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Comparison of Short-term Outcomes in Anticoagulated Patients with GI Bleeding: Warfarin versus NOACs

Antikoagülan Tedavi Gören Gastrointestinal Kanamalı Hastalarda Kısa Vadeli Sonuçların Karşılaştırılması: Warfarin ve NOAC'lar

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Abstract

Objective: Gastrointestinal (GI) bleeding is a major complication of oral anticoagulant therapy. While non-vitamin K oral anticoagulants (NOACs) offer advantages over warfarin, limited real-world data exist comparing short-term clinical outcomes following GI bleeding events in anticoagulated patients. This study aims to compare clinical characteristics, intervention requirements, hospitalization outcomes, and mortality in patients presenting with GI bleeding while receiving warfarin or NOAC therapy, and to explore differences among individual NOAC agents.

Methods: We conducted a single-center, retrospective, cross-sectional study including 299 adult patients who presented to the emergency department with GI bleeding while on oral anticoagulants. Data collected included demographics, laboratory values, interventions, and clinical outcomes. Subgroup analysis was performed among NOAC agents. Statistical comparisons used appropriate univariate tests; multivariable analysis was not feasible due to limited event counts.

Results: Of 299 patients (mean age 75.8±10.4 years, 52.2% male), 30.1% were receiving warfarin and 69.9% NOACs. Emergency department mortality (2.0%) and in-hospital mortality (7.4%) were similar among the groups (p>0.05). Endoscopic interventions (75.3%) and erythrocyte transfusion needs (56.8%) did not differ significantly by anticoagulant type. Elevated creatinine was independently associated with in-hospital mortality (p=0.016). No significant differences in outcomes were found among individual NOAC agents.

Conclusion: GI bleeding remains a serious but generally manageable event in patients on oral anticoagulants, with comparable short-term outcomes between warfarin and NOAC users. Renal dysfunction is an important predictor of mortality. Larger prospective studies are needed to refine risk stratification and optimize management in this population.

Keywords: Gastrointestinal bleeding, warfarin, NOAC, emergency department

Öz

Amaç: Gastrointestinal (GI) kanama, oral antikoagülan tedavisinin önemli bir komplikasyonudur. Vitamin K içermeyen oral antikoagülanlar (NOAC) warfarine göre avantajlar sunsa da antikoagülan tedavisi gören hastalarda GI kanama olaylarını takiben kısa vadeli klinik sonuçları karşılaştıran sınırlı sayıda gerçek dünya verisi bulunmaktadır. Warfarin veya NOAC tedavisi gören ve GI kanaması geçiren hastaların klinik özelliklerini, müdahale gereksinimlerini, hastaneye yatış sonuçlarını ve mortaliteyi karşılaştırmak ve bireysel NOAC ajanları arasındaki farkları araştırmaktır.

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Öz

Yöntem: Oral antikoagülan tedavisi gören ve GI kanaması ile acil servise başvuran 299 yetişkin hastayı içeren tek merkezli, retrospektif, kesitsel bir çalışma yürüttük. Toplanan veriler demografik bilgiler, laboratuvar değerleri, müdahaleler ve klinik sonuçları içeriyordu. NOAC ajanları arasında alt grup analizi yapıldı. İstatistiksel karşılaştırmalarda uygun tek değişkenli testler kullanıldı; olay sayısının sınırlı olması nedeniyle çok değişkenli analiz yapılamadı.

Bulgular: İki yüz doksan dokuz hastanın (ortalama yaş 75,8±10,4 yıl, %52,2'si erkek) %30,1'i warfarin, %69,9'u NOAC alıyordu. Acil servis mortalitesi (%2,0) ve hastane içi mortalite (%7,4) gruplar arasında benzerdi (p>0,05). Endoskopik müdahaleler (%75,3) ve eritrosit transfüzyonu ihtiyacı (%56,8) antikoagülan türüne göre önemli ölçüde farklılık göstermedi. Yükselmiş kreatinin, hastane içi mortalite ile bağımsız olarak ilişkiliydi (p=0,016). Bireysel NOAC ajanları arasında sonuçlarda önemli bir fark bulunmamıştır.

Sonuç: GI kanaması, oral antikoagülan kullanan hastalarda ciddi ancak genellikle yönetilebilir bir olay olmaya devam etmektedir ve warfarin ve NOAC kullanıcıları arasında kısa vadeli sonuçlar benzerdir. Böbrek fonksiyon bozukluğu, mortalitenin önemli bir belirleyicisidir. Bu popülasyonda risk sınıflandırmasını iyileştirmek ve yönetimi optimize etmek için daha büyük prospektif çalışmalar gereklidir.

Anahtar Kelimeler: Gastrointestinal kanama, warfarin, NOAC, acil servis

Introduction

The use of oral anticoagulant therapy has dramatically increased over recent decades due to the growing prevalence of cardiovascular and thromboembolic disorders, particularly in aging populations. Conditions such as atrial fibrillation (AF), mechanical heart valve replacement, venous thromboembolism, and coronary artery disease (CAD) often necessitate long-term anticoagulation to prevent thromboembolic complications, which can result in significant morbidity and mortality if untreated[1,2].

Historically, vitamin K antagonists (VKAs), primarily warfarin, have served as the cornerstone of oral anticoagulation therapy. However, warfarin's narrow therapeutic window, numerous drug and food interactions, and requirement for frequent monitoring of the international normalized ratio (INR) have posed substantial clinical management challenges. In response to these limitations, non-vitamin K oral anticoagulants (NOACs) have been introduced and increasingly adopted due to their more predictable pharmacokinetic profiles, fewer dietary restrictions, and lack of routine coagulation monitoring requirements[3-5].

Despite these advantages, bleeding complications remain the most feared adverse effect of all oral anticoagulants, with gastrointestinal (GI) bleeding being among the most frequent and clinically significant events[6]. Although large randomized controlled trials have demonstrated lower rates of intracranial hemorrhage with NOACs compared to VKAs, data on GI bleeding have shown conflicting results, with some studies suggesting comparable or even slightly increased rates of GI bleeding in NOAC users, particularly with certain agents[7-9].

GI bleeding in anticoagulated patients presents complex management dilemmas for clinicians. These include decisions on temporary or permanent discontinuation of anticoagulation, timing of endoscopic evaluation, reversal strategies, transfusion thresholds, and balancing the competing risks of thrombosis and rebleeding. Furthermore, patient-specific factors such as age, comorbidities, renal function, and polypharmacy contribute additional layers of complexity to clinical decision-making[10-12].

Although numerous studies have evaluated the overall bleeding risks associated with anticoagulant use, data comparing short-term clinical outcomes specifically among patients presenting with GI bleeding while on either warfarin or NOACs remain relatively limited[13]. Most prior investigations have focused on bleeding incidence rates, with less emphasis on the real-world outcomes following acute GI bleeding episodes requiring emergency care and hospitalization[14].

The primary objective of this study was to compare the clinical characteristics, intervention requirements, hospitalization courses, and mortality outcomes of patients presenting to the emergency department with GI bleeding while receiving either warfarin or NOAC therapy. Additionally, we aimed to assess potential differences in outcomes among individual NOAC agents. By addressing these questions in a real-world, emergency care setting, this study seeks to provide valuable insights into the acute management and prognostic implications of GI bleeding in anticoagulated patients.

Materials and Methods

Study Design and Population

This single-center, retrospective, cross-sectional study was conducted in the University of Health Sciences Türkiye, İzmir Tepecik Education and Research Hospital, Department of Emergency between January 2020 and December 2023. A

total of 299 adult patients (≥18 years old) who presented to the emergency department with GI bleeding while receiving oral anticoagulant therapy were included in the study. The anticoagulants evaluated included VKA (warfarin) and NOACs, specifically apixaban, rivaroxaban, dabigatran, and edoxaban (Table 1).

Patients who were using oral anticoagulant therapy and presented with either upper or lower GI bleeding were eligible for inclusion. Exclusion criteria comprised patients under 18 years of age, those with traumatic bleeding, and individuals with incomplete medical records regarding their anticoagulant use or bleeding diagnosis.

Data Collection

Data were retrospectively extracted from electronic medical records and included the following parameters: additionally, data regarding concomitant antiplatelet therapy, non-steroidal anti-inflammatory drug usage, proton pump inhibitor co-medication, and detailed endoscopic bleeding lesion characteristics were not available, which may act as unmeasured confounding variables impacting outcomes.

- Demographic data (age, sex),
- Type and indication of anticoagulant therapy,
- Laboratory parameters at admission [white blood cell count (WBC), hemoglobin, platelet count, urea, creatinine, aspartate aminotransferase, alanine aminotransferase, INR, activated partial thromboplastin time, and prothrombin time],
- Consultations performed (gastroenterology, anesthesiology, surgery, cardiology, internal medicine),
- Interventional procedures [endoscopy, colonoscopy, erythrocyte transfusion (ERT)],
- Emergency department outcomes (discharge, hospitalization, intensive care unit admission, death, transfer, and treatment refusal),
- In-hospital mortality and length of stay.

The primary clinical indications for anticoagulation included AF, mechanical valve replacement, CAD, ischemic stroke, pulmonary embolism, and deep vein thrombosis. Final clinical diagnoses were categorized into upper GI bleeding, lower GI bleeding, anemia-related causes, malignancy-related causes, and other rare etiologies (Tables 1-3).

Outcome Measures

The primary outcomes of interest were emergency department mortality, in-hospital mortality, duration of stay in the emergency department, total hospital length of stay, and the requirement for endoscopic or transfusion interventions. Subgroup analyses were performed based on the type of anticoagulant used (warfarin vs. NOACs, and among the individual NOAC agents) (Tables 4, 5).

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics software (version 26, IBM Corp., Armonk, NY, USA). Continuous variables were presented as mean ± standard deviation, median, minimum, and maximum values. Categorical variables were expressed as numbers and percentages. Comparisons between groups were conducted using the Pearson's chi-square test or Fisher's exact test for categorical variables, depending on the expected frequencies. For continuous variables, normality was assessed, and appropriate tests were applied: Mann-Whitney U test for two-group comparisons and Kruskal-Wallis test for multiple group comparisons. A two-tailed p-value of <0.05 was considered statistically significant.

Due to the limited number of mortality events, multivariate regression analyses could not be performed to adjust for potential confounders such as age, renal function,

Table 1. Baseline characteristics of study population (n=299)

Characteristic	n (%) or mean ± SD
Age (years)	75.8±10.4
Male sex	156 (52.2%)
Female sex	143 (47.8%)
Warfarin	90 (30.1%)
NOACs total	209 (69.9%)
- Apixaban	67 (22.4%)
- Rivaroxaban	90 (30.1%)
- Edoxaban	30 (10.0%)
- Dabigatran	22 (7.4%)
AF	94 (31.4%)
Valve replacement	63 (21.1%)
Coronary artery disease	47 (15.7%)
AF + CAD	36 (12.0%)
SVO	12 (4.0%)
Others	Remaining 15.8%

SD: Standard deviation, NOACs: Non-vitamin K oral anticoagulants, AF: Atrial fibrillation, CAD: Coronary artery disease, SVO: Cerebrovascular disease

comorbidities, and medication co-use. Future studies incorporating larger sample sizes are necessary to allow for robust multivariate modeling.

Ethical Considerations

The study was approved by the Institutional Review Board of University of Health Sciences Türkiye, İzmir Tepecik Education and Research Hospital Ethics Committee approval no: 2023/12-22, 10.01.2024 and was conducted in accordance with the principles of the Declaration of Helsinki.

Results

Patient Characteristics

A total of 299 patients were included in the study, with a mean age of 75.8±10.4 years (range 40-95 years). Of these, 52.2% were male (n=156), and 47.8% were female (n=143). Warfarin was used in 30.1% of patients (n=90), while 69.9% (n=209) were receiving NOACs: apixaban (22.4%), rivaroxaban (30.1%), edoxaban (10.0%), and dabigatran (7.4%).

Table 2. Emergency department interventions and outcomes

Intervention	Warfarin (n=90)	NOAC (n=209)	Total (n=299)	p-value
ED mortality (%)	2 (2.2%)	4 (1.9%)	6 (2.0%)	1.000
Gastroenterology consult	88 (97.8%)	205 (98.1%)	293 (98.0%)	-
Endoscopy performed	62 (68.9%)	163 (78.0%)	225 (75.3%)	0.175
Colonoscopy performed	0	1	1 (0.3%)	-
ERT performed	57 (63.3%)	112 (53.6%)	169 (56.8%)	0.119
Median ED stay (minutes)	668	612	-	0.329

ED: Emergency department, ERT: Erythocyte replacement transfusion

Table 3. In-hospital mortality and outcomes

Outcome	Warfarin (n=90)	NOAC (n=209)	Total (n=299)	p-value
In-hospital mortality (%)	7 (7.8%)	15 (7.2%)	22 (7.4%)	0.855
Median hospital stay (days)	5	5	-	0.931
Discharged	48 (53.3%)	107 (51.2%)	155 (51.8%)	0.543
ICU admission	19 (21.1%)	34 (16.3%)	53 (17.7%)	-

NOAC: Non-vitamin K oral anticoagulant, ICU: Intensive care unit

Table 4. Laboratory parameters associated with mortality

Parameter	Mortality (+) (n=22)	Mortality (-) (n=277)	p-value
WBC (×10³/µL)	12.67±6.51	10.20±5.04	0.055
Creatinine (mg/dL)	2.19±1.54	1.51±0.97	0.016
Hemoglobin (g/dL)	7.58±2.59	8.18±2.52	0.216
Platelets (×10³/µL)	271±105.73	248±96.05	0.291

WBC: White blood count

Table 5. NOAC subgroup outcomes (n=209)

NOAC agent	ED mortality (%)	In-hospital mortality (%)	Endoscopy performed (%)	ERT (%)	Median hospital stay (days)
Apixaban	0	9.0%	83.6%	50.7%	5
Rivaroxaban	1.1%	8.9%	71.1%	52.2%	5
Dabigatran	0	4.5%	81.8%	54.5%	5
Edoxaban	3.3%	6.7%	83.3%	63.3%	4

NOAC: Non-vitamin K oral anticoagulant, ED: Emergency department, ERT: Erythocyte replacement transfusion

Emergency Department Outcomes

The overall mortality rate in the emergency department was 2.0% (6/299), with no significant difference between warfarin (2.2%) and NOAC users (1.9%) (p=1.000). Most patients (97.3%) required consultation, with gastroenterology being the most frequent specialty involved (98.0%). Endoscopic evaluation was performed in 75.3% of patients. Colonoscopy was rarely utilized (0.3%). ERT was administered in 56.8% of patients; however, there was no statistically significant difference observed in the comparative outcomes (Table 2).

In-hospital Outcomes

In-hospital mortality occurred in 22 patients (7.4%). Mortality rates were similar between warfarin (7.8%) and NOAC users (7.2%) (p=0.855). Median hospitalization duration was 5 days in both groups, with no significant difference (p=0.931) (Table 3).

Laboratory Parameters and Mortality

Deceased patients had significantly higher creatinine levels (2.19±1.54 mg/dL vs. 1.51±0.97 mg/dL; p=0.016). Elevated WBC was marginally significant (p=0.055). Other laboratory values showed no significant differences (Tables 4, 5).

NOAC Subgroup Analysis

No statistically significant differences were found among individual NOAC agents regarding emergency department mortality, in-hospital mortality, endoscopic intervention rates, transfusion needs, or discharge outcomes (all p>0.05) (Table 5).

Discussion

In this study, we analyzed the clinical characteristics, intervention needs, and short-term outcomes of patients presenting to the emergency department with GI bleeding while receiving oral anticoagulant therapy. Our findings demonstrated that both warfarin and NOAC users experienced comparable rates of emergency department mortality, in-hospital mortality, endoscopic interventions, transfusion requirements, and hospitalization duration.

The rising prevalence of anticoagulation use, particularly NOACs, has brought increasing attention to their associated bleeding risks. Several randomized trials have shown that while NOACs are generally associated with lower rates of intracranial hemorrhage than warfarin, GI bleeding remains a common and clinically significant complication for both drug classes[15-17]. Our study reinforces this observation by demonstrating that GI bleeding continues to be a frequent cause of emergency admission among anticoagulated patients, irrespective of the anticoagulant type used. However, the lack of data on timing of endoscopic intervention, antiplatelet therapy, or ulcer characteristics limits deeper mechanistic interpretation.

Consistent with previous research, AF was the predominant indication for anticoagulation in our cohort[18]. The clinical spectrum of bleeding sources was also in line with existing data, with upper GI bleeding being the most frequent presentation, followed by lower GI bleeding and anemia-related presentations. This distribution reflects the well-established vulnerability of the upper GI tract to anticoagulation-associated mucosal injury[19].

Importantly, both emergency department and in-hospital mortality rates were relatively low in our population (2.0% and 7.4%, respectively). These findings are consistent with prior studies suggesting that most anticoagulation-related GI bleeding events, when appropriately managed, do not result in fatal outcomes[20,21]. Furthermore, the absence of significant differences in mortality between warfarin and NOAC users supports the accumulating evidence that NOACs do not substantially increase the severity of GI bleeding compared to warfarin[22,23].

Endoscopic intervention rates were high (75.3%) in our study, reflecting current best practice guidelines that recommend early endoscopic evaluation for most cases of GI bleeding in anticoagulated patients[24]. Similarly, ERT was frequently required, but again with no significant differences between warfarin and NOAC users, suggesting comparable clinical severity of bleeding episodes across drug classes.

One of the notable findings in our study was the association between elevated creatinine levels and in-hospital mortality. Renal dysfunction has previously been identified as a significant predictor of adverse outcomes in patients with both GI bleeding and anticoagulation use[25,26].

This may be attributed to impaired drug clearance, accumulation of active drug levels, and overall increased frailty in patients with renal impairment. In addition, renal dysfunction may indirectly reflect overall frailty, sarcopenia, or impaired drug metabolism capacity, all of which have been linked to poor outcomes in elderly anticoagulated patients experiencing GI bleeding.

Our subgroup analysis among different NOAC agents revealed no statistically significant differences in clinical outcomes, including mortality, endoscopy rates, transfusion requirements, or hospitalization duration. Although certain observational studies have suggested differential GI bleeding risk profiles between individual NOAC agents (with dabigatran and rivaroxaban potentially having higher GI bleeding rates than apixaban)[27,28], our real-world data indicate that once GI bleeding occurs and leads to emergency care, the clinical course may be similar across NOAC agents. This finding aligns with several recent meta-analyses that question the clinical relevance of minor variations in bleeding risk between NOAC agents, particularly regarding major bleeding occurrences[29].

Furthermore, our data suggest that individualized bleeding risk stratification incorporating renal function, polypharmacy, and possibly frailty indices may improve patient selection and early intervention planning.

Our findings emphasize the need for vigilant monitoring and prompt management of GI bleeding in all anticoagulated patients, regardless of the anticoagulant agent. Early gastroenterology consultation and endoscopic intervention remain cornerstone approaches in minimizing morbidity and mortality. Additionally, careful assessment of renal function may help identify patients at higher risk for adverse outcomes and guide individualized treatment strategies.

Study Limitations

The strengths of this study include its real-world, emergency department-based design and inclusion of both warfarin and multiple NOAC agents in a single cohort, allowing direct comparison of short-term clinical outcomes. However, several limitations warrant consideration. First, the retrospective nature of the study may have introduced selection or documentation biases. Second, the relatively small number of mortality events limited the statistical power for subgroup analyses, particularly for NOAC agents. Third, unmeasured variables such as concomitant antiplatelet use, endoscopic timing, or specific bleeding lesion characteristics were not captured and may have influenced outcomes. Another limitation is that we did not assess the timing of anticoagulation interruption or resumption post-bleeding, which can influence both thromboembolic risk and rebleeding events. Finally, the single-center design may limit generalizability to broader populations.

Conclusion

In conclusion, our study demonstrates that GI bleeding in anticoagulated patients represents a serious but generally manageable clinical challenge, with comparable outcomes between warfarin and NOAC users. Renal dysfunction remains a relevant prognostic factor for mortality. Future prospective, multicenter studies with larger sample sizes are warranted to further refine risk stratification and optimize management strategies for this complex patient population.

Ethics

Ethics Committee Approval: The study was approved by the Institutional Review Board of University of Health Sciences Türkiye, İzmir Tepecik Education and Research Hospital Ethics Committee approval no: 2023/12-22, 10.01.2024 and was conducted in accordance with the principles of the Declaration of Helsinki.

Informed Consent: This study is single-center, retrospective, and cross-sectional study.

Footnotes

Authorship Contributions

Concept: O.S., Design: O.S., N.Y.O., Data Collection or Processing: N.Y.O., Analysis or Interpretation: O.S., Literature Search: O.S., N.Y.O., Writing: O.S.

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

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