ORIGINAL INVESTIGATION

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Assessing Antiaggregant, Anticoagulant, and Blood Product Transfusion Use in Patients Admitted to Intensive Care for Gastrointestinal Bleeding

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Abstract

Aim: Acute gastrointestinal (GI) bleeding is one of the most common gastrointestinal causes of hospitalization. Several risk factors have been shown to contribute to the development of GI bleeding. The aim of this study was to determine the rate of use of new oral anticoagulants (NOACs), warfarin, and acetylsalicylic acid (ASA), and to evaluate the need for transfusion of erythrocyte suspension (ES), fresh frozen plasma (FFP), platelet suspension, and intensive care unit (ICU) outcomes in patients hospitalized in the intensive care unit due to acute non-variceal upper gastrointestinal bleeding.

Study Design: Patients admitted to the ICU for GI bleeding were divided into two groups: survivors and non-survivors. Demographic data, blood product transfusion needs, and prior antiplatelet and anticoagulant drug use were analyzed retrospectively. Differences between survivors and non-survivors were evaluated.

This single-center, retrospective observational study examined all antiaggregant and anticoagulant therapies used by patients admitted to the ICU for gastrointestinal bleeding between January 2019 and January 2023.

Results: Of the 397 patients included in the study, 59 (14.8%) died. The mean age of deceased patients was 75.5±11.9 years, and 25 (42.4%) were female. Anticoagulant or antiaggregant drugs were used by 165 (41.6%) of all patients and 39 (66.1%) of the patients who died. The most commonly used drugs were ASA (16.6%) and NOACs (12.8%). There were no differences between survivors and non-survivors in terms of gender (p=0.483), decrease in hemoglobin levels (p=0.087), or duration of intensive care unit stay (p=0.243). Additionally, no differences were observed in the transfusion of red blood cells (p=0.092) or platelet suspension (p=0.215) between survivors and non-survivors. The predictive factors for mortality were FFP transfusion (odds ratio [OR], 95% confidence interval [CI]: 0.253, [0.116-0.551], p<0.01), shorter ICU length of stay (OR: 1.127, 95% CI: [1.034-1.228], p<0.01), high pulse rate (OR: 0.970, [0.954-0.987], p<0.01), and lower systolic blood pressure (OR: 1.013, [1.00-1.026], p<0.04).

Conclusions: Despite the fact that FFP transfusion, shorter ICU stay, higher heart rate, and lower systolic blood pressure were strong predictors of mortality, no relationship was identified between ICU mortality and erythrocyte suspension (ES), thrombocyte transfusion, anticoagulant use or type, or hemoglobin level in patients admitted to the ICU with gastrointestinal bleeding.

Keywords: Critical care; Gastrointestinal bleeding; Blood transfusion; Mortality.

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Introduction

Acute gastrointestinal bleeding is the most common gastrointestinal cause of hospitalization. Globally, the incidence of upper gastrointestinal (GI) bleeding has decreased over the last two decades due to increased accessibility to endoscopy, the success of endoscopic treatments, and the eradication of Helicobacter pylori (HP).[1] However, there are cases of gastrointestinal bleeding where the source cannot be identified through endoscopy or colonoscopy. This can lead to increased hospitalization and morbidity.[2]

With a high hospitalization rate and a mortality rate of 10%, GI bleeding remains a serious health concern.[3] Several risk factors have been identified that increase the likelihood of GI bleeding. These include advanced age, chronic liver and kidney disease, smoking, alcohol consumption, certain lifestyle factors, and the use of specific medications such as steroids, non-steroidal anti-inflammatory drugs (NSAIDs), antiaggregants, and anticoagulants.[4] Patients presenting with active bleeding and two or more comorbidities have a mortality rate exceeding 10% and require observation in the ICU. Intensive care monitoring plays a critical role in managing patients with GI bleeding who are at high risk due to severe bleeding, comorbidities, drug use history, and endoscopy findings. Evaluating factors such as medication use and blood product transfusion in patients hospitalized in the intensive care unit for GI bleeding can assist in prioritizing triage from the emergency department. Continued use of acetylsalicylic acid (ASA) has been associated with lower mortality compared to patients who discontinued ASA after experiencing bleeding.[2] The incidence of clopidogrel-induced GI bleeding is lower than that associated with ASA, but dual antiplatelet therapy with ASA and clopidogrel increases the risk of recurrent GI bleeding.[5] Gastrointestinal bleeding occurs in 1-3% of patients on oral anticoagulants.[6] New oral anticoagulants (NOACs), developed in response to high bleeding rates, are a preferred alternative to warfarin due to their predictable pharmacodynamics and safer side-effect profile.[7] However, it has been observed that the incidence of gastrointestinal bleeding is higher in NOAC users compared to warfarin users, although mortality rates are similar.[8–10]

Recent studies have provided outcomes for patients managed in emergency departments and wards for gastrointestinal bleeding, as well as those who developed complications during intensive care unit stay. The present study offers valuable insights by analyzing the outcomes of patients who initially sought emergency department care for gastrointestinal bleeding and subsequently required intensive care unit admission. The aim of this study was to determine the rate of use of NOACs, warfarin, and ASA, and to evaluate the need for transfusion of erythrocyte suspension (ES), fresh frozen plasma (FFP), and platelet suspension, as well as intensive care unit (ICU) outcomes in patients hospitalized due to acute non-variceal upper gastrointestinal bleeding.

Materials and Methods

This study employed a single-center, retrospective observational design. The study population consisted of patients admitted to the intensive care unit for gastrointestinal bleeding between January 2019 and January 2023. The antiaggregant and anticoagulant treatments administered to these patients were analyzed. Critically ill patients aged 18 years or older, who had gastrointestinal bleeding and were hospitalized for more than 24 hours, were included in the study. Patients were excluded if they met any of the following criteria: age under 18 years, pregnancy, or a history of gastrointestinal bleeding or imminent death within 24 hours of admission. The primary data source for the study was the hospital's clinical information system, Probel.

Patients for whom complete information was available were included in the analysis. Data collected from the Probel system included patient demographics (age, gender), Acute Physiology and Chronic Health Evaluation (APACHE) II scores, treatment data (ES, FFP, platelet suspension transfusions), laboratory data (hemoglobin (Hb) measurements and international normalized ratio [INR]), endoscopy reports, and outcomes (ICU length of stay [LOS] and mortality). Patient anamnesis, obtained from the patients and their relatives, included information on the use of NOACs, warfarin, ASA, clopidogrel, low molecular weight heparin (LMWH), and dual antiaggregant therapies. The decrease in Hb level was calculated as the difference between the Hb level at admission to the emergency department and the lowest Hb level during hospitalization. The aim of the study was to compare the mortality rates and transfusion requirements of ICU patients with gastrointestinal bleeding who used NOACs, warfarin, and other anticoagulant drugs. The primary outcomes of the study were to determine the length of stay in intensive care and the mortality rates. As this was a retrospective study, the requirement for informed consent was waived. The study received approval from the İzmir Katip Celebi University Non-Interventional Clinical Research Ethics Committee (Approval

Number: 0193, Date: 25.04.2024). Patient confidentiality was maintained throughout the study, and the study adhered to the ethical principles of clinical research in accordance with the Declaration of Helsinki. I declare that I have not used artificial intelligence (AI)-assisted technologies (such as Large Language Models [LLM], chatbots, or image generators) in the production of the submitted article.

Statistical Analysis

The statistical analysis for this study was conducted using the IBM Statistical Package for the Social Sciences (SPSS) software, version 24.0 (IBM Corp., USA). Patient characteristics were analyzed using descriptive statistics. Categorical variables were expressed as frequencies and percentages (n (%)), while numerical variables were described using mean, standard deviation (mean ± SD), minimum, maximum, and median values. For independent groups, the Student's t-test and Mann-Whitney test were used to determine whether there were any significant differences in the measurements between the groups. The chi-square test was employed to analyze relationships between grouped variables.

Results

Of the 397 patients admitted to the intensive care unit due to upper gastrointestinal bleeding with available data, 59 (14.8%) died. The mean age of the non-surviving patients was higher than that of the surviving patients (75.5±11.9 vs. 66.9±16.1 years, respectively, p<0.01). The APACHE II scores were similar between non-survivors and survivors (16.3±1.4 vs. 13.4±0.8, p=0.51). A summary of the demographic data for the patients included in the study is provided in Table 1. There were no significant differences between the non-surviving and surviving groups in terms of gender (p<0.48), decrease in Hb count (3.3±1.4 vs. 2.9±1.3, p=0.087), or ICU length of stay (4.5±4.4 vs. 5.2±4.2, p=0.243). The most common etiologies of gastrointestinal bleeding were peptic ulcer disease (n=137, 46.7%) and erosive gastritis and esophagitis (n=83, 28%). Endoscopic findings for the patients included in the study are summarized in Table 2. Erythrocyte suspension transfusion was performed in 284 (84%) of the surviving patients and in 54 (91.5%) of the non-surviving patients. Transfusion analysis showed no significant difference between surviving and non-surviving patients in terms of ES and platelet transfusions (p=0.092). ES transfusion was performed in patients with hypotension, tachycardia, and decreased Hb levels due to bleeding. FFP transfusion was administered to patients with INR>1.5 and active bleeding. FFP transfusion was performed in 34 (57.6%) of the non-surviving patients, a statistically significantly higher proportion compared to surviving patients (p<0.01). Blood product transfusion details for the non-surviving patients are summarized in Table 3. Among the non-surviving patients, 14 (23.7%) were using NOACs and 11 (18.6%) were using ASA. In contrast, among the surviving patients, 37 (10.9%) were using NOACs and 55 (16.3%) were using ASA(Table 4) The predictive factors for mortality were FFP transfusion. Of the 397 patients included in the study, 165 (41.6%) had no history of drug use. The drugs most commonly associated with drug use and GI bleeding were ASA (16.6%)

Table 1. Demographic data of non-surviving and surviving patient groups (Mean±SD)

	Non-Survivors	Survivors	p
Gender			
Female (n, %)	25 (42.4)	139 (41.1)	0.483
Male (n, %)	34 (57.6)	199 (58.9)	
Age (Years)	75.5±11.9	66.9±16.1	<0.01
APACHE II	16.3±1.4	13.4±0.8	0.51
ICU Length of Stay (Days)	4.5±4.4	5.2±4.2	0.243
Hemoglobin (Hb) (g/dL)	6.7±1.9	7.3±1.9	<0.05
Decrease in Hb Count (g/dL)	3.3±1.4	2.9±1.3	0.087
INR	2.7±3.7	1.8±2.4	<0.05
Heart Rate (/min)	104.1±23.4	92.3±18.1	<0.01
Systolic BP	105.5±25.2	116.2±24.7	<0.01

Table 2. Endoscopic findings of patients

	Non-Survivors (n, %)	Survivors (n, %)
Peptic Ulcer Disease	8 (2.2)	129 (32.4)
Erosive Gastritis/Esophagitis	9 (2.3)	74 (18.6)
Esophageal Varices	8 (2.1)	37 (9.3)
Malignancy	5 (1)	23 (5.9)
Others (AVM, Mallory-Weiss Syndrome, Polyps)	2 (0.5)	23 (5.8)
Obscure Gastrointestinal Bleeding	27 (6.8)	52 (13.1)

Table 3. The need for blood product transfusion between two groups

	Non-Survivors (n, %)	Survivors (n, %)	p
ES Transfusion (n, %)	54 (91.5)	284 (84.0)	0.092
FFP Transfusion (n, %)	34 (57.6)	96 (28.4)	<0.01

ES: Erythrocyte Suspension; FFP: Fresh Frozen Plasma.

Table 4. A comparison of drug use between two groups

	Non-Survivors (n, %)	Survivors (n, %)	p
No Drug Use	20 (12.1)	145 (87.9)	0.046
NOACs	14 (23.7)	37 (10.9)	
Warfarin	5 (8.5)	34 (10.1)	
ASA	11 (18.6)	55 (16.3)	
Clopidogrel	3 (5.1)	18 (5.3)	
Low Molecular Weight Heparin	5 (8.5)	16 (4.7)	
Dual Antiplatelet (ASA+Clopidogrel)	1 (1.7)	33 (9.8)	

NOACs: New Oral Anticoagulants; ASA: Acetylsalicylic Acid.

Table 5. Multivariate analysis showing associated factors of mortality

	OR	p	(95% CI)
ES Transfusion	0.688	0.568	0.191-2.483
FFP Transfusion	0.253	<0.01	0.116-0.551
ICU Length of Stay	1.127	<0.01	1.034-1.228
Hemoglobin (g/dL)	0.979	0.865	0.764-1.254
INR	1.016	0.756	0.918-1.124
Decrease in Hb Count (g/dL)	1.120	0.491	0.812-1.544
Heart Rate (10/min)	0.970	<0.01	0.954-0.987
Systolic BP (10 mmHg)	1.013	0.043	1.00-1.026

ES: Erythrocyte Suspension; FFP: Fresh Frozen Plasma; ICU: Intensive Care Unit; Hb: Hemoglobin; BP: Blood Pressure; OR: Odds Ratio; CI: Confidence Interval.

and NOACs (12.8%). A comparison of NOAC and warfarin use with ASA use revealed no significant difference between the two groups (p=0.298).

Mortality was analyzed as the dependent variable, and logistic regression analysis was performed using age, gender, ES transfusion, FFP transfusion, ICU length of stay, admission Hb, admission INR, Hb decrease, pulse rate, and systolic blood pressure (BP) as independent variables. The predictive factors for mortality were FFP transfusion (odds ratio [OR], 95% confidence interval [CI]: 0.253, [0.116-0.551], p<0.01), shorter ICU length of stay (OR: 1.127, 95% CI: [1.034-1.228], p<0.01), higher pulse rate (OR: 0.970, [0.954-0.987], p<0.01), and lower systolic blood pressure (OR: 1.013, [1.00-1.026], p<0.04) (Table 5).

Discussion

In this study, we found that 14.9% of patients admitted to the ICU for upper gastrointestinal (UGI) bleeding died. The current literature reports a mortality rate of 8-10% for patients presenting with upper GI bleeding, with this rate increasing to as high as 35% among hospitalized patients. It is evident that the mortality rate for non-esophageal variceal upper GI bleeding is lower compared to variceal bleeding involving the esophagus.[2,11]

In the context of the present study, a higher mean age was observed in non-surviving patients compared to surviving patients (p<0.01). The ASPREE study (Aspirin in Reducing Events in the Elderly) demonstrated an association between age and an increased risk of bleeding in patients undergoing antiplatelet therapy with ASA. This study indicated that the risk of GI bleeding is elevated by 60% in patients aged 75-79 years compared to those under 74 years of age when using ASA. Furthermore, the risk is increased threefold in patients over 80 years of age. This increased risk may be attributed to the prevalence of comorbidities associated with a higher risk of mortality, such as hypertension, diabetes, and coronary artery disease, in the elderly population. Additionally, the use of antithrombotic agents, either as monotherapy or in combination with other drugs, tends to increase with advancing age.[12–14] The risk of mortality following bleeding and perforation due to peptic ulcer disease also increases significantly with age. A study reported that 32.7% of 2,732 patients presenting with bleeding peptic ulcers were aged 80 years or older, with 71.2% of patients being 65 years or older. The 30-day mortality rate was 4.3% for patients younger than 65 years, compared to 16.9% for those aged 80 years or older.[15] In line with the findings of other studies, our investigation revealed that age is a predictive factor for mortality.

The findings of our study also showed a statistically significant decrease in mean systolic blood pressure and an increase in mean heart rate in non-surviving patients compared to survivors. Several previous studies have associated low blood pressure and increased heart rate with an elevated risk of mortality.[16-19] As demonstrated in similar studies, low systolic blood pressure and tachycardia were identified as significant factors influencing mortality.

The lowest mean Hb levels in survivors were higher, and their INR levels were lower than those of non-survivors. However, there was no statistically significant difference between the two groups in the degree of hemoglobin reduction during follow-up.

In previous studies, it was reported that 20% of patients with GI bleeding had an elevated INR requiring FFP

transfusion, and coagulopathy was associated with poor prognosis.[20-22]

The 2021 guidelines published by the European Society for Gastrointestinal Endoscopy (ESGE) recommended a restrictive ES transfusion strategy.[23,24] The results of our study indicated no statistically significant difference between surviving and non-surviving groups in terms of ES transfusion strategy. The Hb threshold for transfusion was 6.7 g/dL in non-surviving patients and 7.3 g/dL in surviving patients. In another study, it was reported that 90.5% of non-surviving patients and 53.1% of discharged patients received ES transfusions.[22] In patients with upper GI bleeding, ES transfusion may indicate recurrent bleeding and adverse clinical outcomes. Other studies have associated a high requirement for ES transfusion with an increased risk of rebleeding, independent of mortality. Studies have shown that ES transfusion is associated with increased mortality in patients hospitalized in the intensive care unit.[25-27] After admission to the intensive care unit, a restrictive transfusion strategy was implemented for the patients in accordance with guideline recommendations. In our study, both groups received transfusions following the same strategy, with more ES transfusions performed in the non-surviving group. However, no statistically significant difference was identified in transfusion rates between the two groups. Thus, ES transfusion does not constitute a predictor of mortality.

Several studies have reported a correlation between increased FFP transfusion and higher mortality risk.[28] In our study, FFP was transfused in 57.6% of non-surviving patients compared to 28.4% of surviving patients. Due to limited data, the relationship between the number of FFP units transfused and mortality risk could not be evaluated.

In our study, platelet transfusion was performed in only 11 patients across the entire cohort. Consequently, statistical evaluation was not conducted. In a retrospective cohort study, it was reported that the length of hospital stay was weakly associated with mortality.[31] In our study, no statistically significant difference was observed in the length of stay in the intensive care unit between the two groups.

The mortality rate in the patient group using NOACs was higher than in the groups using other antiaggregant or anticoagulant drugs. The second-highest mortality rate was observed in the group using ASA. The elevated mortality rate may be attributed to the prevalence of NOAC use among elderly patients and the heightened risk of NOACs-associated GI bleeding with advancing age. The mortality rates observed in patients treated with NOACs and warfarin were not significantly different from those observed in patients treated with ASA. The ASPREE study reported that ASA use increased the risk of serious GI bleeding by 60% in elderly patients, while low-dose ASA (75-325 mg) may increase the risk of non-fatal GI bleeding.[12] In a study by Flacker et al.,[32] the efficacy of apixaban was compared to low-dose ASA, demonstrating no statistically significant difference in GI bleeding between the two cohorts.

It is important to acknowledge several potential limitations of the present study. The first limitation is its retrospective observational design. Secondly, a significant number of patients hospitalized for gastrointestinal were excluded from the study due to inaccessible medical records. This resulted in a relatively small number of patients being included in the analysis.

Conclusion

In conclusion, the study found that the non-surviving patient group had a higher mean age, greater need for FFP transfusion, hemodynamic instability on admission, lower hemoglobin levels, and higher INR levels. No difference in mortality was observed between patients with and without anticoagulant or antiaggregant drug use. The predictive factors for mortality were identified as advanced age, FFP transfusion, shorter ICU hospitalization duration, elevated pulse rate, and reduced systolic blood pressure.

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