DOI: 10.4149/BLL_2023_020

Bratisl Med J 2023; 124 (2)

128 – 132

CLINICAL STUDY

Risk of bleeding after ground-level falls in elderly patients with atrial fibrillation and warfarin therapy

Branislav BEZAK[1,2,9], Marianna BARBIERIK VACHALCOVA[3,10], Viera KISSOVA[6], Peter MICHALEK[2,3], Jan STEVLIK[4], Peter JACKULIAK[7], Milos STEVOVE[5], Tomas UHER[3,5], Allan BOHM[1,3,8]

East Slovak Institute of Cardiovascular Diseases and Pavol Jozef Safarik University, Kosice, Slovakia. **marianna.vachalcova@gmail.com**

ABSTRACT

OBJECTIVES: The aim of this study was to investigate bleeding risk in patients treated with VKAs after ground-level falls, considering the type and severity of bleeding.

METHODS: The study was designed as a retrospective cohort study and included a total of 204 elderly patients aged > 65 years treated for AF continuously with warfarin for more than 3 years. Data were obtained from hospital registries in Bratislava, Slovakia. A 5-year assessment of death/survival was performed to determine mortality.

RESULTS: There was no statistically significant difference in severe bleeding (2.13 % with falls vs 2.55 % without, p=1) and 5-year mortality (45 % and 38 % respectively, p=0.3987) based on the presence of falls. Multivariate analysis, after adjustment for age, CHA_2DS_2VASc, HASBLED, stroke history, labile INR and number of falls showed that only HASBLED score was a statistically significant contributor (CI: 1.0245 – 1.0919, p=0.0007) to severe bleeding. There was statistically significant difference in severe bleeding (18 % vs 0 %, p=0.0132) between patients suffering from spontaneous and bleeding after falls and also when comparing individual bleeding episodes (12 % vs 1 %, p < 0.0001). There was no statistically significant difference in 5-year mortality between the two groups (43 % vs 42 % respectively, p=0.3931).

CONCLUSIONS: Our results show that occurrence of falls in AF patients treated with VKAs have no significant impact on the incidence of severe bleeding and 5-year mortality and that spontaneous bleeding was associated with a significantly higher risk of severe bleeding compared to bleeding after falling *(Tab. 4, Ref. 30)*. Text in PDF *www.elis.sk*

KEY WORDS: atrial fibrillation, vitamin K antagonists, bleeding, elderly patients, falling.

Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia affecting approximately 5 % of population over 65 years and it is a significant risk factor for ischemic stroke and death (1). This risk can be effectively reduced with appropriate long-term oral anticoagulation therapy (2–4). However, almost half of eligible older patients with AF are not treated with anticoagulant therapy due to clinicians' concerns over potential treatment-related harms (5–8). Several studies have shown that the main concern is over possible risk of fall with consequent traumatic intracranial damage (9). Community dwelling individuals over 65 years have 1–2 % risk of falling per year and 5 % of them result in fracture and hospitalization (10). Many physicians often consider this risk of falls and potential intracranial hemorrhage to be a contraindication for oral anticoagulant (OAC) (11–13). Although vitamin K antagonists (VKAs) are being increasingly replaced by the novel oral anticoagulants (NOACs) (14–16) in patients with non-valvular AF, VKAs are still widely used (17–19) and remain the agents of choice for patients with atrial fibrillation in the setting of rheumatic valvular disease and those with mechanical heart valves (2, 20, 21). Furthermore, many countries (e.g. Slovakia) still have prescription limitations for NOACs, reserving them as second-line treatment for patients not tolerating VKAs (22). The risk evaluation of both ischemic adverse events and bleeding is important to guide the selection of the most appropriate patient treatment (23). For this purpose, several scoring systems (e.g. HAS-BLED or CHA_2DS_2-VASc) have been developed (2).

[1]National Institute of Cardiovascular Diseases, Bratislava, Slovakia, [2]Comenius University, Faculty of Medicine, Bratislava, Slovakia, [3]Premedix Academy, Bratislava, Slovakia, [4]University Hospital Bratislava, Bratislava, Slovakia, [5]Comenius University, Bratislava, Slovakia, [6]Comenius University, Faculty of Medicine, First Department of Internal Medicine, Bratislava, Slovakia, [7]Comenius University in Bratislava, Faculty of Medicine, 5. Department of Internal Medicine, University Hospital Bratislava, Bratislava, Slovakia, [8]Comenius University in Bratislava, Faculty of Medicine, 3. Department of Internal Medicine, University Hospital Bratislava, Bratislava, Slovakia, [9]Slovak Medical University, Bratislava, Slovakia, and [10]East Slovak Institute of Cardiovascular Diseases and Pavol Jozef Safarik University, Kosice, Slovakia

Address for correspondence: Marianna Barbierik VACHALCOVÁ, MD, PhD, East Slovak Institute of Cardiovascular Diseases and Pavol Jozef Safarik University, Ondavská 8, SK-040 13 Kosice, Slovakia.
Phone: 055/7891410, Fax: 055/7891413

According to the latest version of European Society of Cardiology (ESC) Clinical Practice Guidelines for Atrial Fibrillation, the risk of stroke without OAC exceeds the bleeding risk on OAC, even in the elderly, patients with cognitive dysfunction or patients with frequent falls or frailty (2). However, these recommendations are based on studies considering the risk of ground-level falls and reliable results considering the type and majority of bleeding are still missing and an unambiguous answer to the question of whether the benefit of therapy always outweighs the potential risk associated with falls is still not available.

The aim of this study was to evaluate the risk of severe bleeding in patients with atrial fibrillation treated by VKAs (warfarin) after ground-level falls, to compare the severity of bleeding and mortality between patients with and without falls and to compare the severity of bleeding and mortality in patients after spontaneous bleeding and bleeding caused by ground-level falls.

Material and methods

The study was designed as a retrospective cohort study. Study population included patients hospitalized with atrial fibrillation during years 2012–2014. Data were obtained from two hospital registries in Bratislava, Slovakia. Elderly patients aged > 65 years treated continuously with warfarin for atrial fibrillation for more than 3 years were included.

The exclusion criteria were:

1. Hemorrhagic diathesis of any etiology (vasculopathy, thrombocytopathy, thrombocytopenia, etc.) except for diathesis based on appropriate dose of warfarin
2. Discontinuation of anticoagulation therapy during observed period of time, except for discontinuation due to bleeding
3. Dialyzed patients

The number of falls, incidence of episodes of spontaneous bleeding, and bleeding outcomes during the last 3 years were acquired from medical records and an interview with patients or their legal representatives. The list of questions is in the annex.

In the case of discontinuation of anticoagulation therapy with VKA the reason of bleeding and its level were verified. In the case of death, it was verified if the cause of death was bleeding.

The bleeding was classified according the ISTH/SSC (24) classification:

1. No bleeding
2. Minor bleeding: bleeding without complications, not requiring medical attention (e.g. epistaxis with spontaneous resolution, simple hematomas, etc.)
3. Intermediate bleeding: bleeding with complication requiring medical attention that does not satisfy the conditions for major bleeding (e.g. epistaxis requiring a tamponade, infected hematoma, asymptomatic gastrointestinal bleeding, etc.)
4. Major bleeding
   a. Bleeding accompanied by ≥ 12.5 mmol/l decrease in hemoglobin
   b. Bleeding requiring administration of erythrocyte concentrate
   c. Symptomatic bleeding in a critical area (intracranial, intraspinal, retroperitoneal, intraocular, pericardial, compartment syndrome)
   d. Lethal bleeding

Tab. 1. Comparison of patients after falls and without falls.

Characteristics (n=204)	Falls (n=47)	Without falls (n=157)	p
Age (years)	**79.45(±7.2)**	75.72(±7.65)	**0.0031**
Female sex (%)	32 (68 %)	95 (61 %)	0.3939
Heart failure (%)	35 (74 %)	105 (67 %)	0.3736
Hypertension (%)	46 (98 %)	153 (97 %)	1
Diabetes Mellitus (%)	18 (38 %)	55 (35 %)	0.7299
Vascular disease[1] (%)	19 (40 %)	43 (27 %)	0.1044
Abnormal renal parameters[2] (%)	10 (21 %)	26 (17 %)	0.5135
Stroke history (%)	**5 (11 %)**	5 (3 %)	**0.0527**
Labile INR[3] (%)	**27 (57 %)**	47 (30 %)	**0.0009**
Medication Usage Predisposing to Bleeding (%)[4]	3 (6 %)	13 (8 %)	1
Alcohol consumption[5] (%)	3 (6 %)	11 (7 %)	1
Pulmonary embolism (%)	4 (9 %)	6 (4 %)	0.2433
Anticoagulation (months)	53.47 (±19.99)	50.98 (±16.65)	0.5892
AF period (months)	56.79 (±27.03)	56.47 (±37.28)	0.4849
CHA_2DS_2VASc	**5.23 (±1.54)**	4.59 (±1.62)	**0.0107**
HASBLED	**3 (±0.98)**	2.69 (±0.85)	**0.0234**
Total episodes of bleeding after fall	94	0	–
Total episodes of spontaneous bleeding	12	22	0.0752
Total episodes of bleeding	106	22	–
Severe (ISTH/SSC 4) bleeding	**1 (2.13 %)**	**4 (2.55 %)**	**1**
Lethal bleeding	0	1 (1 %)	1
5-year mortality	21 (45 %)	59 (38 %)	0.3987

[1]Previous MI, peripheral arterial disease or aortic plaque, [2]Renal disease, dialysis, transplant, Cr >200 µmol/L, [3]TTR<60 % or 2>INR>3 in more than 2 out of 5 controls, [4]≥ antithrombotic medication, non-steroidal anti-inflammatory drugs, [5]≥ 8 drinks/week, AF – atrial fibrillation; Cr – creatinine; INR – international normalized ratio; MI – myocardial infarction; TTR – time in therapeutic range

Patient data were analyzed, and patients were divided into two cohorts according to presence or absence of falls. A total of 204 patients were included in the study, of which 47 had history of falls. 21 patients had history of only spontaneous bleeding and 38 of bleeding only after falls. Patient cohorts are summarized in Table 1. The incidence of major bleeding and the proportion of major bleeding (to all bleedings) were compared between the two cohorts, and the risk of major bleeding after a fall was determined. Based on the results, two other subsets of patients were created: patients who suffered only spontaneous bleeding and those who suffered bleeding only after falls. Patient cohorts are summarized in Table 2. Individual bleeding episodes were analyzed and compared.

Assessment of death/survival after 5 years (average 64.77±0.96 months) was performed in order to determine patient mortality using the e-tool of Health Care Surveillance Authority *(available at https://emortes.portaludzs.sk/web/emortes/vyhladavanie-umrti).*

Tab. 2. Comparison of patients with only spontaneous bleeding and bleeding only after falls.

Characteristics (n=59)	Spontaneous (n=21)	After falls (n=38)	p
Age (years)	74.67(±6.9)	**79.53(±7.64)**	**0.0213**
Female sex (%)	11 (52 %)	27 (71 %)	0.1687
Heart failure (%)	16 (76 %)	26 (68 %)	0.7647
Hypertension (%)	21 (100 %)	37 (97 %)	1
Diabetes Mellitus (%)	6 (29 %)	16 (42 %)	0.4023
Vascular disease[1] (%)	6 (29 %)	17 (45 %)	0.2728
Abnormal renal parameters[2] (%)	6 (29 %)	8 (21 %)	0.5378
Stroke history (%)	3 (14 %)	1 (3 %)	0.1242
Labile INR[3] (%)	8 (38 %)	20 (53 %)	0.4146
Medication usage Predisposing to bleeding (%)	0 (0 %)	1 (3 %)	1
Alcohol consumption[4] (%)	3 (14 %)	2 (5 %)	0.3365
Pulmonary embolism (%)	1 (5 %)	4 (11 %)	
CHA2DS2VASc	4.62 (±2.09)	5.08 (±1.53)	0.1712
HASBLED	2.86 (±0.85)	2.79 (±0.78)	0.882
Anticoagulation (months)	57.76 (±26.42)	51.29 (±17.16)	0.4136
AF period (months)	57.76 (±26.42)	55.39 (±26.84)	0.6768
Total episodes of bleeding	22	78	–
Severe (ISTH/SSC 4) bleeding	**4 (18 %)**	**0 (0 %)**	**0.0132**
Lethal bleeding	1 (5 %)	0 (0 %)	0.3559
5-year mortality	9 (43 %)	16 (42 %)	0.3931

[1]Previous MI, peripheral arterial disease or aortic plaque, [2]Renal disease, dialysis, transplant, Cr >200 µmol/L, [3]TTR<60 % or 2>INR>3 in more than 2 out of 5 controls, [4]≥ antithrombotic medication, non-steroidal anti-inflammatory drugs, [5]≥ 8 drinks/week, AF – atrial fibrillation; Cr – creatinine; INR – international normalized ratio; MI – myocardial infarction; TTR – time in therapeutic range

Tab. 3. Multivariate analysis.

	CI	p
Age (years)	0.9948–1.0011	0.1986
CHA_2DS_2VASc	0.9992–1.0332	0.0637
HASBLED	**1.0245–1.0919**	**0.0007**
Stroke history	0.8625–1.0221	0.1474
Labile INR[1]	0.9121–1.0175	0.1825
Number of falls	0.9736–1.0147	0.5632

[1]TTR < 60 % or 2 > INR >3 in more than 2 out of 5 controls, CI – confidence interval; INR – international normalized ratio; TTR – time in therapeutic range.

Tab. 4. Comparison of individual episodes of bleeding.

Bleeding	Number of episodes	Severe (ISTH/SSC 4)	Lethal
Spontaneous	34	4 (12 %)	1 (3 %)
Fall with head trauma	33	1 (3 %)	0 (0 %)
Fall with different injury	71	0 (0 %)	0 (0 %)
Total injuries	104	1 (1 %)	0

Statistical methods

Continuous variables are presented as means and standard deviations, whereas categorical variables are presented as percentages. Normality of data was assessed using a Shapiro-Wilk test. Unpaired Student t-test and Mann-Whitney test were used to compare continuous variables as appropriate.

The effect of explanatory variables on severe bleeding was evaluated using logistic regression analysis with feature selection based on results from bivariate analysis. The estimates are presented together with the 95 % confidence interval (CI). $p \leq 0.05$ was considered statistically significant. Data were analyzed using StatsDirect statistical software version 3.2.10 (http://www.statsdirect.com) and RStudio 1.2.5033 (RStudio Team (2019). RStudio: Integrated Development for R. RStudio, Inc., Boston, MA URL http://www.rstudio.com/).

Results

Difference in severe bleeding and mortality between patients after falls and without falls:

There was no statistically significant difference in severe bleeding (2.13 % with falls vs 2.55 % without, p=1) and 5-year mortality (45 % with falls vs 38 % without, p=0.3987) between patients based on the presence of falls. The population of patients suffering from falls was significantly older (79.45±7.2 vs 75.72±7.65, p=0.0031), had significantly higher HAS-BLED score (3±0.98 vs 2.69±0.85), p=0.023), significantly higher CHA_2DS_2VASc score (5.23±1.54 vs 4.59±1.62, p=0.01), more labile INR (57 % vs 30 %, p=0.009) and suffered more prior strokes (11 % vs 3 %, p=0.0527). All results are summarized in Table 1. Multivariate analysis, after adjustment for age, CHA_2DS_2VASc, HASBLED, stroke history, liable INR and number of falls showed that only HASBLED score was statistically significant contributor to severe bleeding (CI: 1.0245–1.0919, p=0.0007). All results are summarized in Table 3.

Comparison of individual bleeding episodes:

When comparing individual bleeding episodes (Tab. 4), there was a statistically significantly higher proportion of severe bleeding among spontaneous bleeds compared to those after falls (12 % vs 1 %, $p<0.0001$).

Difference in severe bleeding and mortality between patients suffering from spontaneous bleeding and after falls:

There was statistically significant difference in severe bleeding (18 % vs 0 %, p=0.0132) between patients suffering from spontaneous bleeding compared to patients after falls. There was no statistically significant difference in 5-year mortality between the two groups (43 % vs 42 % respectively, p=0.3931). The population of patients suffering from falls was significantly older (74.67±6.9 vs 79.53±7.64, p=0.02). All results are summarized in Table 2.

Discussion

The results of our study show that occurrence of falls in AF-patients treated with VKAs for prevention of thromboembolism has no significant impact on the incidence of severe bleeding and 5-year mortality despite the fact that the studied population of patients suffering from falls was significantly older, had significantly higher HAS-BLED and CHA_2DS_2VASc score, more labile INR and suffered more prior strokes. These outcomes speak strongly against the notion that the presence of falls in elderly patients con-

traindicates the use of OACs for treatment of AF. These results are also supported by previous studies. A study by Hagerty et al states that perception of high risk of falling in elderly should not be considered as justification for withholding anticoagulation in otherwise suitable candidates for such therapy (25). According to Gage et al patients with $CHADS_2$ score of 2 or higher benefit from anticoagulation with warfarin, whether or not they are considered to be at risk for falls, despite the fact that the history of falls or documented high risk of falling was associated with a 1.9 times higher risk of intracranial hemorrhage during follow-up (26). In another study it was estimated that an individual would have to fall 295 times in 1 year for the risk of fall related major bleeding to outweigh the benefit of warfarin in reducing the risk of stroke (27).

In our population spontaneous bleeding was associated with a significantly higher risk of severe bleeding compared to bleeding after falling. Furthermore, the only fatal bleeding in our patient population was also the result of spontaneous bleeding. Based on our results, we assume that patients with normal, healthy haemocoagulation are not significantly endangered by falls despite being treated with VKAs. Patients with coagulation disorders (presenting as episodes of spontaneous bleeding) are at much greater risk of bleeding, independent of falls. Therefore, we believe that it is essential to stratify patients based on their individual bleeding risk using scoring systems such as HAS-BLED. In our study this system has also proved to be the only independent contributor to severe bleeding. Nevertheless, it is important to remark that compared to other scoring systems (HEMORR2HAGES, ATRIA, or ORBIT), the HAS-BLED score distributed more major bleeding events into the "low" or "moderate" risk categories (28).

The use of warfarin is limited by the narrow therapeutic interval, necessitating frequent monitoring and close adjustments, but VKAs, when delivered with adequate time in therapeutic range, are effective for stroke prevention (29). Bleeding is more likely to occur in patients treated more intensively (higher therapeutic range between 2.5 and 3.5 INR) that in those treated in less intense therapeutic range (2–3 INR) (30). Although VKAs are being increasingly replaced by the novel oral anticoagulants (NOACs) in patients with non-valvular AF, VKAs remain the agents of choice for patients with atrial fibrillation in the setting of rheumatic valvular disease and those with mechanical heart valves (2, 21). In addition, VKAs still remain to be used in many health care systems due to local health care policy or their economic aspects.

Conclusions

Our results show that occurrence of falls in AF patients treated with VKAs has no significant impact on the incidence of severe bleeding and 5-year mortality and that spontaneous bleeding was associated with a significantly higher risk of severe bleeding compared to bleeding after falling.

Study limitations

The major limitation of our study was patient selection based on surveying. Even though a thorough examination of patient documentation was performed, valuable data may have been unintentionally not mentioned by patients. Larger study population, especially patient subgroups of different bleeding causes, would provide more reliable results.

References

1. Lernfelt G, Mandalenakis Z, Hornestam B et al. Atrial fibrillation in the elderly general population: a 30-year follow-up from 70 to 100 years of age. Scand Cardiovasc J 2020; 54: 232–238.

2. 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 of Cardio-Thoracic Surgery (EACTS). Eur Heart J 2020. 2020/08/30. DOI: 10.1093/eurheartj/ehaa612.

3. Garkina SV, Vavilova TV, Lebedev DS, Mikhaylov EN. Compliance and adherence to oral anticoagulation therapy in elderly patients with atrial fibrillation in the era of direct oral anticoagulants. J Geriatr Cardiol 2016; 13: 807–810.

4. Wändell P, Carlsson AC, Holzmann MJ et al. Warfarin treatment and risk of stroke among primary care patients with atrial fibrillation. Scand Cardiovasc J 2016; 50: 311–316.

5. Glader EL, Sjölander M, Eriksson M, Lundberg M. Persistent use of secondary preventive drugs declines rapidly during the first 2 years after stroke. Stroke 2010; 41: 397–401.

6. Cavallari I, Patti G. Efficacy and safety of oral anticoagulation in elderly patients with atrial fibrillation. Anatol J Cardiol 2018; 19: 67–71.

7. Lee IH, Kim H, Je NK. Underutilization of warfarin for stroke prophylaxis in patients with atrial fibrillation or atrial flutter in Korea. J Cardiol 2015; 66: 475–481.

8. de Almeida J, Martinho AS, Girão A et al. Novel anticoagulants in an older and frail population with atrial fibrillation: the effect of inappropriate dosing on clinical outcomes. Eur Geriatr Med 2020; 11: 813–820.

9. Lotze U, Liebetrau J, Malsch I et al. Medical treatment of patients with atrial fibrillation aged over 80 years in daily clinical practice: influence of age and CHADS(2) score. Arch Gerontol Geriatr 2010; 50: 36–41.

10. Rubenstein LZ. Falls in older people: epidemiology, risk factors and strategies for prevention. Age Ageing 2006; 35 Suppl 2: ii37–ii41. 2006/08/24. DOI: 10.1093/ageing/afl084.

11. Hylek EM, D'Antonio J, Evans-Molina C, Shea C, Henault LE, Regan S. Translating the results of randomized trials into clinical practice: the challenge of warfarin candidacy among hospitalized elderly patients with atrial fibrillation. Stroke 2006; 37: 1075–1080.

12. Veronese N, Argusti A, Canepa E et al. Evaluating the effectiveness and risks of oral anticoagulant treatments in multimorbid frail older subjects with atrial fibrillation using the multidimensional prognostic index: the EURopean study of older subjects with atrial fibrillation – EUROSAF. European Geriatric Medicine 2018; 9. DOI: 10.1007/s41999–018-0026-6.

13. Annoni G, Mazzola P. Real-world characteristics of hospitalized frail elderly patients with atrial fibrillation: can we improve the current prescription of anticoagulants? J Geriatr Cardiol 2016; 13: 226–232.

14. Kim IS, Kim HJ, Kim TH et al. Non-vitamin K antagonist oral anticoagulants have better efficacy and equivalent safety compared to warfarin in elderly patients with atrial fibrillation: A systematic review and meta-analysis. J Cardiol 2018; 72: 105–112.

15. Antza C, Doundoulakis I, Akrivos E et al. Non-vitamin K oral anticoagulants in nonvalvular atrial fibrillation: a network meta-analysis. Scand Cardiovasc J 2019; 53: 48–54.

16. Nishida T, Okumura Y, Yokoyama K et al. Oral anticoagulant use and clinical outcomes in elderly Japanese patients: findings from the SAKURA AF Registry. Heart Vessels 2019; 34: 2021–2030.

17. Koretsune Y, Yamashita T, Yasaka M et al. Comparative effectiveness and safety of warfarin and dabigatran in patients with non-valvular atrial fibrillation in Japan: A claims database analysis. J Cardiol 2019; 73: 204–209.

18. Yamagishi M, Tsuda T, Kato T, Furusho H, Hayashi K. Cost-effectiveness for prevention of thromboembolism by anticoagulants in non-valvular atrial fibrillation: additional analysis from the Hokuriku-Plus AF Registry. Heart Vessels 2019; 34: 1024–1030.

19. Tagaya M, Yoshikawa D, Sugishita Y et al. Prescription patterns of oral anticoagulants for patients with non-valvular atrial fibrillation: experience at a Japanese single institution. Heart Vessels 2016; 31: 957–962.

20. Turan B, Demir H, Mutlu A, Daşlı T, Erkol A, Erden İ. Inappropriate combination of warfarin and aspirin. Anatol J Cardiol 2016; 16: 189–196.

21. Loo SY, Dell'Aniello S, Huiart L, Renoux C. Trends in the prescription of novel oral anticoagulants in UK primary care. Br J Clin Pharmacol 2017; 83: 2096–2106.

22. Ministry of Health of the Slovak Republic. Categorization and official pricing of medicinal products not included in the list of categorized medicinal products. http://kategorizacia.mzsr.sk/Lieky/Common/DecisionDetails/1316.

23. Gorin L, Fauchier L, Nonin E, Charbonnier B, Babuty D, Lip GYH. Prognosis and guideline-adherent antithrombotic treatment in patients with atrial fibrillation and atrial flutter: implications of undertreatment and overtreatment in real-life clinical practice; the Loire Valley Atrial Fibrillation Project. Chest 2011; 140: 911–917.

24. Kaatz S, Ahmad D, Spyropoulos AC, Schulman S, the Subcommittee on Control of A. 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. Journal of Thrombosis and Haemostasis 2015; 13: 2119–2126.

25. Hagerty T, Rich MW. Fall risk and anticoagulation for atrial fibrillation in the elderly: A delicate balance. Cleve Clin J Med 2017; 84: 35–40.

26. Gage BF, Birman-Deych E, Kerzner R, Radford MJ, Nilasena DS, Rich MW. Incidence of intracranial hemorrhage in patients with atrial fibrillation who are prone to fall. Am J Med 2005; 118: 612–617.

27. Man-Son-Hing M, Nichol G, Lau A, Laupacis A. Choosing antithrombotic therapy for elderly patients with atrial fibrillation who are at risk for falls. Arch Intern Med 1999; 159: 677–85. 1999/04/28.

28. Zeng J, Yu P, Cui W, Wang X, Ma J, Zeng C. Comparison of HAS-BLED with other risk models for predicting the bleeding risk in anticoagulated patients with atrial fibrillation: A PRISMA-compliant article. Medicine (Baltimore) 2020; 99: e20782. 2020/06/23. DOI: 10.1097/md.0000000000020782.

29. Sjögren V, Grzymala-Lubanski B, Renlund H et al. Safety and efficacy of well managed warfarin. A report from the Swedish quality register Auricula. Thromb Haemost 2015; 113: 1370–1377.

30. Breen AB, Vaskinn TE, Reikvam A, Skovlund E, Lislevand H, Madsen S. [Warfarin treatment and bleeding]. Tidsskr Nor Laegeforen 2003; 123: 1835–1837.

Received September 7, 2022.
Accepted September 21, 2022.