocardiography (ECG) and 24-hour Holter ECG monitoring, medical records were reviewed, and ECG recordings from the current follow-up period were analyzed. During the in-hospital phase, recurrences of atrial fibrillation (AF) in the early postoperative period were noted in 24 patients (40%). Among them, three patients required electropulse therapy, while in other cases, sinus rhythm was restored pharmacologically. A complication in the form of bleeding during heparin therapy in the early postoperative period was observed in two patients (4%), necessitating revision on the first day after surgery.

and transfusion of fresh frozen plasma. The source of bleeding was identified as collateral from the left internal mammary artery. There were no perioperative myocardial infarctions (MIs). Post-CABG surgery, drug therapy encompassed standard postoperative treatment for CHD along with the administration of antiarrhythmic drugs (class III) immediately after patient extubation. Following the operation, therapy with unfractionated heparin was initiated, and after a day of observation, patients were transitioned to oral anticoagulant therapy. The choice of anticoagulant was determined by the attending physician, considering the patient's comorbidities, perceived compliance, preferences regarding drug cost and dosing frequency, as well as the feasibility of monitoring the INR on an outpatient basis. For patients receiving warfarin, parenteral heparin was discontinued immediately after achieving an INR of 2.0. Given the high risk of thromboembolic complications (TEC) (with an average CHA<sub>2</sub>DS<sub>2</sub>-VASc score of  $3.8 \pm 1.1$ ), all patients were prescribed anticoagulants indefinitely post-surgery.

The patients were categorized into two groups: those receiving warfarin (group 1) and those receiving NOACs (group 2). Table 2 outlines the clinical and anamnestic characteristics of the patients

**Table 2 Clinical and anamnestic characteristics of patients taking warfarin (group 1) and rivaroxaban (group 2)**

Indicators	Group 1 (n = 21)	Group 2 (n = 13)	p
Age, years, M $\pm$ SD	62.3 $\pm$ 8.2	65.3 $\pm$ 7.2	0.10
Persistent form of FP, n (%)	18 (86)	D (69)	0.45
CHA <sub>2</sub> DS <sub>2</sub> -VASc, Points, M $\pm$ SD	3.8 $\pm$ 1.1	3.7 $\pm$ 1.1	0.96
HAS-BLED, points, M $\pm$ SD	2.0 $\pm$ 0.7	2.1 $\pm$ 0.7	0.84
Left ventricular ejection fraction, %, M $\pm$ SD	58.2 $\pm$ 10.8	60.3 $\pm$ 6.7	0.84
Left atrium size, mm, M $\pm$ SD	43.7 $\pm$ 3.5	45.6 $\pm$ 5.5	0.82
Prior history: PICS/PCI, n (%)	9/3 (43/14)	10/4 (76/30)	0.23/0.30
CHF FC according to NYHA I/II/III/IV, n (%)	8/10/3/0 (38/48/14/0)	4/7/2/0 (31/54/15/0)	0.52/0.53/ 0.64/-
Syntax Coronary Lesion Volume, Scores, M $\pm$ SD	27.1 $\pm$ 3.5	20.9 $\pm$ 4.3	0.25
Euroscore, points, M $\pm$ SD	2.0 $\pm$ 0.0	2.1 $\pm$ 0.9	0.84

At 12- and 24-months following enrollment in the study, the vital status (alive/deceased) of patients was determined through telephone interviews conducted with patients or their relatives.

Out of the 44 patients (100%) followed up after 12 months, no deaths were reported. However, after 24 months, two patients died post-operation, one due to acute myocardial infarction (AMI) and the other due to prostate cancer with multiple metastases. Regarding arrhythmia management, sinus rhythm was maintained in 35 patients (79%) after 12 months, but after 24 months, only 10 patients (23%) remained free of atrial fibrillation (AF) episodes following CABG. All patients received anticoagulants for thromboembolic event prevention, including either warfarin or NOACs (rivaroxaban, dabigatran, apixaban). Upon hospital discharge, the optimal dosage of warfarin was determined for patients, and regular INR monitoring once every 4 weeks on an outpatient basis was recommended, targeting an INR level of 2.0–2.5. During the follow-up period, 34 patients (77%) continued anticoagulant therapy. However, ten patients opted to discontinue warfarin after discharge due to difficulties in INR control or financial constraints preventing NOAC usage, instead continuing with dual antiplatelet therapy (DAPT) comprising aspirin and clopidogrel. A coagulogram comprises several tests utilized to evaluate blood clotting disorders. Among these, prothrombin time (PT) is a crucial parameter. To assess blood

coagulation, a simple PT test is conducted to calculate the INR. Warfarin dosage is adjusted based on INR values. During PT analysis, a specific tissue factor (thromboplastin) is introduced into the blood sample, and the time required for clot formation is measured.

In many post-Soviet countries, blood coagulation is often expressed as a "prothrombin index" (PTI), calculated by comparing the prothrombin time (PT) of a patient's blood sample to that of a control sample. In healthy individuals, the PTI typically falls within the range of 70-100%. For effective stroke prevention while on warfarin therapy, the PTI should ideally be around 25-45%. Lower PTI values present an increased risk of bleeding, while higher values show a heightened risk of blood clots. Various methods have been developed to determine PTI, and the activity of the thromboplastin added to blood samples during PT testing can vary between manufacturers. Consequently, PTI measurement results may differ significantly on the kind of tissue factor (thromboplastin) reagent utilized by individual laboratories. Another standardized measure of blood clotting, INR, has been introduced into clinical practice to standardize prothrombin time (PT) test results. INR control results are consistent across clinical laboratories, providing a stable measure of blood clotting status. For patients receiving direct and indirect anticoagulants, maintaining the blood INR level within specific limits is crucial. Lower INR values render prevention ineffective, while higher values rise the risk of bleeding, outweighing the benefits of thrombosis prevention. The optimal range for INR has been established through extensive clinical trials involving hundreds of thousands of participants worldwide. Effective warfarin therapy necessitates ongoing monitoring of INR levels and precise dosing adjustments based on these measurements. Thus, determining the correct dose involves assessing the blood clotting time (INR).

An INR of 1 indicates a normal level typically found in individuals who are not taking warfarin or any anticoagulant medication;

An INR value of 2 signifies that the blood clotting time is approximately twice as long as the normal time;

An INR value of 3 indicates that the blood clotting time is approximately three times longer than normal.

The optimal INR value varies depending on the patient's condition. For people with AF, the recommended range typically falls between 2 and 3.

One component of antithrombotic therapy for 21 patients (48%) was warfarin. The initial dose for patients who had not previously used warfarin was 5 mg/day (2 tablets) for the first 4 days. On the 5th day of treatment, INR was determined, and based on this value, patients were typically prescribed a maintenance dose ranging from 2.5 to 7.5 mg/day (1 to 3 tablets).

Thirteen patients (29%) were prescribed NOACs, specifically rivaroxaban at a dosage of 20 mg/day, within 24 months after surgery. Among them, six patients underwent interventional treatment for atrial fibrillation (AF), during which no evidence of intracardiac thrombosis was detected.

The incidence of endpoints in patients taking warfarin (group 1) and NOAC (group 2) is summarized in Table 3.

**Table 3 the incidence of endpoints in patients taking warfarin and NOACs**

Indicators Parameters	Group 1 (n = 21)	Group 2 (n = 13)	p
ACVA	2 (9)	0	0.41
Thrombosis of LP	0	0	-
Bleeding Small, large	10 (48). 1 (5)	5 (38). 1 (7,7)	0.58 -

Death within 12 months	0	0	-
Death within 24 months	1 (5)	0	0.62

Note: p – comparison between groups 1 and 2, ACVA – acute cerebrovascular accident, LP – left atrium.

Vitamin K antagonists and NOACs (X-factor inhibitors and thrombin inhibitors) are currently available as oral anticoagulants. Vitamin K antagonists are among the primary medications utilized for stroke and systemic thromboembolism prevention, with their use associated with a 67% reduction in the relative risk of ischemic stroke [12]. However, warfarin therapy presents several challenges: its pharmacokinetics and pharmacodynamics are unpredictable due to both genetic factors and the specifics of drug metabolism, necessitating regular laboratory monitoring, and it requires a prolonged period before achieving therapeutic effect [13]. In many instances, stroke can occur during the interruption of vitamin K antagonists or when INR values are subtherapeutic [13]. Studies comparing NOACs to warfarin, such as ROCKET-AF with rivaroxaban [14, 16, 19, 21], have indicated that the time spent within the therapeutic range of INR (2-3) for patients on warfarin in clinical trials was only 64%. Nonetheless, findings from these clinical trials suggest that NOACs is effective like warfarin in preventing thromboembolic complications, while also boasting a better safety profile and greater ease of use [14, 15, 22]. Presently, prescribing NOACs alongside antiplatelet therapy following PCI have been thoroughly investigated [17, 18, 20]. In our study, only minor bleeding events were observed among patients taking NOACs, including one case of hemorrhoids and four cases of nasal bleeding, none of which required hospitalization, medical intervention, or discontinuation of anticoagulant therapy. Thromboembolic complications were not observed in patients receiving NOACs. However, it is important to acknowledge the limits, including the small sample size and the initially non-randomized nature of the study when prescribing NOACs and warfarin. Further research, particularly safety studies on new oral anticoagulants, is warranted to establish them as a viable alternative to vitamin K antagonists in antithrombotic therapy following CABG in patients with atrial fibrillation.

The observational study conducted on a limited patient sample, those receiving NOACs as part of antithrombotic therapy post-CABG exhibited a lower incidence of thromboembolic complications (TEC) and hemorrhagic complications compared to patients treated with warfarin. Nevertheless, clinical trials involving a larger patient population in this regard show promise.

Medication intake was closely monitored during each visit, and adjustments were made as necessary. The majority of patients enrolled in the study received statins for both CHD and nephroprotection. Additionally, ACEI or ARB were prescribed for nephroprotection once renal function was stabilized. Due to the high prevalence of anemia, some patients were recommended iron supplements, and therapy with erythropoietin preparations was initiated in consultation with a nephrologist. In cases of acute kidney injury requiring parenteral iron and/or erythropoietin, a joint consultation with a nephrologist was conducted. The table outlining the groups of drugs used for treatment and their frequency of use is presented in Table 4.

**Table 4 List of groups of medications taken**

Pharmacological group	Warfarin Group (21) abs.,(%)	Rivaroxaban group (13) abs.,(%)	p
ACEI/ARB II	9 (42%)	5 (40%)	0,67
Calcium channel blocker	14 (69%)	9 (70%)	1
Loop diuretic	11 (53%)	5 (41%)	0,34
Thiazide diuretic	6 (31%)	2 (22,5%)	0,063
β-adrenergic blocker	19 (92%)	10 (77,5%)	0,13

Hypoglycemic drug	5 (22%)	2 (22,5%)	1
Insulin	3 (13,9%)	1 (10%)	0,52
Statin	20 (97%)	11 (85%)	0,09
Erythropoietin	2 (8%)	1 (10%)	1
Iron supplements	14 (67%)	8 (60%)	0,69
Proton Pump Inhibitor	9 (42%)	6 (47,5%)	0,78
A drug that affects the metabolism of uric acid	15 (72%)	7 (55%)	0,12

In the warfarin group, a Time in TTR of over 70% was achieved in 94% of patients. Following the attainment of at least three consecutive INR results within the range of 2-3 in the laboratory, a subset of patients (n=9) transitioned to INR monitoring using a portable coagulometer. On average, each patient required 57 INR measurements over an 18-month period to sustain the target TTR.

Patients receiving warfarin demonstrated a significantly higher likelihood of experiencing minor bleeding according to the BARC and ISTH scales, as well as all clinically significant bleeding events (including major and minor clinically significant bleeding) according to the ISTH scale (refer to Table 5).

**Table 5 Bleeding in the rivaroxaban (n=13) and warfarin (n=21) group**

Bleeding Scale	Rivaroxaban group, abs (%) - 13	Warfarin group, abs. (%) -21	p
<b>BARC</b>			
Small	6 (42,5%)	15 (72,2%)	<0,01
Small clinically significant	1 (7,7%)	2 (8,33%)	0,043
Big	1 (7,7%)	2 (8,33%)	0,048
All clinically significant	2 (15,3%)	3 (16%)	0,045
<b>ISTH</b>			
Small	4 (32,5%)	12 (55,6%)	0,01
Small clinically significant	1 (7,7%)	4 (19,4%)	0,043
Big	1 (7,7%)	2 (8,33%)	0,03
All clinically significant	4 (32,5%)	6 (27,7%)	0,03

It is noteworthy that the number of readmissions for all causes was 5 (42.5% of patients) in the rivaroxaban group and 11 (48% of patients) in the warfarin group (p=0.57). Among these, 4 (35%) and 9 (40%) readmissions (in the rivaroxaban and warfarin groups, respectively) were due to emergency reasons (p=0.96). Additionally, the case of bleeds in the warfarin group was higher than in the rivaroxaban group.

### Conclusion:

1. The frequency of anticoagulant prescription in hospitalized people with CAD complicated by atrial fibrillation reveals that the dose of the prescribed new oral anticoagulant exceeded the therapeutic dose in 16% of cases. Studies comparing NOACs, such as ROCKET-AF with rivaroxaban, to warfarin have shown that the time spent in the therapeutic range of INR (2-3) among patients participating in the clinical trial taking warfarin was only 64%. Despite this, in these clinical studies, it has been demonstrated that NOACs are no less effective than warfarin in preventing thromboembolic complications (TECs). Furthermore, they exhibit a better safety profile and are easier to use.

2. Patients taking warfarin were found to be significantly more likely to develop minor bleeding according to the BARC and ISTH scales, as well as all clinically significant (major and minor clinically significant) bleeding according to the ISTH scale. Regarding readmissions for all causes, there were 5 (42.5% of patients) in the rivaroxaban group and 11 (48% of patients) in the warfarin group ( $p=0.57$ ). Among these readmissions, 4 (35%) and 9 (40%) occurred due to emergency reasons in the rivaroxaban and warfarin groups, respectively ( $p=0.96$ ).
3. Continuous monitoring of INR in people getting warfarin is deemed inconvenient for assessing the efficacy of therapy. Factors such as its low impact on the restoration of renal function and the potential side effect of increased blood loss provide a basis for considering the effective use of rivaroxaban instead.

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