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Original Article

Comparison of Bleeding Risk Scores in Atrial Fibrillation Patients on Direct-Acting Oral Anticoagulants: A Real-Life Study

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Abstract

Objective: Hemorrhagic complications continue to be a major clinical challenge among individuals with atrial fibrillation (AF) receiving direct-acting oral anticoagulants (DOACs). This research sought to evaluate and contrast the accuracy of various risk assessment models in forecasting bleeding incidents within this specific patient cohort.

Methods: We enrolled 447 subjects diagnosed with AF who were prescribed DOAC therapy (including apixaban, dabigatran, edoxaban, or rivaroxaban). By retrospectively reviewing institutional electronic health records, we computed the ORBIT, ATRIA, and HEMORR$_2$HAGES risk indices for each participant. The main outcome measures were defined as the occurrence of clinically relevant minor or major hemorrhages. Consequently, we analyzed how accurately these scoring systems could foresee the specified endpoints.

Results: The cohort's average age stood at 75.6±10.1 years, comprising predominantly women (62.2%). During a 12-month observation period, 6.7% of the participants (n=30) encountered one or more major hemorrhagic events. When forecasting severe bleeding, the ATRIA, ORBIT, and HEMORR$_2$HAGES frameworks exhibited comparable predictive accuracies without any statistically notable variations. Upon conducting a multivariate logistic regression, independent variables linked to a heightened likelihood of bleeding encompassed prior hemorrhagic episodes (odds ratio [OR]: 3.101, p=0.019) and the presence of heart failure (OR: 2.028, p=0.009). In addition, anemia emerged as a significant factor (OR: 0.366, p=0.049), alongside elevated evaluations in both the HEMORR$_2$HAGES (OR: 1.535, p=0.006) and ORBIT (OR: 1.849, p<0.014) scales.

Conclusion: Both the ORBIT and HEMORR$_2$HAGES models proved to be valuable independent indicators for future hemorrhagic complications. Integrating these tools into routine cardiovascular care can optimize therapeutic strategies and enhance the overall safety of AF patients on anticoagulation.

Keywords: ATRIA score; atrial fibrillation; bleeding risk; direct-acting oral anticoagulants; HEMORR$_2$HAGES score; ORBIT score.

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Direkt Etkili Oral Antikoagülan Kullanan Atriyal Fibrilasyon Hastalarında Kanama Risk Skorlarının Karşılaştırılması: Bir Gerçek Yaşam Çalışması

Özet

Amaç: Direkt etkili oral antikoagülan (DOAK) tedavisi alan atriyal fibrilasyon (AF) olgularında kanama komplikasyonları ciddi bir klinik sorun teşkil etmeyi sürdürmektedir. Bu araştırmanın temel hedefi, söz konusu hasta grubunda kanama riskini tahmin etmek amacıyla kullanılan farklı skorlama araçlarının öngörü doğruluklarını birbirleriyle kıyaslamaktır.

Yöntem: Çalışma kapsamında AF tanısı taşıyan ve DOAK (apiksaban, dabigatran, edoksaban veya rivaroksaban) kullanan 447 birey incelenmiştir. Hastane veritabanı taranarak katılımcıların ORBIT, ATRIA ve HEMORR$_2$HAGES skorları geriye dönük olarak hesaplanmıştır. Araştırmanın birincil sonlanım noktası, klinik olarak anlamlı minör veya majör kanamaların meydana gelmesi olarak tanımlanmış ve risk skorlarının bu olayları ne derece doğru öngörebildiği analiz edilmiştir.

Bulgular: Çalışma grubunun yaş ortalaması 75,6±10,1 yıl olarak saptanmış ve popülasyonun büyük bir kısmını kadın hastalar (%62,2) oluşturmuştur. Bir yıllık izlem periyodu içerisinde 30 olguda (%6,7) en az bir kez majör kanama tablosu gelişmiştir. Majör kanama olaylarını tahmin etme açısından HEMORR$_2$HAGES, ATRIA ve ORBIT modellerinin doğruluk payları arasında istatistiksel yönden belirgin bir ayrım tespit edilmemiştir. Yapılan çok değişkenli analizler sonucunda; kalp yetersizliği varlığı (OR: 2,028, p=0,009), kanama geçmişi (OR: 3,101, p=0,019), anemi (OR: 0,366, p=0,049) ile birlikte yüksek HEMORR$_2$HAGES (OR: 1,535, p=0,006) ve ORBIT (OR: 1,849, p<0,014) skorlarının kanama açısından bağımsız risk faktörleri olduğu saptanmıştır.

Sonuç: Elde edilen veriler ışığında, HEMORR$_2$HAGES ve ORBIT skorlarının gelecekteki kanama riskini belirlemede bağımsız öngörücüler olarak işlev görebileceği anlaşılmıştır. Bu araçların günlük kardiyoloji pratiğine entegre edilmesi, hekimlerin klinik karar alma süreçlerine katkı sağlayarak antikoagülan kullanan hastaların genel yönetimini ve klinik gidişatını iyileştirebilir.

Anahtar sözcükler: ATRIA skoru; atriyal fibrilasyon; kanama riski; direkt etkili oral antikoagülanlar; HEMORR$_2$HAGES skoru; ORBIT skoru.

Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia worldwide and is directly associated with increased mortality and morbidity due to cerebrovascular events.[1] The use of direct-acting oral anticoagulants (DOACs) has become widespread in the management of AF due to their efficacy and convenience compared to traditional Vitamin K antagonists (VKAs). However, bleeding remains a significant concern with DOAC therapy. According to the recommendation of clinical guidelines, long-term use of oral anticoagulant agents reduces the thromboembolic risk; however, bleeding remains a significant problem.[2,3]

Evidence from randomized controlled studies demonstrates that DOACs match the efficacy of VKAs for both primary and secondary stroke prophylaxis in AF. Notably, these newer agents reduce the likelihood of intracranial hemorrhage by approximately 50% compared to traditional therapies.[4,5] Despite robust data from phase IV investigations and extensive meta-analyses confirming the overall safety profile of DOACs, susceptibility to gastrointestinal (GI) bleeding remains a notable clinical apprehension.[6] Literature suggests that the annual incidence of GI hemorrhage attributable to DOAC therapy in the AF population ranges from 0.4% to 0.7%.[7] Conversely, a contemporary meta-analysis indicated that substituting VKAs with DOACs does not elevate the bleeding hazard among patients with a history of stroke.[8]

Because the frequency of severe hemorrhagic events linked to DOAC administration is far from negligible, clinicians must carefully weigh the risk-benefit balance before initiating therapy.[9] To gauge this susceptibility, researchers have designed several distinct prognostic models, such as the HEMORR$_2$HAGES, ORBIT, and ATRIA indices.[10–12] By integrating diverse demographic factors and clinical parameters, these frameworks attempt to quantify a given patient's vulnerability to bleeding complications. Nevertheless, there is a scarcity of comprehensive head-to-head evidence evaluating how accurately these scoring systems perform specifically within the DOAC-treated AF cohort.

Objectives

The primary goal of the current research was to evaluate and contrast the prognostic accuracies of the ORBIT, HEMORR$_2$HAGES, and ATRIA bleeding risk indices explicitly among individuals undergoing DOAC therapy.

Materials and Methods

Study Design and Population

We retrospectively included 447 patients who were initiated on non-VKAs oral anticoagulants (DOACs), including dabigatran, rivaroxaban, apixaban, or edoxaban, for the management of non-valvular AF at the cardiology clinic between June 2011 and June 2019. To guarantee a sufficient observational window, eligibility was restricted to individuals maintaining DOAC therapy for at least half a year. Criteria for exclusion comprised the presence of prosthetic heart valves or rheumatic mitral stenosis. Furthermore, subjects were disqualified if they had a history of hematological, autoimmune, or inflammatory disorders, or if they had experienced a stroke, acute coronary syndrome, unstable angina, hemodynamic compromise, surgical procedures, or inpatient admissions during the 6 months before enrollment. Individuals prescribed DOACs exclusively for the management of venous thromboembolism, such as pulmonary embolism or deep vein thrombosis, were similarly excluded. All research activities complied with the ethical tenets set forth in the Declaration of Helsinki. The study protocol was approved by the İstanbul University-Cerrahpaşa Ethics Committee (date: June 02, 2020, and number: 59491012-604.01.02, Decision No: A-35).

Baseline patient profiles, including demographic details, concurrent pharmacological treatments, and laboratory test results, were systematically extracted from the institution's digital health records. To monitor longitudinal clinical occurrences and ascertain underlying comorbidities, we cross-referenced the computerized hospital registry and performed telephonic follow-up interviews. This comprehensive chart review supplied the requisite clinical, demographic, and serological variables needed to compute the HEMORR$_2$HAGES, ORBIT, and ATRIA indices.

Bleeding Definitions

Within the scope of this investigation, a severe hemorrhagic event (major bleeding) was classified as any clinically pertinent blood loss satisfying a minimum of one of the subsequent conditions: First, any bleeding involving critical anatomical sites (intracranial, intraocular, or urinary) that necessitated active medical intervention. Second, events triggering a drop in systolic arterial pressure below 90 mmHg, thereby causing hemodynamic

compromise. Third, a documented reduction in hemoglobin concentration by ≥2 g/dL. Finally, any GI hemorrhage requiring packed red blood cell transfusions. Conversely, non-major (minor) bleeding was assigned to events failing to meet these strict severity thresholds. Such episodes typically involved less severe, localized bleeding that resolved without requiring aggressive interventions, blood transfusions, or resulting in hemodynamic instability. Minor hemorrhages could present as superficial bruising, self-limiting epistaxis (nosebleeds), or mild GI bleeding that did not mandate a transfusion strategy.[13]

Bleeding Risk Assessment

Each patient's bleeding risk was assessed based on the criteria. The ATRIA score incorporates age, prior bleeding history, hypertension, diabetes, heart failure, and renal impairment to estimate bleeding risk.[10] To compute the HEMORR$_2$HAGES index, several clinical and demographic variables are evaluated: Liver or kidney impairment, alcohol overconsumption, oncological history, advanced age, impaired platelet functionality or thrombocytopenia, systemic hypertension, low hemoglobin levels, hereditary bleeding predispositions, high susceptibility to falls, and a history of cerebrovascular accidents.[11] The ORBIT score includes age, renal function, anemia, prior bleeding, bleeding diathesis, and hypertension as variables for predicting bleeding risk.[12]

Outcome Measures

The main clinical outcome for this investigation was defined as the manifestation of either severe or non-severe hemorrhages among the DOAC-treated AF cohort. We identified these hemorrhagic episodes by examining hospital charts and conducting direct patient communications, including follow-up phone calls. Furthermore, within the specific subset of individuals who suffered a bleeding complication, we performed a comparative analysis to assess and contrast the prognostic capabilities of the distinct scoring models.

Statistical Analysis

Data computation and all subsequent statistical evaluations were carried out utilizing the IBM Statistical Package for the Social Sciences software package, version 19.0 (IBM Corp., Armonk, NY, USA). To determine the normality of continuous variables, the Kolmogorov–Smirnov method was applied. Variables following a normal distribution were expressed as the mean±standard deviation, whereas skewed quantitative data were detailed using medians alongside their respective interquartile ranges. Qualitative parameters were presented as frequencies and percentages (%). For the comparison of categorical data, Pearson's Chi-squared test was implemented. Depending on the normality of the underlying distributions, continuous variables between unrelated cohorts were evaluated via either the Mann–Whitney U test or the independent Student's t-test. To pinpoint independent clinical predictors linked to hemorrhagic complications, both univariable and multivariable logistic regression models were executed. The outputs from these regression models were detailed using odds ratios (ORs) paired with their 95% confidence intervals (CIs). Furthermore, we constructed receiver operating characteristic (ROC) curves to pinpoint the ideal threshold limits for the HEMORR$_2$HAGES, ORBIT, and ATRIA tools, aiming to maximize their combined specificity and sensitivity in anticipating bleeding events. A probability threshold of $p<0.05$ was accepted as the indicator of statistical significance.

Results

The initial clinical and demographic profiles of the cohort are outlined in Table 1. This research enrolled 447 individuals di-

Table 1. Characteristics of patients and clinical risk factors for major bleeding

	Major bleeding (n=30)	No bleeding (n=417)	p
Male	16 (53.3)	153 (36.7)	0.069
Diabetes mellitus	33.3 (10)	35 (146)	0.852
Hypertension (diagnosed)	80 (24)	65.5 (273)	0.103
Coronary artery disease	63.3 (19)	37.6 (157)	0.005
Antiplatelet usage	9 (30.0)	60 (14.4)	0.022
Reduced platelet count	3 (10.0)	20 (4.8)	0.213
Left ventricular dysfunction (LVEF <%40)	7 (23.3)	55 (13.2)	0.121
Liver impairment	1 (3.3)	4 (1.0)	0.232
Renal impairment (CrCl <30 mL/min)	17 (56.7)	144 (34.5)	0.015
Alcohol usage	1 (3.3)	32 (7.7)	0.380
Malignancy	1 (3.3)	18 (4.3)	0.797
Anemia	21 (70.0)	151 (36.2)	<0.001
Fragility (fall risk)	21 (70.0)	181 (43.4)	0.005
Previous stroke	11 (36.7)	52 (12.5)	<0.001
A history of bleeding	13 (43.3)	33 (7.9)	<0.001
Hypertension (SBP >160 mmHg)	12 (40.0)	53 (12.7)	0.000
Age ≥75 years	25 (83.3)	231 (55.4)	0.003

Values are mean±SD or n (%). Reduced platelet count defined as <150.000 platelets. Anemia is defined as hemoglobin <13 g/dL in men and <12 g/dL in women. CrCl: Creatinine clearance; SBP: Systolic blood pressure; SD: Standard deviation.

agnosed with AF who were prescribed DOAC therapy. These subjects were monitored over 12 months to track the manifestation of any hemorrhagic complications. Throughout this initial year of observation, 6.7% of the cohort (n=30) suffered from at least one severe bleeding event. The average age across the study population stood at 75.6±10.1 years, with a predominant female representation (62.2%).

Individuals who encountered major bleeding demonstrated a markedly greater frequency of concurrent coronary artery disease (63.3% vs. 37.6%, p=0.005), concomitant antiplatelet therapy (30.0% vs. 14.4%, p=0.022), diminished platelet counts (10.0% vs. 4.8%, p=0.213), renal dysfunction (56.7% vs. 34.5%, p=0.015), anemia (70.0% vs. 36.2%, p<0.001), a documented history of stroke (36.7% vs. 12.5%, p<0.001), prior hemorrhagic episodes (43.3% vs. 7.9%, p<0.001), and severe hypertension characterized by systolic readings above 160 mmHg (40.0% vs. 12.7%, p<0.001). Furthermore, the likelihood of suffering a severe hemorrhage was considerably elevated in subjects aged 75 or above when contrasted with younger counterparts (83.3% vs. 55.4%, p=0.003) (Table 1).

Regarding the specific anticoagulant regimens, rivaroxaban was the most frequently prescribed agent (57%, n=255), followed by apixaban (31.3%, n=140), dabigatran (10.7%, n=48), and edoxaban (0.9%, n=4). Notably, elevated values across all three evaluated risk indices strongly correlated with the occurrence of bleeding (p<0.001) (Fig. 1).

Table 2 illustrates how the study population was categorized into varying risk tiers utilizing the ATRIA, ORBIT, and HEMORR$_2$HAGES frameworks. This table also details the proportion of subjects with and without major hemorrhagic episodes across these specific risk classifications. When examining the high-risk brackets of each model, severe bleeding incidents were observed in 80% of patients categorized by the HEMORR$_2$HAGES system, 66.7% by the ATRIA index, and 63.3% according to the ORBIT scale (Table 2).

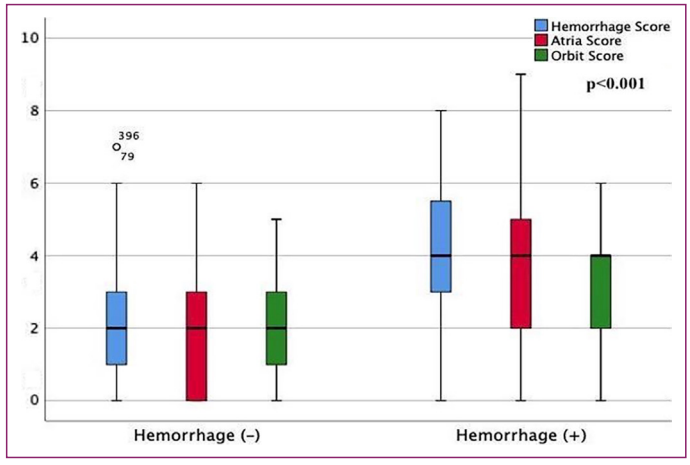

Figure 1. Comparison of patients with and without bleeding according to bleeding scores.

A detailed appraisal of these predictive tools, incorporating ROC evaluations, is provided in Table 3. By computing the area under the curve (AUC) for each respective model, we determined that the HEMORR$_2$HAGES index yielded the most superior predictive performance with an AUC of 0.843 (p<0.001). The ORBIT framework ranked second (AUC: 0.816, p<0.001), whereas the ATRIA tool recorded an AUC of 0.784 (p<0.001) (Table 3). A head-to-head evaluation of the prognostic capabilities of these indices concerning severe hemorrhagic events is detailed in Table 4.

Although the contrast in forecasting accuracy between the HEMORR$_2$HAGES and ATRIA models trended toward statistical significance (p=0.058), overall, the three frameworks demonstrated statistically equivalent predictive strengths. No meaningful disparity was detected in the AUC metrics when contrasting the HEMORR$_2$HAGES and ORBIT tools (Difference in AUC: 0.026,

Table 2. Patients stratified by the risk groups according to HEMORR$_2$HAGES, ATRIA, and ORBIT scores

	Risk group	Major bleeding (+), n (%)	No bleeding events, n (%)
HEMORR$_2$HAGES	Low (≤1)	1 (3.3)	138 (33.1)
	Intermediate (2–3)	5 (16.7)	175 (42)
	High (>3)	24 (80)	104 (24.9)
ATRIA	Low (≤1)	6 (20)	308 (73.9)
	Intermediate (2–3)	4 (13.3)	16 (3.8)
	High (>3)	20 (66.7)	93 (22.3)
ORBIT	Low (≤1)	5 (16.7)	273 (65.5)
	Intermediate (2–3)	6 (20)	67 (16.1)
	High (>3)	19 (63.3)	77 (18.5)

Values are n (%). HEMORR$_2$HAGES, Hepatic or Renal Disease, Ethanol Abuse, Malignancy, Older Age, Reduced Platelet Count or Function, Re-Bleeding, Hypertension, Anemia, Genetic Factors, Excessive Fall Risk, and Stroke; ATRIA: Anticoagulation and risk factors in atrial fibrillation; ORBIT: Outcomes registry for better informed treatment.

Table 3. Evaluation of the bleeding risk scores and ROC analysis

Risk score	AUC	p	Sensitivity (%)	Specificity (%)	95% CI
HEMORR$_2$HAGES	0.843	0.001	80	75.1	0.806–0.876
ATRIA	0.784	0.001	80	73.9	0.743–0.822

ROC: Receiver operating characteristic; AUC: Area under the curve; CI: Confidence interval.

Table 4. Comparison of the predictive power of the bleeding risk scores used to assess the risk of major bleeding

Bleeding risk score	AUC difference	95% CI	p
ORBIT versus HEMORR$_2$HAGES	0.0268	0.0112–0.0649	0.167
ORBIT versus ATRIA	0.0320	0.0132–0.0772	0.165
HEMORR$_2$HAGES versus ATRIA	0.0588	0.00209–0.120	0.058

AUC: Area under the curve; CI: Confidence interval

Table 5. Multivariate logistic regression analysis to identify predictors of major bleeding

	Multivariate analysis		
Variable	OR	95% CI	p
Heart failure (LVEF <%40)	2.028	1.072–3.229	0.009
Previous bleeding	3.101	1.203–7.998	0.019
Anemia	0.366	0.134–0.999	0.049
HEMORR$_2$HAGES score	1.535	1.131–2.082	0.006

LVEF: Left ventricular ejection fraction; OR: Odds ratio.

95% CI: 0.0112–0.0649, p=0.167). A parallel lack of significance was noted between the ORBIT and ATRIA systems (Difference in AUC: 0.0320, 95% CI: 0.0132–0.0772, p=0.165). The margin of difference between the ATRIA and HEMORR$_2$HAGES curves stood at 0.0588 (95% CI: 0.00209–0.120, p=0.058) (Table 4).

To isolate independent clinical variables forecasting severe hemorrhages, we executed a multivariable logistic regression model. This evaluation underscored several distinct parameters as notable indicators of major bleeding. These included a documented history of bleeding (OR: 3.10, 95% CI: 1.20–7.99; p=0.019), left ventricular dysfunction representing heart failure (LVEF<40%) (OR: 2.02, 95% CI: 1.07–3.22; p=0.009), and the presence of anemia (OR: 0.36, 95% CI: 0.13–0.99; p=0.049). Furthermore, elevated categorizations within the HEMORR$_2$HAGES (OR: 1.53, 95% CI: 1.13–2.08; p=0.006) and ORBIT frameworks (OR: 1.84, 95% CI: 1.13–3.02; p=0.014) independently signaled future bleeding events. Specifically, prior hemorrhages and concomitant heart failure amplified the likelihood of severe bleeding, whereas anemia appeared to correlate with a risk-reducing or protective pattern in this cohort. Expectedly, advancing risk tiers in both the ORBIT and HEMORR$_2$HAGES models firmly correlated with heightened bleeding vulnerabilities (Table 5).

Discussion

Although multiple prognostic models exist to gauge hemorrhagic vulnerabilities in individuals with AF undergoing oral anticoagulation therapy, consensus regarding the optimal predictive instrument is still lacking.[4] This investigation was designed to identify the most precise scoring metric by leveraging real-world clinical datasets, ultimately aiming to mitigate DOAC-associated bleeding complications. The primary clinical takeaways from our analysis are twofold : First, applying the HEMORR$_2$HAGES criteria categorized the bulk of the cohort (71.4%) into the moderate-to-high-risk stratum. Conversely, evaluations using the ORBIT and ATRIA models designated the majority of subjects as low-risk (62.2% and 70.4%, respectively). Second, subsequent comparative appraisals via the c-statistic indicated that while the prognostic capability of the HEMORR$_2$HAGES tool approached significance when evaluated against the ATRIA index (p=0.058), there was no statistically meaningful divergence among the three instruments in forecasting severe hemorrhages. Third, multivariable modeling confirmed that a prior hemorrhagic event, diminished left ventricular function (heart failure), anemia, and advanced tiers in both the ORBIT and HEMORR$_2$HAGES indices acted as robust, independent determinants of future bleeding (heart failure OR: 2.028, p=0.009; bleeding history OR: 3.101, p=0.019; anemia OR: 0.366, p=0.049; HEMORR$_2$HAGES score OR: 1.535, p=0.006; ORBIT score OR: 1.849, p<0.014). Although DOACs provide substantial protection against ischemic stroke through targeted anticoagulation, they inherently elevate the likelihood of hemorrhagic complications in susceptible individuals. Consequently, a variety of prognostic tools, such as the ATRIA, ORBIT, and HEMORR$_2$HAGES frameworks, have been formulated to quantify this vulnerability.[14–17] In a retrospective study conducted by Yao et al.,[18] which examined a cohort of 39,539 DOAC-treated individuals with non-valvular AF over a 5-year period (2010–2015). Their findings indicated an annual severe bleeding rate of 2.9% (n=665). Furthermore, their comparative evaluation of multiple indices (including ATRIA, ORBIT, HAS-BLED, CHADS2, and CHA2DS2-VASc) failed to establish the definitive superiority of any single model. These results align closely with our current findings; our head-to-head comparison of the ATRIA, ORBIT, and HEMORR$_2$HAGES frameworks yielded no statistically definitive disparities in predicting severe hemorrhages. We did note, however, that the predictive accuracy of the HEMORR$_2$HAGES model trended closely toward significance when matched against the ATRIA tool (p=0.058).

In the study conducted by Proietti et al.,[19] the data from the RE-LY study were analyzed, involving a total of 18,113 patients. During the 2-year follow-up, 1182 patients (6.5%) experienced major bleeding. The ORBIT risk scoring system was identified as the most valuable tool for predicting both major bleeding and intracranial bleeding. In our study, through multivariate analysis, we identified the HEMORR$_2$HAGES and the ORBIT score as statistically significant independent predictors of bleeding de-

velopment. In the study conducted by Lip et al.,[20] the ORBIT, HAS-BLED, and ATRIA schemes were contrasted, noting only marginal variations in performance (c-index metrics around 0.59) over a 12-month follow-up. In their cohort, the HAS-BLED model yielded a markedly higher sensitivity (62.8%) for detecting critical bleeds relative to ORBIT (37.1%) and ATRIA (29.7%). Distinguishing our research from these earlier investigations, we explicitly incorporated the HEMORR$_2$HAGES framework into our comparative analysis.

A robust body of evidence indicates that individuals suffering from ventricular dysfunction face heightened vulnerabilities not solely to thromboembolic complications, but also to hemorrhagic episodes. Notably, this predisposition persists independently of concurrent variables such as advancing age, diabetic status, elevated cholesterol levels, or the administration of antithrombotic medications.[21–24] In alignment with these prior observations, our multivariable evaluation confirmed that pre-existing heart failure independently escalates the probability of future bleeding.

A primary advantage of the present investigation is our reliance on real-world clinical cohorts rather than strictly controlled trial environments. Furthermore, evaluating three distinct hemorrhagic risk indices concurrently within a uniform participant group yields robust comparative data. The 12-month observational window facilitated a comprehensive tracking of temporal bleeding occurrences, and the application of multivariable modeling enabled the isolation of distinct predictive variables. Consequently, these results deliver practical insights that can assist physicians when managing anticoagulant regimens, reinforcing the translational value of our research for routine cardiovascular care.

Study Limitations

Certain constraints within our research design merit consideration. To begin with, our cohort was relatively modest in scale when contrasted with major multicenter registries, a factor that might restrict the broader extrapolation of our conclusions to the general AF population. Another prominent constraint was our inability to compute the HAS-BLED index, as routine international normalized ratio testing was inherently absent for this DOAC-treated group. Because the HAS-BLED metric frequently serves as a baseline comparator in similar scientific literature, its omission here is an important caveat. Finally, the over-the-counter availability of non-steroidal anti-inflammatory drugs (NSAIDs) in our geographic region complicated the accurate tracking of their consumption. This missing tracking data may have obscured the true impact of NSAIDs on GI hemorrhage rates, potentially altering the perceived predictive accuracy of the evaluated risk models.

Conclusion

To summarize, our analysis of real-world clinical records revealed that the ATRIA, ORBIT, and HEMORR$_2$HAGES frameworks are equally effective at forecasting severe hemorrhagic complications among AF patients receiving DOAC therapy. Notably, the ORBIT and HEMORR$_2$HAGES indices emerged as strong, stand-alone prognostic factors for predicting both severe and non-severe bleeding events. Incorporating these specific tools into daily patient evaluations could substantially aid physicians in quantifying hemorrhagic vulnerability. While the quest for the ultimate prognostic model continues to spark debate and necessitates additional prospective investigations, this research enriches current medical literature by simultaneously evaluating three distinct indices within an extensive, real-world demographic, diverging from earlier reports that heavily relied on strictly controlled trial participants. Furthermore, this paper represents a pioneering effort in head-to-head contrasting of these specific models, which were initially designed as substitutes for the widely used HAS-BLED metric. Ultimately, these outcomes deliver essential practical guidance for utilizing prognostic scores in cardiology, emphasizing the necessity for ongoing scientific exploration in this domain.

Disclosures

Ethics Committee Approval: The study was approved by the İstanbul University-Cerrahpaşa Ethics Committee (no: 59491012-604.01.02, decision no: A-35, date: 02/06/2020).

Informed Consent: Written informed consents were obtained from patients who participated in this study.

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