BIOMEDICINSKA ISTRAŽIVANJA
2025;16(1):1–10

UDK: 616.12-008.31:615.273
DOI: 10.59137/BII202501462T

Original article

Prescribing patterns of anticoagulants in patients with atrial fibrillation in primary care

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Primljen – Received: 24/01/2025
Prihvaćen – Accepted: 11/06/2025

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Summary

Introduction. Anticoagulants have the key role in prevention of thromboembolism including ischemic stroke, in patients with non-valvular atrial fibrillation (NVAF). The European Association of Cardiology (ESC) recommends new oral anticoagulant drugs (NOACs) as first choice therapy because of approved effectiveness and safety profile compared to vitamin K antagonists (VKAs). The aim of this study was to evaluate the frequency of prescribing anticoagulants in patients with NVAF, and the compatibility of the therapy with current recommendations for stroke prevention.

Methods. Our cross-sectional study, conducted from June 2023 to June 2024, included 238 patients with NVAF registered in the Primary Health Centre Banja Luka. Patients' medical records were used as the data source. The CHA2DS2-VASc and HAS-BLED instruments were used for the assessment of risk of stroke and bleeding.

Results. The majority of respondents were aged 65–84. Patients ≤ 65 years have a significantly lower risk of stroke (p=0.000). According to the CHA2DS2-VASc score, 219 patients were supposed to use anticoagulant therapy, however 73.5% of patients had adequate treatment. Mostly prescribed anticoagulants were VKAs (44.1%), followed by NOACs (29.4%), while 26.5% of patients did not use anticoagulants. The majority of patients with unregulated international normalized ratio (INR) were >75 years, and those with regulated INR were 65–74 years old (p=0.03). The risk of bleeding (HAS-BLED ≥ 3) was present in 40% of patients using anticoagulants.

Conclusion. Stroke prevention in patients with NVAF and prescribing NOACs are partially aligned with clinical recommendations. Insufficient NOACs usage has been noticed, despite their approved advantages. Additional activities are needed aiming anticoagulant therapy optimization, particularly in elderly and those with high risk for stroke.

Key words: atrial fibrillation, anticoagulant therapy, vitamin K antagonists, stroke

Introduction

Cardiovascular diseases (CVDs) remain the leading cause of morbidity and mortality worldwide, with atrial fibrillation (AFib) being a major contributor to thromboembolic complications, particularly stroke. Family physicians play a key role in preventing these complications through risk stratification and appropriate anticoagulant therapy [1, 2].

AFib is the most common supraventricular arrhythmia, with a prevalence ranging from 2% to 4% in adults, increasing significantly with age. The irregular atrial contractions in AFib lead to blood stasis and thrombus formation, which can result in embolic events such as ischemic stroke or transient ischemic attack (TIA). Effective anticoagulation is essential in reducing these risks [3–5].

Oral anticoagulant therapy includes vitamin K antagonists (VKAs) and new oral anticoagulants (NOACs). While NOACs are recommended as first-line therapy in most patients with non-valvular AFib, studies suggest that prescribing patterns may not always align with clinical guidelines. The CHA2DS2-VASc and HAS-BLED scores are widely used tools for assessing stroke and bleeding risk, respectively, yet their application in real-world clinical practice varies. Since 2018 family medicine teams in Republic of Srpska, Bosnia and Herzegovina have had the possibility to implement the clinical guideline named The Usage of Anticoagulant Therapy in Atrial Fibrillation and Venous Thromoembolism [3].

This study aims to evaluate the prescribing patterns of anticoagulants in patients with non-valvular AFib, to assess the adherence to clinical guidelines, and to analyze the effectiveness of VKAs in achieving target International Normalized Ratio (INR) values. Understanding these factors can contribute to optimizing stroke prevention strategies in primary care.

Methods

Study design and setting

This cross-sectional study was conducted at the Educational Centre of the Primary Health Care (PHC) Centre Banja Luka from June 1, 2023, to June 30, 2024.

Participants

The study included all patients diagnosed with non-valvular atrial fibrillation (AFib) registered at the Educational Centre. Patients were divided into four age groups: ≤ 64, 65–74, 75–84, and ≥ 85 years.

Data collection

Family medicine teams in PHC Banja Luka recorded patients' data in electronic medical records within Web Medic electronic system till November 2023, and afterwards within The Integrated Health Information System (IZIS).

Data were collected from electronic health records, including:

- Demographics: Age, sex, education level, employment status;
- The value of international normalized ratio (INR) was classified as regulated (2,0–3,0) and unregulated (< 2,0 and > 3,0);
- Comorbidities and Therapy: Presence of cardiovascular and other chronic diseases, ongoing anticoagulant therapy.

Risk assessment

Stroke risk was assessed using the CHA2DS2-VASc score, where a score of ≥ 2 indicated the need for anticoagulation.

Bleeding risk was evaluated using the HAS-BLED score, with a score of ≥ 3 suggesting a need for cautious anticoagulant use and possible cardiology consultation [2, 3].

Statistical analysis

Data were processed using Microsoft Excel and SPSS v.23. Descriptive statistics (frequencies, percentages) were used for categorical variables. The Chi-square test was applied for categorical comparisons, while ANOVA was used for analyzing mean differences between age groups. A p-value < 0.05 was considered statistically significant.

Ethical considerations

The study was approved by the Ethics Committee of the Primary Health Care Centre Banja Luka, and consent was obtained from the institution management before data collection.

Results

There were 238 respondents in our research, with equal representation of both sexes. The age ranged from 31 to 94 years, the mean age was 73.4 ± 10.35, where more than half of the respondents were less than 75 years old. The percentile representation of patients aged 64 or less and patients aged 85 or over was equal (15.1%), while the largest number of patients belonged to the age group from 65 to 74 years (36.1%), and a slightly smaller percentage were patients aged 75–84 (33.6%). The average age of men was 70.20 ±11.28, the average age of women was 74.57 ±10.21. The largest number of male patients belonged to the age group of 65 to 74 years of age, while the largest number of female patients belonged to the age group of 75 to 84 years of age. The largest number of respondents obtained secondary education level (65.5%) (Table 1).

Table 1. Socio-demographic characteristics of respondents

Characteristics	N(%)	Arithmetic mean	SD	Max/min	Median	Male N (%)	Female N (%)
Sex							
Male	119 (50)						
Female	119 (50)						
Age		73.4	10.35	31–94	74		
≤ 64	36 (15.1)					21 (17.6)	15 (12.6)
65–74	86 (36.1)					45 (37.8)	41 (34.5)
75–84	80 (33.6)					37 (31.1)	43 (36.1)
≥ 85	36 (15.1)					16 (13.4)	
Level of education							
Primary school	29 (12.2)						
Secondary school	156 (65.5)						
Community college	38 (16)						
University degree	12 (5)						
Working status							
Retired	202 (84.9)						
Employed	2.9 (12.2)						
Unemployed	7 (2.9)						

Anticoagulant therapy prescribing in the largest percentage (44.1%) included VKAs, while NOACs were prescribed in 29.4% of patients, and 26.5% of patients did not use anticoagulant drugs. The prescription of NOACs and VKAs had no statistically significant differences in relation to the age and sex of the subjects (Table 2).

According to the CHA2DS2-VASc score, 219 patients should use anticoagulant therapy, 13 patients should be considered for anticoagulant therapy and six patients were not supposed to use anticoagulant therapy. Patients younger than 65 years of age had a significantly lower risk of cerebrovascular insult (CVI) as compared to patients aged 65 or older. The majority of patients (N=165) using anticoagulant therapy had a CHA2DS2-VASc score of 2 or higher. Two patients with the score of nearly zero used anticoagulant therapy. The number of patients who did not use anticoagulant therapy was 63, and according to the CHA2DS2-VASc score, 54 of the mentioned number of patients should have necessarily taken anticoagulant therapy, while in five patients it was necessary to consider the introduction of therapy (Table 3).

The highest percentage (34.6%) of patients with documented INR values belonged to the age groups of 65–74 and 75–85 years of age, with the same number of patients in both groups. A significantly larger number of patients aged 65-74 had regulated INR values as compared to other age groups (p=0.03). The largest number of patients with unregulated INR values belonged to the age group of 75 to 84 years of age. Unregulated INR values were confirmed in a greater number in female respondents, while regulated INR values were confirmed in a greater number in their male counterparts, but the difference was not statistically significant (Table 4).

There was no statistically significant influence of the presence of CVDs or DM as well as appropriate therapy for the mentioned comorbidities in relation to INR values (not presented in table).

There was no statistically significant difference in the CHA2DS2-VASc score between patients with unregulated and regulated INR values, because the majority of patients in both groups had a score of over 2 (Table 5). More than half of patients using anticoagulant therapy had HAS BLED score less than 3, therefore there was no increased risk of bleeding. The risk of bleeding was present in 40% of patients out of the total number of patients using anticoagulant therapy. Patients using VKA had a higher percentage of bleeding risk compared to patients using NOAC (Table 6).

Table 2. Anticoagulant therapy prescription in relation to the age and sex

Anticoagulant drug group	N	%	Age (N/%)				p value	Sex		p value
			≤ 64	65–74	75–84	≥ 85		Female N (%)	Male N (%)	
NOAC	70	29.4	8 (11.4)	28 (40)	25 (35.7)	9 (12.9)		37 (52.9)	33 (47.1)	
VKA	105	44.1	13 (12.4)	39 (58.2)	32 (30.5)	21 (20)	0.6	57 (54.3)	48 (45.7)	0.8
Overall	175	73.5	21 (12)	67 (38.3)	57 (32.6)	30 (17.1)		94 (53.7)	81 (46.3)	
NO therapy	63	26.5								

*NOAC - New Oral Anticoagulant; VKA - Vitamin K antagonist

Table 3. Distribution of CHA2DS2-VASc and anticoagulants prescribing scores in relation to age and sex

CHA_2DS_2-VASc	Frequency	Percentage	Cumulative percentage	Frequency	Percentage	Patients without anticoagulant therapy	
				CHA2DS2-VASc			
				1	≥ 2	1	≥ 2
0	6	2.5	2.5				
1	13	5.5	8.0	13	5.5		
2	30	12.6	20.6				
3	84	35.3	55.9				
4	76	31.9	87.8	219	92.0	5 (8.5)	54 (91.5)
5	22	9.2	97.1				
6	6	2.5	99.6				
7	1	0.4	100.0				
Overall	238	100.0		232	97.5		

Age				Anticoagulant drugs			
	CHA2DS2-VASc				CHA2DS2-VASc		
	1	≥ 2	p value		1	≥ 2	p value
≤ 64	10 (33.3)	20 (66.7)	0.0	NOAC	3 (4.3)	67 (95.7)	0.5
65–74	1 (1.2)	85 (98.8)		VAK	5 (4.9)	98 (95.1)	
75–84	1 (1.3)	79 (98.7)					
≥ 85	1 (2.8)	35 (97.2)		Overall	8 (4.6)	165 (95.4)	

Table 4. Presentation of the regulation of INR values in relation to the age and sex

INR	N (%)	Midpoint	SD	Max	Min
patients	107	2.3	0.86	7.06	0.99

INR	age				sex		Overall
	<64	65-74	75-84	>85	male	female	
Unregulated	5 (9.6)	12 (23.1)	24 (46.2)	11 (21.2)	25 (48.1)	27 (51.9)	52 (100)
Regulated	5 (9.1)	25 (45.5)	13 (23.6)	12 (21.8)	32 (58.2)	23 (41.8)	55 (100)
Overall	10 (9.3)	37 (34.6)	37 (34.6)	23 (21.5)	57 (53.3)	50 (46.7)	107 (100)

*INR - International Normalized Ratio

Table 5. Display of INR values in relation to the CHA2DS2VASc score

INR values	CHA2DS2VASc score N		
	1	≥ 2	p value
Unregulated	3	47	0.5
Regulated	2	53	

Table 6. Relationship between HAS BLED score and type of anticoagulant therapy

HAS BLED score	Frequency	Percentage	Cumulative percentage	Anticoagulant drugs		p
				NOAC	VAK	
0	5	2.1	2.9			
1	23	9.7	16.0	44 (41.9)	61(58.1)	
2	77	32.4.	60.0			0.5
3	57	23.9	92.6			
4	11	4.6	98.9	26(37.1)	44(62.9)	
5	2	0.8	100.0			
Total	175	73.5		175		

Discussion

The results of our study showed that the majority of patients with atrial fibrillation were between the ages of 65 and 84, with the larger percentage in the age group from 65 to 74 (36.1%), followed by a slightly smaller percentage of patients aged 75–84 (33.6%). Similar results were shown by a French research with the largest number of patients aged 65 to 74, followed by the group of patients older than 80 years [6]. These data indicate that atrial fibrillation affects older population, and the results of our study indicate that first manifestations of AFib coincide with the age of increased risk for CVI. Considering that, it is possible to conclude that older age is a risk factor for the onset of atrial fibrillation [2].

The insight into sex representation appeared engaging. Although referenced data indicate that AFib is more frequent in males [2], the results of our study and aforementioned French study, indicated that both sexes were equally affected [6]. This may point out to the specificity of the researched population, and potential variations in diagnostic approach and the therapy between different countries and health systems.

The analysis of age groups in relation to sex reveals that the largest percentage of males in our study belonged to the age group of 65 to 74, while the largest percentage of females belonged to the age group of 75 to 84 years. These results indicate that the development of CVI is age-dependent in women, which is in accordance with the recommendations of The European Society of Cardiology (ESC) [2]. Women have a specific pattern for the disease onset, and therefore prevention and close monitoring of cardiovascular diseases, including AFib, are often necessary to reduce the risk of severe complications.

Considering anticoagulant therapy, the greatest number of patients in our study were prescribed warfarin (VKAs), while NOACs were prescribed in about one quarter of patients. There is a significant difference in findings of our study in relation to other countries, like Netherlands, where it was noted that NOACs were prescribed in a higher percentage in patients with AFib than VKAs [7]. This may point out to the differences in treatment approach depending on health politics and recommendations in various countries.

A national study in France revealed that introduction of NOACs resulted in increased administration of oral anticoagulant therapy, especially in elderly patients and patients with an increased risk of stroke [6].

In our study, risk assessment according to CHA2DS2-VASc instrument, showed that 219 patients were candidates for the anticoagulant

therapy administration, while six patients were excluded. However, two of six patients, who were not candidates for this therapy according to CHA2DS2-VASc instrument, were using VKAs. This may indicate to suboptimal therapy administration or other factors that may have influence on treatment options, like comorbidities or age. Out of 219 patients who had indication for the anticoagulant therapy, 165 patients were using anticoagulants. This shows that following of guidelines is good, with the possibility of improving, and in some cases adjusting of recommendations.

Analysis of INR values in patients using VKAs showed that the greatest number of patients with unregulated INR values belonged to the older age groups. That is an additional indication for the introduction of NOACs, having the advantage due to an easier administration and minor dependence on food and other drugs intake. The results of a meta-analysis of 10 clinical studies indicate that NOACs, compared to conventional therapy, are equally or more effective in older patients, with low risk of side effects [7, 8]. A systematic review of meta-analyses from six databases confirmed that NOACs are more effective in elderly patients with unstable INR values, what decreases the risk of stroke [9].

VKAs have a narrow therapeutic range, meaning that precise dosing and regular monitoring of INR values have the key role in effectiveness of the therapy. This is particularly important in elderly patients due to variations in diet, interactions with other drugs and changes in physiological functions [9]. The risk from bleeding in these patients is significant, what makes NOACs more attractive treatment option, as often INR monitoring is not necessary and interactions with food and other drugs are less present [10].

The risk from bleeding is one of the key factors in the treatment of AFib, and it is being assessed in accordance with HAS-BLED scoring. The results of our study showed that 40% of patients using anticoagulants were at the increased risk of bleeding, with the majority of that percentage favoring patients using VKAs. This result stresses the necessity of better control and monitoring over the risk of bleeding in order to prevent side effects. HAS BLED instrument has been recommended for achieving better control and regulation of risk factors that can increase the possibility of bleeding, but not for excluding the patient from anticoagulant therapy. The purpose of the usage of this instrument is to enhance the control of risk of bleeding and to administer safe therapy [2, 9]. Apart from clinical effectiveness, the advantage of NOACs in relation to VKAs, is reflected in fixed dosage, predictable effectiveness, lesser interaction with other drugs and food, as well as fast onset. That makes them suitable for elderly patients [9]. However, it is mandatory to assess the renal function before introducing NOACs into therapy, as inappropriate dosing can lead to severe side effects, such as bleeding and thrombosis [11, 12].

In our society, anticoagulant therapy has mainly been prescribed at the secondary health care level, based on the regulation defined by the Health Insurance Fund of Republic of Srpska. Though acetylsalicylic acid (ASA) has been recommended as antiplatelet therapy, the usage of ASA AFib is not in accordance with international recommendations that favor the usage of oral anticoagulants as the first line therapy [6].

Prevention of CVI requires a comprehensive and multidisciplinary approach in the management of patients with atrial fibrillation, with the aim of implementing valid international clinical recommendations, and timely alignment of the therapy based on specific needs of the patient [13, 14].

Study limitations

The study included small number of patients with Afib, therefore large-scale investigation would be more relevant for confirmation of therapy necessity and efficiency.

Conclusion

The results of this study lead to the following conclusions:

The majority of patients with atrial fibrillation (AF) are treated with anticoagulant therapy.

Non-vitamin K antagonist oral anticoagulants (NOACs) are prescribed less frequently than vitamin K antagonists (VKAs) in the AF patient population.

The use of NOACs for stroke prevention in AF patients is only partially aligned with current clinical guidelines.

Therapeutic INR values were achieved in approximately half of the AF patients treated with VKAs.

In Republic of Srpska, the Health Insurance Fund limits NOAC reimbursement to a six-month period, after which these medications must be purchased out-of-pocket.

Despite clinical recommendations favoring NOACs, acetylsalicylic acid (ASA) continues to be used among AF patients, particularly among those unwilling or unable to afford continued anticoagulant therapy.

Funding source. The authors received no specific funding for this work.

Ethical approval. The Ethics Committee of the Primary Health Care Centre Banja Luka, Republic of Srpska, Bosnia and Herzegovina, approved the study and informed consent was obtained from all individual respondents. The research was conducted according to the Declaration of Helsinki.

Conflicts of interest. The authors declare no conflict of interest.

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Učestalost propisivanja antikoagulanasa kod pacijenata sa atrijalnom fibrilacijom u porodičnoj medicini

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Uvod. Antikoagulantni lijekovi ključni su u prevenciji tromboembolijskih komplikacija, uključujući ishemijski moždani udar, kod pacijenata s nevalvularnom atrijalnom fibrilacijom (NVAF). Evropsko udruženje kardiologa preporučuje nove oralne antikoagulanse (NOAK) kao terapiju izbora zbog njihove dokazane efikasnosti i povoljnijeg sigurnosnog profila u odnosu na antagoniste vitamina K (VKA). Cilj ovog istraživanja bio je procijeniti učestalost propisivanja antikoagulantnih lijekova pacijentima s NVAF-om i usklađenost terapije s važećim kliničkim smjernicama za prevenciju moždanog udara.

Metode. Ovo presječno istraživanje provedeno je u periodu od juna 2023. do juna 2024. godine i obuhvatilo je 238 pacijenata s NVAF-om registrovanih u Edukativnom centru Doma zdravlja Banja Luka. Podaci su prikupljeni iz zdravstvenih kartona pacijenata. Rizik od moždanog udara procijenjen je korišćenjem CHA_2DS_2-VASc skale, dok je rizik od krvarenja procijenjen HAS-BLED skalom.

Rezultati. Većina ispitanika bila je starosti između 65 i 84 godine, sa sličnom zastupljenošću oba pola. Pacijenti mlađi od 65 godina imali su značajno niži rizik od moždanog udara (p = 0,000). Prema CHA_2DS_2-VASc skoru, 219 pacijenata imalo je indikaciju za antikoagulantnu terapiju, ali samo 73,5% njih je primilo odgovarajuću terapiju. Najčešće propisivani antikoagulansi bili su antagonisti vitamina K (44,1%), zatim NOAK (29,4%), dok 26,5% pacijenata nije primalo nikakav antikoagulantni lijek. Veći broj pacijenata starijih od 75 godina imao je neregulisane INR vrijednosti, dok su pacijenti u starosnoj grupi 65–74 godine češće imali stabilne INR vrijednosti (p=0,03). Rizik od krvarenja (HAS-BLED ≥ 3) zabilježen je kod 40% pacijenata na antikoagulantnoj terapiji.

Zaključak. Rezultati pokazuju da je propisivanje antikoagulantnih lijekova pacijentima s NVAF-om djelimično usklađeno s važećim kliničkim preporukama. Uočeno je nedovoljno korišćenje NOAK-a, unatoč njihovim dokazanim prednostima. Potrebne su dodatne mjere za optimizaciju antikoagulantne terapije, naročito kod starijih pacijenata i onih s visokim rizikom od moždanog udara.

Ključne riječi: atrijalna fibrilacija, antikoagulantna terapija, vitamin K antagonisti, moždani udar