The incidence of bleeding in patients with nonvalvular atrial fibrillation using anticoagulants: a real-world report with the biggest Vietnamese data

Bui The Dung,[1] Cao Ngoc Mai Han,[1] Tran Hoa,[2] Nguyen Thanh Hien[1]

[1]Department of Cardiology, University Medical Center HCMC, Ho Chi Minh City; [2]Department of Internal Medicine, Faculty of Medicine, University of Medicine and Pharmacy at Ho Chi Minh City, Vietnam

ABSTRACT

This is a retrospective descriptive study carried out on 1036 patients with nonvalvular atrial fibrillation who took oral anticoagulants and visited the cardiology clinic of the University of Medicine and Pharmacy Hospital, Ho Chi Minh City, from 01/01/2021 to 30/06/2021. The objective was to investigate the incidence of bleeding in these patients. The average age of the study population was 72±12 years, with an average CHA_2DS_2VASc score of 4.2±1.8 and an average HAS-BLED score of 1.26±0.03. Rivaroxaban was the most prescribed anticoagulant, with a total of 463 cases, accounting for 44.7%. There were 99 bleeding events recorded; of these, 37 (37.4%) cases were severe bleeding, and 62 (62.6%) were minor bleeding. Gastrointestinal bleeding was the most common site in both severe and minor bleeding groups. The group who had an overdose of anticoagulants had a severe bleeding rate of 52.4%, similar to the group whose anticoagulant dose could not be assessed (55.6%), nearly twice as high as the group who took the standard dose (30.6%) and the group who took a lower dose than recommended (30.0%). Of the 37 cases of severe bleeding, 14 (37.8%) were using rivaroxaban, 12 (32.4%) were using vitamin K antagonists, 5 (13.5%) were using dabigatran, and 6 (16.2%) were using a combination of anticoagulants and antiplatelets. To conclude, gastrointestinal bleeding was a very common event in patients using anticoagulants for nonvalvular atrial fibrillation. Non-vitamin K antagonist oral anticoagulants should be preferred in patients with a high risk of bleeding (dabigatran may have advantages over rivaroxaban). It is important to assess the patient's weight and renal function to determine the appropriate anticoagulant dose according to recommendations to reduce the risk of severe bleeding.

Correspondence: Nguyen Thanh Hien, Department of Cardiology, University Medical Center HCMC, Ho Chi Minh City, Vietnam.
E-mail: hien.nt1@umc.edu.vn

Key words: nonvalvular atrial fibrillation, anticoagulant, major bleeding.

Contributions: all the authors made a substantial intellectual contribution, read and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

Conflict of interest: the authors declare that they have no competing interests, and all authors confirm accuracy.

Ethics approval and consent to participate: the study was approved by the Ethics Committee of University Medical Center Ho Chi Minh City.

Informed consent: written informed consent was obtained from all patients.

Patient consent for publication: all patients provided written informed consent for publication of their data.

Availability of data and materials: data and materials are available from the corresponding author upon request.

Funding: none.

Received: 24 September 2024.
Accepted: 18 November 2024.

Licensee PAGEPress, Italy
Italian Journal of Medicine 2025; 19:1807
doi:10.4081/itjm.2025.1807

Introduction

Atrial fibrillation is one of the most common arrhythmias in clinical practice. The aging population, coupled with advancements in screening for atrial fibrillation, has significantly increased the incidence of atrial fibrillation worldwide. It is estimated that by 2050, there will be up to 72 million cases of atrial fibrillation in Asia alone.[1] Concurrently, there is an increase in the disease burden associated with atrial fibrillation, including heart failure, stroke, and other systemic thromboembolic events. The hospital admission rate for atrial fibrillation is also expected to increase by 5-42% annually in the Asia-Pacific countries.[1]

The introduction of oral anticoagulants, especially non-vitamin K antagonist oral anticoagulants [non-vitamin K antagonist oral anticoagulants (NOACs)], has significantly reduced the incidence of thromboembolic events related to atrial fibrillation. However, an undesired side effect during

the use of anticoagulants, which is bleeding events, is quite common among the Asian population.[2] Some studies have shown that using oral anticoagulants at the recommended standard dose can help reduce the risk of thromboembolism as well as bleeding in patients while using a dose lower than recommended may increase the risk of thromboembolism but does not help reduce bleeding rates.[2,3] Therefore, using anticoagulants appropriately according to liver and kidney function is an important factor in the process of anticoagulant usage.

Because there is not much real-world evidence of clinical bleeding relating to NOACs in developing Southeast Asian countries so far, we conducted this study to investigate bleeding events in patients using anticoagulants for atrial fibrillation not caused by valvular heart disease.

Materials and Methods

Research subjects

The study included 1036 patients aged ≥18 years diagnosed with nonvalvular atrial fibrillation, who visited the cardiology clinic of the University Medical Center HCMC, Ho Chi Minh City, from 01/01/2021 to 30/06/2021, and were prescribed oral anticoagulants ($CHA_2DS_2VASc \geq 1$ in men or $CHA_2DS_2VASc \geq 2$ in women). People who had paroxysmal atrial fibrillation because of treatable conditions (acute coronary syndrome, sepsis, hyperthyroidism, or after surgery) and whose echocardiograms did not show any structural abnormalities in the atrium and whose subsequent electrocardiogram Holter monitoring did not record recurrent atrial fibrillation were not included. Neither were patients who did not have enough data collected (for example, those who went to the University Medical Center HCMC for tests and the results were not saved in their electronic record); nor were people who needed to be anticoagulated for other reasons (venous thromboembolism, pulmonary embolism, *etc*.).

Research methods

The main variables used in this retrospective descriptive study are the following. i) nonvalvular atrial fibrillation: atrial fibrillation not accompanied by a mechanical valve or new biological valve replacement ≤3 months, or mitral stenosis with valve area <1.5 cm^2; ii) duration of anticoagulant use: the time from the start of anticoagulation to the occurrence of the bleeding event (group 1: ≤7 days; group 2: 8-30 days; group 3: 1-3 months; group 4: 3 months-1 year; group 5: >1 year); iii) for cases that had changed several types of anticoagulants before the bleeding event, only the duration of the last type of anticoagulant used immediately before the bleeding event was counted; iv) major bleeding according to the International Society on Thrombosis and Hemostasis criteria, satisfied by one of the following standards: bleeding that leads to death, bleeding with symptoms in a critical area or organ such as intracranial, intraspinal, intraocular, retroperitoneal, intra-articular, or pericardial, or intramuscular with compartment syndrome, or bleeding causing a decrease in hemoglobin level of 2 g/dL or more, or leading to the transfusion of two or more units of whole blood or red cells. In cases where a patient had multiple bleeding sites at the same time, the most severe bleeding site was recorded; v) the recommended dose of anticoagulant was determined according to the 2020 European Society of Cardiology (ESC) guidelines on the management and treatment of atrial fibrillation (Table 1); vi) if Rivaroxaban dosing is determined according to the J-ROCKET AF study, the standard dose is considered to be 15 mg, and the reduced dose is 10 mg; vii) vitamin K antagonist anticoagulants are deemed to be below the standard dose when international normalized ratio (INR)<2.0 and overdosed when INR>3.0.

Continuous sampling of patients meeting the selection criteria during the period 01/2021–06/2021, with information obtained from electronic records, was used.

Collected data were entered and processed using SPSS software version 25.0 (IBM, Armonk, NY, USA). Quantitative variables were presented as mean values with standard deviation (or median and interquartile range if not normally distributed). Qualitative variables were presented as percentages. The independent sample *t*-test was used to compare two means, and a one-way analysis of variance was used to compare multiple means. The Chi-square test was employed to examine the relationship between two qualitative variables. The relationship of independent variables to the dependent variable (binary) was determined using logistic regression models, with results presented as odds ratios (OR) and 95% confidence intervals (CI). All tests, analyses, and comparisons mentioned above were considered statistically significant if $p<0.05$ with a 95% CI.

Table 1. Non-vitamin K antagonist oral anticoagulant doses according to the 2020 European Society of Cardiology guidelines.

	Dabigatran	Rivaroxaban	Apixaban
Standard dose	150 mg twice daily	20 mg once daily	5 mg twice daily
Low dose	110 mg twice daily	-	-
Reduced dose	-	15 mg once daily	2,5 mg twice daily
Dose reduction criteria	The 110 mg dose is recommended if the patient meets at least one of the following criteria: i) age ≥80 years; ii) concurrent use of verapamil; ii) high risk bleeding	A reduced dose is recommended for patients with a creatinine clearance (CrCl) of 15-49 mL/min	The reduced dose is recommended if the patient meets at least 2 of the following criteria: i) age ≥80 years; ii) body weight ≤60 kg; iii) serum creatinine ≥1.5 mg/dL (133 µmol/L). Alternatively, for patients with a CrCl <30 ml/min.

Results

Out of the 1036 cases collected, 127 (12%) had a history of bleeding, but only 83 (8%) patients were on anticoagulants before the bleeding event occurred. Of these, 71 (85%) cases had one bleeding event, 8 (10%) had two bleeding events, and 4 (5%) had three bleeding events, totaling 99 bleeding events recorded after anticoagulant use. The group with a history of bleeding had an average age of 76±11, CHA_2DS_2VASc score of 4.98±1.68, and HAS-BLED score of 1.98±0.93, which are significantly higher than the group without a history of bleeding (respectively, 71±12 years, 4.11±1.75 points, and 1.16±0.79 points), with p<0.001. The group with a history of bleeding was five times less likely to be prescribed oral anticoagulants compared to those without a history of bleeding (95% CI 2.56-8.71), regardless of whether these patients were on anticoagulants before the bleeding event (Table 2).

The demographic characteristics of atrial fibrillation patients with bleeding events after taking oral anticoagulants are presented in Table 3. About one-third of the cases with bleeding events were very old patients (>80 years old). The group using vitamin K antagonist anticoagulants had a bleeding event rate twice as high as that of rivaroxaban and dabigatran users (19.4% compared to 9.2% and 8.7%). This group was younger on average than the NOAC group, and nearly 50% of these cases were on medication before visiting the University Medical Center HCMC, Ho Chi Minh City (the duration of medication use before the bleeding event was unclear). After the bleeding event, 12 out of 25 (48%) cases using vitamin K antagonist anticoagulants were switched to NOACs. Most NOAC cases had bleeding events occurring after >3 months of medication use. However, when combining NOACs and antiplatelet drugs, this complication appeared earlier, with 57.1% of cases being skin and mucosal bleeding.

Gastrointestinal bleeding was the most common site in both groups, with severe and minor bleeding levels. Nine out of 30 cases of gastrointestinal bleeding were prescribed proton pump inhibitors. Compared to vitamin K antagonists, rivaroxaban and dabigatran had a higher rate of gastrointestinal bleeding complications (60% and 50% compared to 40%). While most cases of bleeding after NOAC use were minor, the vitamin K antagonist group had a >50% rate of severe bleeding. Most bleeding cases had an INR>3.0, yet there were cases of bleeding with INR within or below the therapeutic range (including two cases due to combination with antiplatelet drugs).

Severe bleeding requiring surgical/interventional procedures occurred only in the group using vitamin K antagonist anticoagulants and the group taking rivaroxaban, mainly gastrointestinal bleeding and cerebral hemorrhages. Both cases using vitamin K antagonists had an INR>5.0. The group that assumed rivaroxaban had four patients on the recommended doses and two cases on a dose below the ESC recommended one (if calculated according to the J-ROCKET AF study standards, then all 6 cases were on a dose of rivaroxaban appropriate for renal function). The highest rate of cases requiring blood transfusion was in the vitamin K antagonist group (50%), while the group that took dabigatran only had 9.1% of cases requiring transfusion.

Over half of the patients were restarted on anticoagulants within 1 month after the bleeding event. Patients >80 years old were three times more likely to discontinue anticoagulants for >1 year after the bleeding event compared to those ≤80 years old (95% CI 1.09-8.14). For gastrointestinal bleeding events, 32.7% of cases were restarted on anticoagulants within one week, and 26.5% of cases within 2-4 weeks. Even with minor gastrointestinal bleeding, only 46.7% of patients were prescribed anticoagulants again within one week.

Nearly one-third of the cases with severe bleeding complications assumed an overdose of anticoagulants compared to the recommendation (Table 4). The age and weight of the group with a prescribed overdose or a dose below the recommended one were equivalent to the group with a prescribed dose according to the recommendation. The lowest renal function was observed in the group that overdosed on anticoagulants compared to the recommendations (Table 5).

Table 2. General characteristics of the study population.

Characteristics	Total (n=1036)	No anticogulants (n=187)	Antivitamin K (n=129)	Rivaroxaban (n=463)	Dabigatran (n=253)	Apixaban (n=4)	Chi-square test
Age, mean±SD	72±12	70±14	68±11	74±11	71±12	81±7	<0.001
Female, n (%)	542 (52.3)	98 (52.4)	65 (50.4)	252 (54.4)	124 (49.0)	3 (75.0)	0.578
Heart failure, n (%)	326 (31.5)	52 (27.8)	49 (38.0)	150 (32.4)	72 (28.5)	3 (75.0)	0.078
Hypertension, n (%)	838 (80.9)	138 (73.8)	88 (62.8)	397 (85.7)	211 (83.4)	4 (100.0)	<0.001
Diabetes, n (%)	321 (31.0)	42 (22.5)	37 (28.7)	152 (32.8)	88 (34.8)	2 (50.0)	0.031
Coronary artery disease, n (%)	623 (60.1)	108 (57.8)	67 (51.9)	281 (60.7)	164 (64.8)	3 (75.0)	0.141
peripheral artery disease, n (%)	56 (5.4)	10 (5.3)	2 (1.6)	31 (6.7)	13 (5.1)	0	0.198
Stroke, n (%)	219 (21.1)	20 (10.7)	24 (18.6)	108 (23.3)	65 (25.7)	2 (50.0)	<0.001
Chronic kidney disease, n (%)	300 (29.0)	48 (25.7)	39 (30.2)	148 (32.0)	61 (24.1)	4 (100.0)	0.005
Cirrhosis, n (%)	26 (2.5)	10 (5.3)	5 (3.9)	7 (1.5)	4 (1.6)	0	0.042
Concomitant antiplatelet use, n (%)	126 (12.2)	105 (56.1)	7 (5.4)	10 (2.2)	3 (1.2)	1 (25.0)	<0.001
CHA_2DS_2VASc score, mean±SD	4.2±1.8	3.7±1.8	3.7±1.7	4.5±1.7	4.3±1.8	6.0±2.2	<0.001
HAS-BLED score, mean±SD	1.3±0.85	1.2±0.98	1.6±0.98	1.2±0.76	1.2±0.79	2±0.82	<0.001
History of bleeding, n (%)	127 (12.3)	42 (22.5)	12 (9.3)	41 (8.9)	30 (11.9)	2 (50.0)	<0.001

SD, standard deviation.

Table 3. Characteristics of atrial fibrillation patients with bleeding events after oral anticoagulant therapy.

	Antivitamin K (n=18)	Antivitamin K + antiplatelet (n=7)	Rivaroxaban (n=43)	Dabigatran (n=22)	Apixaban (n=2)	NOAC + antiplatelet (n=7)	Total (n=99)
Age, mean±standard deviation	70±8	69±10	76±12	82±8	78±8	74±8	76±11
Time to bleeding while on anticoagulant therapy, n (%)							
Not specified	9 (50.0)	2 (28.6)	2 (4.7)	1 (4.5)	0	0	14 (14.1)
≤1 month	1 (5.6)	0	10 (23.3)	3 (13.5)	1 (50.0)	1 (14.3)	16 (16.2)
2-3 months	1 (5.6)	1 (14.3)	6 (14.0)	4 (18.2)	0	3 (42.9)	15 (15.2)
4-12 months	1 (5.6)	2 (28.6)	14 (32.6)	5 (22.7)	1 (50.0)	3 (42.9)	26 (26.3)
>1 year	6 (33.3)	2 (28.6)	11 (25.6)	9 (40.9)	0	0	28 (28.3)
Time to resume anticoagulant therapy after bleeding, n (%)							
Continuous anticoagulant therapy after bleeding	1 (5.6)	0	15 (34.9)	5 (22.7)	2 (100.0)	3 (42.9)	26 (26.3)
<1 week	4 (22.2)	3 (42.9)	3 (7.0)	3 (13.6)	0	0	13 (13.1)
2-4 weeks	5 (27.8)	3 (42.9)	5 (11.6)	7 (31.8)	0	3 (42.9)	23 (23.2)
2-3 months	2 (11.1)	0	5 (11.6)	0	0	1 (14.3)	8 (8.1)
4-12 months	1 (5.6)	0	5 (11.6)	3 (13.6)	0	0	9 (9.1)
>1 year	0	0	3 (7.0)	1 (4.5)	0	0	4 (4.1)
Not specified	5 (27.8)	1 (14.3)	7 (16.3)	3 (13.6)	0	0	16 (16.2)
Minor bleeding location, n (%)							
Gastrointestinal bleeding	3 (16.7)	2 (28.6)	17 (39.5)	8 (36.4)	0	0	30 (30.3)
Urinary bleeding	0	1 (14.2)	4 (9.3)	2 (9.1)	1 (50.0)	0	8 (8.1)
Intramuscular bleeding	2 (11.1)	0	0	2 (9.1)	0	0	4 (4.0)
Subcutaneous and mucosal bleeding	1 (5.6)	1 (14.2)	6 (13.9)	4 (18.2)	0	4 (57.1)	16 (16.2)
Haemoptysis	0	0	2 (4.6)	1 (4.5)	0	0	3 (3.0)
Vaginal bleeding	0	0	0	0	1 (50.0)	0	1 (1.0)
Major bleeding location, n (%)							
Gastrointestinal bleeding	5 (27.8)	0	9 (20.9)	3 (13.6)	0	2 (28.6)	19 (19.2)
Urinary bleeding	0	0	0	0	0	0	0
Intramuscular bleeding	3 (16.7)	1 (14.2)	0	1 (4.5)	0	0	5 (50.1)
Subcutaneous and mucosal bleeding	0	0	0	0	0	0	0
Haemoptysis	0	0	0	0	0	0	0
Vaginal bleeding	0	0	0	0	0	0	0
Intracranial hemorrhage	4 (22.2)	2 (28.4)	4 (9.3)	1 (4.5)	0	1 (14.3)	12 (12.1)
Hemothorax	0	0	1 (2.3)	0	0	0	1 (1.0)
Bleeding treatment, n (%)							
Hospital admission	17 (94.4)	5 (71.4)	24 (55.8)	11 (50.0)	0	3 (42.9)	60 (60.6)
Blood transfusion	9 (50)	1 (14.2)	5 (11.6)	2 (9.1)	0	2 (28.6)	19 (19.2)
Surgery/procedure	2 (11.1)	0	7 (16.3)	0	0	0	9 (9.1)
Temporary cessation of anticoagulation	4 (22.2)	0	6 (13.9)	5 (22.7)	0	1 (14.3)	16 (16.2)
Switching to a different anticoagulant	7 (38.9)	5 (71.4)	11 (25.6)	4 (18.2)	1 (50.0)	1 (14.3)	29 (29.3)

NOAC, novel oral anticoagulant.

Table 4. Incidence of severe bleeding by anticoagulant dose group.

Dose of NOACs	Antivitamin K (n=12)	Antivitamin K + antiplatelet (n=3)	Rivaroxaban (n=14)	Dabigatran (n=5)	NOAC + antiplatelet (n=3)	Total (n=37)
Below recommended dose, n (%)	0	1 (33.3)	1 (7.1)	0	0	2 (5.4)
Recommended dose, n (%)	2 (16.7)	1 (33.3)	10 (71.4)	3 (60.0)	3 (100.0)	19 (51.4)
Over recommended dose, n (%)	7 (58.3)	1 (33.3)	2 (14.3)	1 (20.0)	0	11 (29.7)
Not specified, n (%)	3 (25.0)	0	1 (7.1)	1 (20.0)	0	5 (13.5)

NOAC, novel oral anticoagulants.

Table 5. Characteristics of patient groups prescribed anticoagulants at the recommended dose compared to those prescribed below or above the recommended dose.

	Below recommended dose	Recommended dose	Over recommended dose	Chi-square test
Age (mean±SD)	74±11	76±11	76±9	0.888
Weight (mean±SD)	64±10	60±9	61±14	0.547
Creatinine (mean±SD)	0.83±0.19	1.18±0.47	1.39±0.64	0.034
Creatinine clearance (mean±SD)	66±22	46±18	41±19	0.015

SD, standard deviation.

Discussion

The rising incidence of atrial fibrillation can be attributed to enhanced detection rates, the aging population, and the presence of multiple comorbid conditions. Patients with nonvalvular atrial fibrillation are increasingly older, facing risks such as kidney failure, falls, dementia, and numerous comorbidities. In our study, the median age of patients was 72 years, which was higher than the median age of Asian patients in studies like RE-LY, ROCKET AF, ARISTOTLE, and ENGAGE AF TIMI-48.[2]

The prevalence of atrial fibrillation is lower in Asians than in Caucasians. However, due to Asia's large population, the burden of atrial fibrillation is higher than in Europe. Approximately 2.9 million Asians will suffer strokes due to atrial fibrillation by 2050 if not treated with anticoagulants. Asian patients have a higher rate of stroke and embolism compared to non-Asian patients, and Asians are also more susceptible to bleeding complications.[4,5]

In our study, the rate of bleeding after the use of oral anticoagulants in patients with nonvalvular atrial fibrillation was 8%, with severe bleeding accounting for 3.6%, which is equivalent to or lower than the rates reported in other global studies.[6,7] A history of bleeding was one of the factors limiting the prescription rate of anticoagulants (OR=5.10, 95% CI 2.56-8.71). A study conducted at the Gia Dinh People's Hospital in 2018, involving 431 nonvalvular atrial fibrillation cases, also showed that in the high stroke risk group, 6% of patients had not been prescribed anticoagulants due to complications or bleeding risk.[8]

Global studies consistently report gastrointestinal bleeding as the most common bleeding site in patients with nonvalvular atrial fibrillation who have been prescribed oral anticoagulants,[2] similar to the findings of our study. Since the introduction of NOACs, there has been an increase in anticoagulation use and a decrease in cardioembolic event rates in patients with new nonvalvular atrial fibrillation, including Asian patients.[9] However, the literature also notes an increase in gastrointestinal bleeding events in patients using rivaroxaban and dabigatran compared to warfarin, while apixaban reduces this risk. Therefore, the RE-LY and ROCKET-AF studies excluded patients with a history of gastrointestinal bleeding.[2] Although our study had limited cases prescribed on apixaban, it still showed a higher rate of gastrointestinal bleeding in the rivaroxaban and dabigatran groups compared to the vitamin K antagonist group (60% and 50% *vs*. 40%). Asian patients have a higher rate of intracranial hemorrhage than non-Asian patients, and developing countries bear 80% of the global burden of intracranial hemorrhage.[4] The rate of intracranial hemorrhage in our study was 12.1%, ranking second after gastrointestinal bleeding.

Moreover, restarting anticoagulation after a bleeding event is crucially important to protect patients against thromboembolic events. Some studies have shown that resuming NOACs in patients with a history of gastrointestinal bleeding not only reduces the risk of stroke but also reduces severe bleeding events and the rate of recurrent gastrointestinal bleeding.[2] However, the timing of anticoagulation resumption remains a controversial issue. Some studies suggest restarting at the time of hospital discharge or after 7 days from the gastrointestinal bleeding event to reduce the rate of thromboembolic events without increasing the risk of recurrent bleeding compared to restarting anticoagulation after 30 days.[2] Keys to safely restarting anticoagulation are controlling bleeding risk factors, such as eliminating medications that increase bleeding risk (antiplatelets, non-steroidal anti-inflammatory drugs, and corticosteroids), adding proton pump inhibitors, or performing surgical/interventional treatment for the bleeding source (such as tumor removal, hemorrhoidectomy). At the University Medical Center HCMC, the resumption of anticoagulation after gastrointestinal bleeding is often delayed beyond a week, even in cases of minor bleeding, possibly due to uncontrolled bleeding conditions (patient refusal of endoscopy, recurrent gastrointestinal bleeding).

Excessive dosing of anticoagulants has been shown to increase the risk of severe bleeding in many studies.[10] In our study, about one-third of the severe bleeding cases were on an anticoagulant dose exceeding the recommended one. The current challenge is that our hospital's testing system calculates renal filtration rate using the Chronic Kidney Disease Epidemiology Collaboration formula without readily available creatinine clearance results *via* the Cockcroft-Gault formula, potentially complicating the prescribing process for cardiologists under time constraints due to high patient volumes.

Data from studies around the world show that the therapeutic interval of vitamin K antagonists in Asian patients is low,[5] but INR stabilization does not significantly reduce the risk of stroke/thromboembolism or major bleeding.[11] Asian patients are often susceptible to bleeding events when using vitamin K antagonists, even when the INR is below the therapeutic range.[2,12] This aligned with our findings, where the rate of bleeding post-vitamin K antagonist use was twice as high as that in the rivaroxaban and dabigatran groups. The hospitalization rate for bleeding events with vitamin K antagonists was twice as high as for the NOAC group, approaching 90%. Consequently, current global and Asian guidelines prefer NOACs due to the high cost associated with hospitalizing bleeding events, potentially exceeding NOAC treatment costs. With a high bleeding risk, Asian patients are often prescribed NOACs at doses lower than recommended, but studies have shown that this does not decrease the risk of severe bleeding while significantly increasing the risk of thromboembolic events.[13-15]

Our study was a retrospective one based on electronic health records, and some information could not be collected. Patients had multiple bleeding events, but we only collected data on the most recent bleeding event during the data collection process. Sometimes, patients were admitted to other hospitals for bleeding treatment, and we could not capture that information. Moreover, the anticoagulant medications used by patients changed several times throughout the treatment process. Therefore, we plan to conduct a prospective observational study to monitor patients in the future to update on anticoagulant use, related health events, and anticoagulant usage.

Conclusions

A history of bleeding significantly limits the prescription rate of anticoagulants for patients with nonvalvular atrial fibrillation. Gastrointestinal bleeding is the most common event associated with the use of oral anticoagulants. NOACs (dabigatran may have advantages over rivaroxaban) should

be the preferred choice over vitamin K antagonist anticoagulants in patients at high risk of gastrointestinal bleeding. It is important to assess the patient's weight and renal function to determine the appropriate anticoagulant dosage according to guidelines, which helps reduce the risk of severe bleeding during treatment.

References

1. Biosense Webster. Beyond the burden: the impact of atrial fibrillation in Asia Pacific, 2019 report. Available from: https://www.jnjmedtech.com/system/files/pdf/beyond-the-burden-afib-stroke-statistics-report.pdf.
2. Chiang CE, Chao TF, Choi EK, et al. Stroke prevention in atrial fibrillation: a scientific statement of JACC: Asia (part 1). JACC Asia 2022;2:395-411.
3. Chong DTT, Andreotti F, Verhamme P, et al. Direct oral anticoagulants in Asian patients with atrial fibrillation: consensus recommendations by the Asian Pacific Society of Cardiology on strategies for thrombotic and bleeding risk management. Eur Cardiol 2021;16:e23.
4. Krishnamurthi RV, Feigin VL, Forouzanfar MH, et al. Global and regional burden of first-ever ischaemic and haemorrhagic stroke during 1990-2010: findings from the Global Burden of Disease Study 2010. Lancet Glob Health 2013;1:e259-81.
5. Li YG, Lee SR, Choi EK, Lip GY. Stroke prevention in atrial fibrillation: focus on Asian patients. Korean Circ J 2018;48:665-84.
6. Connolly SJ, Ezekowitz MD, Yusuf S, et al. Dabigatran versus warfarin in patients with atrial fibrillation. N Engl J Med 2009;361:1139-51.
7. Patel MR, Mahaffey KW, Garg J, et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. N Engl J Med 2011;365:883-91.
8. Hai NH. Anticoagulants prescription in nonvalvular atrial fibrillation during the first six month of 2018 in out-patient settings of Gia Dinh Peoples Hospital. Ho Chi Minh City J Med 2018;22:50-5.
9. Chao TF, Chiang CE, Lin YJ, et al. Evolving changes of the use of oral anticoagulants and outcomes in patients with newly diagnosed atrial fibrillation in Taiwan. Circulation 2018;138:1485-7.
10. Camm AJ, Cools F, Virdone S, et al. Mortality in patients with atrial fibrillation receiving nonrecommended doses of direct oral anticoagulants. J Am Coll Cardiol 2020;76:1425-36.
11. Bonde AN, Staerk L, Lee CJ, et al. Outcomes among patients with atrial fibrillation and appropriate anticoagulation control. J Am Coll Cardiol 2018;72:1357-65.
12. Liu X, Huang M, Ye C, et al. The role of non-vitamin K antagonist oral anticoagulants in Asian patients with atrial fibrillation: a PRISMA-compliant article. Medicine 2020;99:e21025.
13. Cho MS, Yun JE, Park JJ, et al. Outcomes after use of standard- and low-dose non-vitamin K oral anticoagulants in Asian patients with atrial fibrillation. Stroke 2019;50:110-8.
14. 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;42:373-498.
15. Hori M, Matsumoto M, Tanahashi N, et al. Rivaroxaban vs. warfarin in Japanese patients with atrial fibrillation – the J-ROCKET AF study. Circ J 2012;76:2104-11.