RESEARCH ARTICLE

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Comparison of Clinical Characteristics, Risk Factors, and Risk Scores of Patients with and without Bleeding Episodes During Warfarin Treatment

Şaban Esen[1], Emre Özdemir[2], Tuncay Kiriş[2], Fatma Esin[2], Muhammet Mücahit Tiryaki[3]

[1]Department of Cardiology, Tunceli State Hospital, Tunceli, Turkey
[2]Department of Cardiology, Atatürk Training and Research Hospital, İzmir Katip Çelebi University, İzmir, Turkey
[3]Department of Cardiology, Muş State Hospital, Muş, Turkey

Abstract

Background and Aim: The annual risk of major bleeding due to anticoagulant use ranges from 2% to 5%, with 0.5% to 1% of these bleedings being fatal. The global usage of oral anticoagulants is 0.65%, with warfarin being the most commonly used oral anticoagulant agent. In our study, we aimed to determine the long-term bleeding risks of patients using warfarin in our clinic and to make treatment and risk factor adjustments according to this risk situation. We investigated the effectiveness of the most commonly used bleeding risk scores and their superiority over one another in this study.

Materials and Methods: This study included patients taking warfarin from January 2010 to January 1, 2022. Demographic data, laboratory parameters, known, and potential bleeding risk factors were recorded for all patients. Pre-treatment CHA_2DS_2-VASc, ATRIA, HAS-BLED, and ORBIT scores were calculated for all patients included in the study, along with their time in therapeutic range (TTR) values during follow-up. Patients were retrospectively monitored for bleeding events.

Results: In our study, we observed that anemia, chronic kidney failure, cancer, and mechanical valves were associated with an increased risk of bleeding compared with other risk factors. We found that among the risk scores assessed in patients, the HAS-BLED risk score more strongly predicted the risk of bleeding than the other risk scores. Additionally, we found that low TTR values were directly associated with bleeding.

Conclusion: Modifying identified risk factors in patients during the warfarin treatment process (such as anemia, chronic kidney failure, etc.) may reduce the risk of bleeding. Similarly, close monitoring of TTR, particularly in patients with high HAS-BLED and ORBIT risk scores assessed before treatment initiation, is considered a safe treatment approach to reduce the risk of bleeding.

Keywords: Warfarin, HAS-BLED, ORBIT, TTR, bledding

INTRODUCTION

Anticoagulant therapy is performed with the aim of preventing thrombus formation in potential vascular structures or areas in the body that may block blood flow. Thrombus formation is a significant clinical condition that occurs in various medical and surgical conditions, such as atherosclerosis, atrial fibrillation (AF), and the presence of mechanical valves. Arterial and venous thromboses are major causes of mortality and morbidity. Arterial thromboses are the most common cause of myocardial infarctions, stroke, and extremity gangrene, whereas venous thromboses can lead to fatal pulmonary embolism (PE) and postphlebitic syndrome. Anticoagulant

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Address for Correspondence: MD Şaban Esen, Department of Cardiology, Tunceli State Hospital, Tunceli, Turkey
E-mail: saban___1064@hotmail.com
ORCID ID: orcid.org/0000-0001-5644-5787

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treatment prevents possible adverse clinical conditions by preventing thrombus formation. However, this also increases the risk of simultaneous bleeding. Most common indications for anticoagulation; acute myocardial infarction, left ventricular thrombus, AF, left ventricular aneurysm, prosthetic heart valve, venous thromboembolism (VTE), prophylaxis, etc.[1] The most commonly used anticoagulant drugs are; unfractionated heparin, low-molecular-weight heparin, bivalirudin, warfarin derivative warfarin, factor Xa inhibitors (apixaban, edoxaban rivaroxaban, fondaparinux), and direct thrombin inhibitors (dabigatran).[1] Warfarin may deplete functional vitamin K reserves and thus reduce the synthesis of factors necessary for coagulation. In particular, the mechanical valve is the only oral anticoagulant agent that can be administered to moderate to severe mitral stenosis.

In patients receiving warfarin therapy for all indications, the annual risk of major bleeding is reported to be between 1-3%.[1] However, in studies involving patients receiving warfarin for AF, this risk is approximately 0.3-0.5%[2], and for VTE, the risk is found to be 1.3%.[2] In observational studies, it has been found that this rate can reach up to 7% in patients taking warfarin who are not followed for study.

Some patients using anticoagulants with similar age and clinical characteristic experience bleeding, whereas others do not. Patients were investigated for known and possible additional risk factors that could explain the difference. Multiple risk scores are used to predict the risk of bleeding in patients taking warfarin. In our daily practice, we researched the HAS-BLED, ORBIT, and ATRIA risk scores because of their easy access to risk factors and straightforward calculation. We investigated the predictive values of these risk scores and compared their superiority to each other. The effect of time in therapeutic range (TTR) value on bleeding risk was also investigated.

MATERIALS AND METHODS

Our study comprised 500 patients who were prescribed warfarin for various reasons (AF, mechanical heart valve, DVT, pulmonary thromboembolism, etc.) and attended regular follow-up appointments at Atatürk Training and Research Hospital, İzmir Katip Çelebi University between 2000 and 2023.

The average age of the patients included in the study was 67.7 years, with 222 (44.4%) males and 278 (55.6%) females. The average follow-up period was 59.4 months (range: 35.9-94 months), with appointments scheduled for checkups every 3 months. In the retrospective follow-up, patients with bleeding were classified into three groups based on the TIMI bleeding criteria: major, minor, and minimal bleeding. Those with intracranial bleeding or a decrease in hemoglobin (Hgb) of 5 g/dL or more were included in the major bleeding group, those with a Hgb decrease of more than 3 g/dL were included in the minor bleeding group, and those with bleeding less than 3 g/dL were included in the minimal bleeding group. The total number of bleeding events was calculated as the sum of all bleeding events. Patients were divided into two groups: those with bleeding and those without bleeding. Patients in the two groups were compared according to risk factors known to increase the risk of bleeding, including anemia, coronary artery disease (CAD), peripheral artery disease, hypertension (HT), chronic kidney disease (CKD), malignancy, and mechanical valve replacement. Additionally, HAS-BLED, ORBIT, and ATRIA risk scores, which provide predictive values for bleeding risk in patients, were calculated. TTR was calculated for each patient to investigate the effect of effective international normalized ratio (INR) presence on bleeding risk. The left atrial (LA) diameter of each patient was measured at the beginning of follow-up. The ATRIA score is commonly used in clinical practice to predict the risk of stroke in patients with AF. In our study, we computed each patient's ATRIA risk score at the outset of the follow-up period to assess its predictive value in predicting bleeding.

TTR Calculation, Bleeding Risk Score Calculation, Bleeding Risk Factors

Patients should ideally maintain a TTR >70% to ensure effective anticoagulation therapy. TTR values below this threshold may indicate irregular treatment adherence, which can compromise the effectiveness of anticoagulation and increase the risk of adverse events, including bleeding complications.

This criterion ensures an adequate representation of the patient's anticoagulation status over time. Patients with fewer than four INR values measured within the specified intervals were excluded from the analysis due to insufficient data for accurate TTR calculation. Additionally, patients with intervals of >60 days between INR measurements were excluded. The diameter of the left atrium (LA) was also examined.

The file scanning included the history of our study and the collection of patient information for follow-up visits. The application file has been submitted to the local Ethics Committee of İzmir Katip Çelebi University for review. Ethics committee approval was granted with decision number 0301, dated 16.06.2022.

Statistical Analysis

Statistical analysis was conducted using the Statistical Package for Social Sciences (SPSS) for Windows version 26.0 (IBM SPSS Inc., Chicago, IL). Descriptive statistics were presented using mean and standard deviation (mean ± standard deviation) for normally distributed variables, whereas median and maximum-minimum values (median/max-min) were used for non-normally distributed variables. Pearson's chi-square test and Fisher's exact test were employed to assess categorical

variables. The normality of continuous variables was assessed using visual (histogram) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk tests). The t-test was used to compare normally distributed variables between the two groups, and the Mann-Whitney U test was used to compare non-normally distributed variables between the two groups. Receiver operating characteristic (ROC) curve analysis was performed to assess the predictive value of bleeding risk scores. Bleeding risks were calculated according to the scoresduring follow-up using the Kaplan-Meier curve.

RESULTS

The study included 500 patients who were prescribed warfarin for various reasons (such as AF, mechanical heart valve, PE, etc.) and attended regular INR monitoring between 2000 and 2023. The average follow-up period was 59.4 months (range: 35.9-94 months), with appointments scheduled for checkups every 3 months. Patients included in the study were evaluated retrospectively. During the follow-up of the patients, bleeding events occurred in 196 (39.2%) patients, whereas no bleeding was detected in 304 (60.8%) patients. When examining patients who experienced bleeding, the findings based on the TIMI bleeding score were as follows: Seven patients experienced major bleeding, 90 patients experienced minor bleeding, and 97 patients experienced minimal bleeding. Additionally, 2 patients experienced both minor and minimal bleeding during follow-up period (Table 1). Mortality occurred in 99 patients (18%) during follow-up. When comparing the two groups, it was found statistically significant that the baseline Hgb values were lower in the bleeding group, whereas the creatinine values were higher. Furthermore, upon examining the left atrium diameter (LA), it was noted that the baseline left atrium diameter was larger in the bleeding group.

The study found that baseline Hgb levels were significantly lower in the group experiencing bleeding, whereas creatinine levels were higher in this group. Therefore, clinical characteristics such as anemia and CKD were identified as risk factors for bleeding in the present study. Baseline Hgb values were lower in the bleeding group than in the non-bleeding group (12.5±1.8 vs. 13.09±2.0, p=0.002). Additionally, creatinine levels were higher in the bleeding group than in the non-bleeding group (1.05±0.72 vs. 0.918±0.25, p=0.003).

Additionally, upon examining the LA diameter, it was observed that the baseline LA diameter was larger in the bleeding group. These findings suggest that increased LA size is a potential predictive factor for bleeding in these patients.

Table 2 presents the statistical analysis performed on these laboratory parameters.

Table 3 presents the statistical analysis of the effect of comorbid conditions on bleeding risk. There was nostatistically significant difference in the increased risk of bleeding between the groups in terms of comorbid conditions, such as CAD, HT, RDW, VTE, aortic valve replacement (AVR), AF, diabetes mellitus, peptic ulcer, cerebrovascular accident (CVA) stroke, or liver dysfunction. Although some of these risk factors have been shown to increase bleeding risk in previous studies, their ineffectiveness in our study could be due to the small number of patients and insufficient patient event records. Mitral valve replacement (MVR) was found to be associated with increased bleeding risk. Additionally, sex and age were found to have no effect on the increased risk of bleeding between groups.

After identifying the risk factors for bleeding in patients, we then examined the risk scores. The average ATRIA scores among the study participants were 3 (ranging from 1 to 6) in the nonbleeding group and 4 (ranging from 1 to 6) in the bleeding group. There was no statistically significant difference between the two groups (p=0.082). However, the HAS-BLED score was significantly higher in the bleeding group than in the non-bleeding group [3 (1-4) vs. 2 (1-3), p=0.001] (Figure 1). The ORBIT score was 0 (ranging from 0 to 2) in the non-

Table 1: Patients' bleeding status and classification according to the TIMI bleeding score

Status	Bledding (-)	Bledding (+)			
		Classification according to the TIMI bleeding score			
Number of patients	n=304	Major bledding	Minor bledding	Minimal bledding	Minor and minimal bleeding
		n=7	n=90	n=97	n=2

TIMI: Thrombolysis in myocardial infarction

Table 2: Laboratory data of the patients

Variables	Bledding (-)	Bledding (+)	p-value
Hemoglobin (g/dL)	13.09±2.0	12.5±1.8	0.002
Kreatinin (mg/dL)	0.918±0.25	1.05±0.72	0.003
LA, mm	43.2±8.3	46.2±7.8	0.001

LA: Left atrium

Table 3. Demographic characteristics of the patients

Variables	Bledding (-) (n=304)	Bledding (+) (n=196)	p-value
CAD, number (%)	68 (22%)	48 (26%)	0.321
PAD, number (%)	14 (4.5%)	2 (1.1%)	0.036
HT, number (%)	239 (47.9%)	158 (31.7%)	0.087
CKD, number (%)	9 (1.8%)	15 (3%)	0.002
MVR, number (%)	53 (17%)	48 (26%)	0.048
Cancer, number (%)	16 (5%)	22 (12%)	0.007
DM, number (%)	88 (17.6%)	56 (11.2)	0.386
SVO, number (%)	63 (20.1)	31 (16.6%)	0.326
Peptic ulcer, number (%)	0 (0%)	1 (0.5%)	0.195
Liver disease, number (%)	1 (0.3%)	3 (1.6%)	0.117
AF valvular, number (%)	65 (20.8%)	49 (26.2%)	0.161
AF non- valvular, number (%)	168 (53.7)	93 (49.7%)	0.393
AVR, number (%)	51 (16.3%)	36 (19.3%)	0.408
VTE, number (%)	25 (8.1%)	13 (7)	0.641
ASA, number (%)	13 (4.2%)	14 (7.5%)	0.115
Klopidogrel, number (%)	2 (0.6%)	4 (2.2%)	0.136
Prasugrel	0	0	-
Tikagrelor, number (%)	1 (0.3%)	0 (0)	0.439
Statin, number (%)	50 (16%)	36 (19.4%)	0.342
PPI, number (%)	9 (2.9%)	2 (1.1%)	0.178
NSAI, number (%)	0	0	
New SVO, number (%)	15 (4.9%)	15 (8.1%)	0.155
Gender, men/women, number	139/172	104/83	0.946
Age	67.2±12.2	68.6±12.5	0.216
HD	0 (0%)	3 (1.6%)	0.002

CAD: Coronary artery disease, PAD: Peripheral arterial disease, HT: Hypertension, CKD: Chronic kidney disease, MVR: Mitral valve replacement, DM: Diyabet mellitus, SVO: Cerebrovascular event, AF: Atrial fibrillation, AVR: Aortic valve replacement, VTE: Venous thromboembolism, ASA: Asetilsalisilik acid, PPİ: Proton pump inhibitor, NSAI: Nonsteroidal anti-inflammatory drug, HD: Hemodialisis

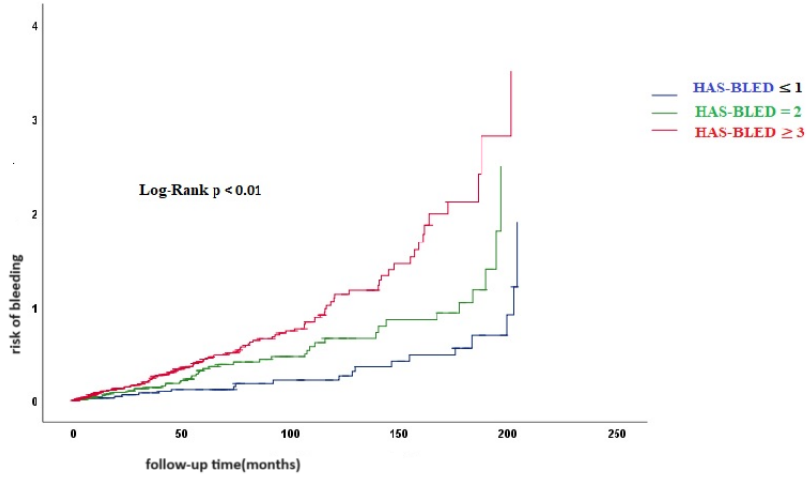

Figure 1: Bleeding risk according to HAS-BLED score

bleeding group and 3 (ranging from 2 to 4) in the bleeding group. There was a statistically significant association between a high ORBIT score and the risk of bleeding (p=0.001) (Figure 2). The HAS-BLED score of the patients included in the study was significantly higher in the group with bleeding compared with the group without bleeding [3 (1-4) vs. 2 (1-3), p=0.001]. Figure 3 presents the ROC curve for bleeding risk.

In our study, the mean TTR value in the nonbleeding group was 80.4±11.2, whereas it was calculated as 47.5±12.5 in the bleeding group. A low TTR value was found to be significantly associated with an increased risk of bleeding (p=0.001) (Table 4).

In the multivariate analysis, HAS-BLED, ORBIT, mechanical valve replacement, TTR, cancer, and left atrium diameter (LA) were identified as independent predictors of bleeding (Table 5).

DISCUSSION

Despite having similar characteristics and risk factors, some patients experience bleeding, whereas others do not. Therefore, in this study, we investigated potential additional risk factors in addition to known risk factors. We found that known risk factors, such as anemia and elevated creatinine levels, were associated with increased bleeding risk. MVR is also associated with increased bleeding risk. However, other known risk factors like CAD, AVR, CVA (stroke), PTE (PE), antiplatelet use and HT were not found to be associated with increased bleeding risk in our study. Some of these risk factors have been shown to increase bleeding risk in previous studies; however, their ineffectiveness in our study could be attributed to the small number of patients included and the inadequacy of follow-up and event records.

The left atrium collects blood during systole and supports the filling of the left ventricle during diastole, playing a crucial physiological role. Given these functions, it provides important prognostic information about cardiac physiology, cardiac

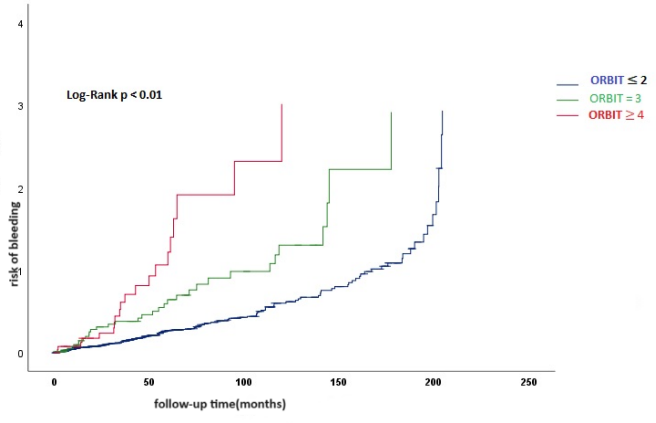

Figure 2: Bleeding risk according to ORBIT score

health, and adverse cardiovascular events (CVE). Increased LA diameter occurs as a result of atrial remodeling and can be associated with increased left ventricular filling pressure (left ventricular diastolic dysfunction), increased volume load, or valvular heart disease. In our study group, we investigated the potential for increased LA size to increase bleeding risk and its predictive value for possible bleeding events. We observed that an increase in LA diameter assessed echocardiographically was associated with increased bleeding risk in our study.

Additionally, we evaluated the effectiveness of bleeding risk scores and compared their performance. Our findings indicate

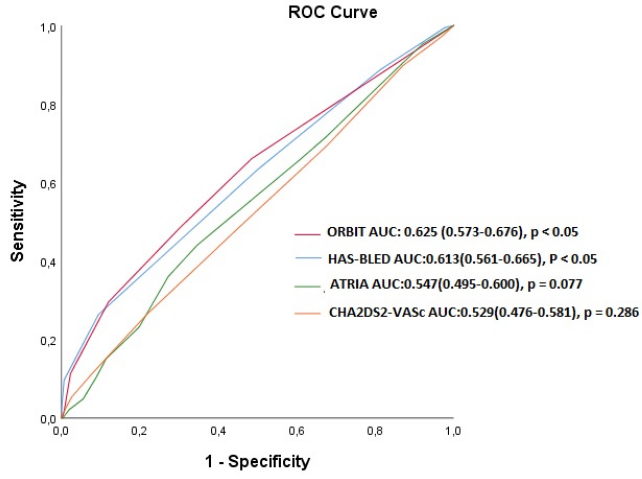

Figure 3: Receiver operating characteristic (ROC) curve for bleeding risk

Table 4: Bleeding risk scores of patients

Variables	Bledding (-) (n=304)	Bledding (+) (n=196)	p-value
TTR	80.4±11.2	47.5±12.5	0.001
HAS-BLED score	2 (1-3)	3 (1-4)	0.001
ATRIA score	3 (1-6)	4 (1-6)	0.082
ORBIT score	0 (0-2)	3 (2-4)	0.001
CHADVASC score	3 (2-4)	3 (2-5)	0.536
TTR: Therapeutic range time			

Table 5: Multivariate analysis of bleeding risk

Variables	Multivariate analysis	p-value
Canser	3.117 (1.228-7.268)	0.007
MVR	1.746 (1.024-2.978)	0.041
LA size (mm)	1.039 (1.009-1.071)	0.011
ORBIT score	1.347 (1.127-1.610)	0.001
TTR	0.982 (0.972-0.993)	0.002
HAS-BLED score	1.422 (1.115-1.815)	0.005
LA: Left atrium, TTR: Therapeutic range time, MVR: Mitral valve replacement		

that the HAS-BLED risk score outperforms the other predictors of bleeding risk. Furthermore, we demonstrated a direct association between low TTR and bleeding in patients.

In 2012, a study was published involving 965 patients[3] patients was associated with an increased risk of bleeding during follow-up. It was determined that a high HAS-BLED score was highly predictive of bleeding. Additionally, the current study revealed that a high HAS-BLED score was predictive of CVE and all-cause mortality. In our study, the average HAS-BLED score in the bleeding group was 3 (ranging from 1 to 4), whereas in the group it was calculated as 2 (ranging from 1 to 3). The difference in scores between the two groups was statistically significant. Our findings align with those of the aforementioned study, indicating that an increase in the HAS-BLED score is associated with a higher bleeding risk, thus confirming its important predictive value.

Similar to our study, a meta-analysis involving 8097 patients was published in 2017. In the analysis, patients were classified into low (0-2 points), medium (3 points), and high (4-7 points) risk categories based on ORBIT score. It was observed that the bleeding risk of patients in these groups increased by 1.21, 1.44, and 1.73 times, respectively. High ORBIT scores in patients taking anticoagulants were found to significantly increase the risk of bleeding, demonstrating statistical significance.[4]

In a study conducted in 2016 on 2293 patients, the HAS-BLED, ATRIA, and ORBIT risk scores were compared to predict bleeding risk. Each score was calculated for each patient, and the statistical significance was evaluated. Patients with HAS-BLED scores ≥3 were found to have a 1.85-fold increased risk of bleeding and a 2.4-fold increased risk of major bleeding. For patients with ATRIA scores ≥4, the increase in bleeding risk was not statistically significant; however, the risk of major bleeding alone increased by 2.4 times. Similarly, in patients with ORBIT scores ≥3, there was no statistically significant increase in bleeding risk, but the risk of major bleeding alone increased by 2.9 times. All three scores were found to be statistically significant in determining major bleeding risk; however, the HAS-BLED score demonstrated a higher predictive value for bleeding risk than the other two scores.[5] Likewise, our study also showed that the HAS-BLED risk score had the highest predictive value.

A study conducted in 2013 involved 937 patients and investigated the effectiveness of ATRIA and HAS-BLED risk scores.[6] In the study, 49% of patients were male and 51% were female, with an average age of 76. The mean HAS-BLED score of these patients was 2 (ranging from 2 to 3), and 35% had a HAS-BLED score ≥3. The mean ATRIA score was 3, and 16% of the patients had a score ≥5. Patients were followed for an average of 952 days, during which an increased risk of bleeding was detected in patients with a HAS-BLED score ≥3. Similarly, although an ATRIA score of 5 or above increases the risk of major bleeding, its effectiveness in predicting bleeding was found to be insufficient. Similar to the results of the previous study, in this study, the scores of the patients in the group with bleeding and the group without bleeding were compared. Accordingly, bleeding rates were increased in the group with a high HAS-BLED score. Similar to our study, the ATRIA risk score was found to be unsuccessful in predicting bleeding.

In a study involving 2233 patients, the predictive value of TTR values for risks such as bleeding, CVA/transient ischemic attack (TIA), and death was investigated.[7] The average age of the patients was 68.4 years, and the average follow-up period was 30 months (ranging from 12 to 36 months).The average number of INR tests performed on patients was 9 (ranging from 5 to 13).

Although it is recommended that the TTR value be >70%, ineffective TTR was not detected in this study. Ineffective TTR was defined as <65%. Additionally, for sensitivity analysis, TTR values were divided into 3 groups. Patients with TTR <45.1% were classified into group 1, those with TTR ranging from 45.1% to 66.8% were classified into group 2, and those with values >66.8% were classified into group 3. Patients with TTR <65% were at increased risk of bleeding, stroke, and death. Moreover, as the subgroups moved from group 3 to group 1, the risk of bleeding, death, and cerebrovascular events increased.

Similar to our study, low TTR treatment was associated with irregularity and increased the risk of bleeding. Studies on bleeding risk factors generally indicate that factors such as cancer, anemia, mechanical valve implantation, elevated creatininelevels, and LA dilation tend to increase the risk of bleeding. The presence of these factors together may indicate an even higher risk of bleeding.

Between 2007 and 2016, a study was conducted involving 6445 patients taking warfarin or NOAC, and it was published in 2020 to investigate the effect of LA enlargement on bleeding and CVA.[8] The group taking warfarin comprised 46.9% of the patients, whereas the group receiving NOAC comprised 48.2%. In this study, the average left atrium diameter was 47 mm. The current study found that the use of NOACs in patients with LA dilatation reduced the risk of cerebrovascular disease.

However, no difference was found between warfarin and NOAC in terms of bleeding risk inthese patients. The current study found that LA enlargement was associated with overall bleeding.

Between 2004 and 2016, a study investigated the effect of warfarin use on increased bleeding risk in patients undergoing mitral valve repair. Of the patients, 754 were receiving vitamin K antagonists (VKA), while 1462 were not. The two groups were

compared in terms of bleeding events. In the VKA group, the risk of major bleeding events related to any cause significantly increased during the 180-day follow-up period (VKA: 8.58% vs. non-VKA: 4.21%; risk ratio, 2.09; p<0.001).[9]

A study conducted between 2008 and 2011, involving 546 patients, aimed to determine whether mechanical valve replacement increased the risk of bleeding. Patients were prospectively followed for the risk of major bleeding, thromboembolism, and death. Among the participants, 398 patients underwent AVR, 122 patients underwent MVR, and 26 underwent both AVR and MVR. In terms of thromboembolism risk, the ratios were 1.8/100 and 2.2/100 in the AVR group and 2.2/100 in the MVR group, indicating a higher risk in the MVR group. Regarding bleeding risk, there was a 4.4% increase in the AVR group and a 4.6% increase in the MVR group. A similar increase in bleeding risk was found in both groups.[10] In our study, 48 patients (26%) who underwent MVR therapy experienced bleeding, while 53 patients (17%) did not.

The presence of MVR wasassociated with a statistically significant increase in the risk of bleeding. In our study, we did not observe an increased risk of bleeding in the AVR group. This finding could be attributed to the small sample size and inadequate event recording and follow-up. Another possible reason could be the lower target INR range in AVR patients compared to MVR patients.

In 2021, a study involving 1512 patients investigated the impact of anemia on bleeding risk. The average Hgb level among the patients was 13.2±1.8 g/dL, and 518 patients were considered to have anemia (Hgb <11 g/dL). Patients were followed-up for an average of 25.8±10.5 months. The study reported rates of 2.9% for ischemic stroke/TIA, 4.9% for major bleeding, 1.8% for CVE, and 9.2% for mortality. A statistical analysis revealed a significant association between anemia and an increased risk of major bleeding.[11]

In a study involving 578 patients, the effect of renal failure on bleeding risk among patients receiving warfarin was investigated. Particularly in patients with moderate-to-severe renal failure, the study found a lower required dose of warfarin and a lower achievement rate of the target INR. Compared with the other groups, patients with severe renal failure were found to have a major bleeding risk twice as high. Compared with the normal patient population, initiating lower starting doses of warfarin and closely monitoring INR may be beneficial in patients with moderate to severe renal failure to reduce potential side effects.[12]

Study Limitations

Increasing the number of patients in the study enhances its representativeness of the population.

Consequently, more accurate and reliable data are obtained, which allows better interpretation. In our study, the

the major bleeding risk scores. However, by expanding the number of risk scores (e.g., GARFIELD-AF, etc.), the risk score with the highest predictive value can be determined, which evaluation of each patient before treatment in daily practice. Despite screening more than 5,000 retrospective cases of warfarin use in the study, many patients were not included due to a lack of regular INR monitoring, follow-up from a single center, and inadequate record-keeping.

CONCLUSION

The TTR value calculated in patients is predictive of bleeding risk. Informing and raising awareness among patients with ineffective TTR values and ensuring more frequent INR monitoring for these patients are crucial for achieving effective TTR and consequently reducing the risk of bleeding. This approach is particularly important for patients with a history of previous bleeding events.

Since our study revealed that HAS-BLED and ORBIT risk scores, in particular, have predictive value for bleeding risk, assessing these scores before initiating warfarin treatment can provide insights into the risk of bleeding. Patients with high scores should be monitored for bleeding events. Modifying factors that increase the risk of bleeding in these patients (such as HT, anemia, etc.), and if necessary, considering alternative treatments (such as NOACs) may be warranted.

In this study, we demonstrated that the LA diameter value exhibits predictive value similar to risk scores in forecasting bleeding. Consequently, it can be regarded as a standalone parameter similar to HAS-BLED or ORBIT risk scores for assessing bleeding risk. The advantage of the proposed score lies in its easy accessibility and simple measurability for eachpatient.

In our study, 22 of the patients with cancer (12%) experienced bleeding, whereas 16 (5%) did not. A statistically significant increase in bleeding risk was associated with the presence of cancer (p=0.007). Chemotherapeutic drugs administered to patients with cancer receiving warfarin therapy may affect their blood INR levels, either increasing or decreasing them. Additionally, interruptions in warfarin therapy due to necessary treatments can hinderthe achievement of effective TTR, thereby increasing the risk of bleeding.

Close monitoring of INR levels and achieving the effective TTR value (TTR >70%) in patientswith high HAS-BLED and ORBIT risk scores, which are assessed before initiating warfarin treatment, are essential to prevent potential major bleeding events in these patients.

Shortening the intervals between INR checks, closely adjusting doses, and considering alternative medications for patients taking concomitant drugs that may affect warfarin levels can help achieve and maintain the target TTR.

Ethics

Ethics Committee Approval: The application file has been submitted to the local Ethics Committee of İzmir Katip Çelebi University for review. Ethics committee approval was granted with decision number 0301, dated 16.06.2022.

Informed Consent: Retrospective study.

Authorship Contributions

Concept: E.Ö., Design: Ş.E., E.Ö., T.K., Data Collection or Processing: Ş.E., T.K., F.E., M.M.T., Analysis or Interpretation: Ş.E., E.Ö., T.K., F.E., M.M.T., Literature Search: Ş.E., T.K., F.E., M.M.T., Writing: Ş.E., E.Ö., M.M.T.

Conflict of Interest: No conflict of interest was declared by the authors.

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