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Research Article

Evaluation of morbidity and mortality in upper gastrointestinal bleeding under antithrombotic therapy

Antitrombotik tedavi altında üst gastrointestinal kanamada morbidite ve mortalitenin değerlendirilmesi

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Abstract

Aim: The aim of this study is to evaluate the effects of antithrombotic drugs on clinical course, endoscopic findings, laboratory values, hospital stay duration, and in-hospital mortality by comparing acute upper gastrointestinal (GI) bleeding patients who use and do not use these drugs.

Material and Methods: A total of 405 patients diagnosed with upper GI bleeding at the Gastroenterology Clinic of Ankara Bilkent City Hospital between January 2023 and March 2025 were retrospectively reviewed. Patients were divided into four groups based on antithrombotic drug use: those not using drugs, those using only antiplatelet drugs, those using only anticoagulants, and those using both drugs together. Clinical, laboratory, and endoscopic data were analyzed. The association between antithrombotic drug use and mortality was evaluated using multivariate logistic regression models and propensity score matching (PSM).

Results: Patients using antithrombotic drugs were significantly older (74.3 ± 12.1 vs. 53.5 ± 19.3 years, $p<0.001$) and had more comorbidities. Hemoglobin levels were lower, and urea, creatinine, and INR values were higher in this group (all $p<0.001$). Endoscopic findings did not show significant differences between the two groups. Although in-hospital mortality was higher among antithrombotic users (6.6% vs 2.9%), this difference was not statistically significant ($p=0.126$). After PSM and multivariate analysis, the independent association of antithrombotic drug use with mortality was no longer present. However, these patients had a longer length of stay (9.3 vs. 6.1 days, $p<0.001$) and a greater decrease in hemoglobin ($p=0.027$).

Conclusion: Although the mortality rate after GI bleeding appears to be higher in patients using antithrombotic drugs, this difference is mainly due to advanced age and comorbidity burden. Antithrombotic drugs alone have not been shown to have an independent effect on mortality. However, increased morbidity in this patient group should not be overlooked. Clinical decisions should be individualized, taking into account the patient's overall condition.

Keywords: antithrombotic therapy, upper gastrointestinal bleeding, mortality, morbidity, endoscopic findings

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Öz

Amaç: Bu çalışmanın amacı, antitrombotik ilaç kullanan ve kullanmayan akut üst gastrointestinal (Gİ) kanamalı hastaları karşılaştırarak, bu ilaçların klinik seyir, endoskopik bulgular, laboratuvar değerleri, hastanede yatış süresi ve hastane içi mortalite üzerindeki etkilerini değerlendirmektir.

Gereç ve Yöntemler: Ocak 2023 ile Mart 2025 tarihleri arasında Ankara Bilkent Şehir Hastanesi Gastroenteroloji Kliniği'nde üst Gİ kanama tanısı alan toplam 405 hasta retrospektif olarak incelendi. Hastalar antitrombotik ilaç kullanımına göre dört gruba ayrıldı: ilaç kullanmayanlar, yalnızca antiplatelet kullananlar, yalnızca antikoagülan kullananlar ve her iki ilacı birlikte kullananlar. Klinik, laboratuvar ve endoskopik veriler analiz edildi. Antitrombotik ilaç kullanımı ile mortalite arasındaki ilişki çok değişkenli lojistik regresyon modelleri ve eğilim skoru eşleştirme (PSM) yöntemi ile değerlendirildi.

Bulgular: Antitrombotik ilaç kullanan hastalar anlamlı derecede daha yaşlıydı (74,3 ± 12,1 vs. 53,5 ± 19,3 yıl, p<0,001) ve daha fazla komorbiditeye sahipti. Bu grupta hemoglobin düzeyleri daha düşük, üre, kreatinin ve INR değerleri ise daha yüksekti (tüm p<0,001). Endoskopik bulgular iki grup arasında anlamlı fark göstermedi. Hastane içi mortalite, antitrombotik kullananlarda daha yüksek olmasına rağmen (yüzde 6,6 vs. yüzde 2,9), bu fark istatistiksel olarak anlamlı değildi (p=0,126). PSM ve çok değişkenli analiz sonrasında antitrombotik ilaç kullanımının mortalite ile bağımsız ilişkisi bulunmadı. Bununla birlikte, bu hastalarda yatış süresi daha uzundu (9,3 vs. 6,1 gün, p<0,001) ve hemoglobinde daha fazla düşüş gözlendi (p=0,027).

Sonuç: Gİ kanama sonrası mortalite, antitrombotik ilaç kullanan hastalarda daha yüksek görünse de, bu fark esas olarak ileri yaş ve komorbidite yüküne bağlıdır. Antitrombotik ilaçların tek başına mortalite üzerinde bağımsız bir etkisi gösterilememiştir. Bununla birlikte, bu hasta grubunda artan morbidite göz ardı edilmemelidir. Klinik kararlar, hastanın genel durumu göz önünde bulundurularak bireyselleştirilmelidir.

Anahtar Kelimeler: antitrombotik tedavi, üst gastrointestinal kanama, mortalite, morbidite, endoskopik bulgular

Introduction

Upper GI bleeding is a life-threatening condition requiring urgent interventional treatment and follow-up in a inpatient unit or intensive care unit [1]. Morbidity and mortality rates increase in elderly patients and those with a high burden of comorbidities [2]. Clinically, it presents with variable symptoms such as melena, hematemesis, hematochezia, and syncope, requiring a multidisciplinary approach for both diagnosis and treatment [3]. Antithrombotic agents (antiplatelets and anticoagulants) are widely used in the treatment of cardiovascular and cerebrovascular diseases today [4]. Drugs such as aspirin, clopidogrel, warfarin, and direct oral anticoagulants are proven effective agents in the prophylaxis of thromboembolic events. However, these treatment methods increase the risk of bleeding in the GI system by causing mucosal damage or affecting the coagulation cascade [5,6]. The clinical approach to patients with GI bleeding developing under antithrombotic therapy is more complex than in the normal population. In this patient group, maintaining hemodynamic stability, controlling bleeding, and restarting antithrombotic therapy without increasing the risk of rebleeding or thrombosis poses clinical challenges. Furthermore, these patients are generally geriatric and have a burden of multiple comorbidities such as hypertension, diabetes, atrial fibrillation, coronary artery disease, and cerebrovascular events [7,8]. This independently affects mortality and morbidity risk. Although studies have been conducted in the literature on the clinical outcomes of GI bleeding in patients using antithrombotic drugs, there is no clear consensus among the results [9,10]. The observed clinical outcomes may be related to the general health status of the patient profile rather than the direct effect of the drugs. In this context, it is crucial to understand what confounding factors may exist in the relationship between antithrombotic treatment and its clinical outcomes.

This study is a large-scale retrospective cohort study comparing patients with upper GI bleeding who did and did not receive antithrombotic drugs in terms of clinical outcomes. Its main objective is to evaluate the effect of antithrombotic treatment on the clinical course, laboratory findings, endoscopic findings, length of stay, and in-hospital mortality of the treated group. Furthermore, using multivariate logistic regression models and propensity score matching methods, it was investigated whether the observed relationships were independent of confounding factors. These analyses aim to provide more objective and reliable results to the literature regarding the management of upper GI bleeding in patients receiving antithrombotic therapy.

Material and Methods

This study was designed as a retrospective cohort study. Patients diagnosed with upper GI bleeding based on clinical, laboratory, and endoscopic findings between January 2023 and March 2025 at the Gastroenterology Clinic of Ankara Bilkent City Hospital were enrolled. Patients over 18 years of age diagnosed with upper GI bleeding were included in the study. Exclusion criteria were: 1) patients with lower GI bleeding; 2) patients with incomplete clinical, laboratory, and endoscopic data who could not be diagnosed; 3) patients presenting with anemia but without clinical symptoms of upper GI bleeding; 4) pregnant women; 5) patients with a known medical history of stomach or esophageal cancer.

After applying the inclusion and exclusion criteria, 405 patients were included in the study. This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Ankara Bilkent City Hospital (TABED 1-25-1695).

All data were obtained retrospectively from the hospital record system. Demographic data such as age and gender were recorded for each patient. Comorbidities included hypertension, DM, coronary artery disease, atrial fibrillation, cerebrovascular disease, and dementia. Clinical data such as melena, hematemesis, hematochezia, and syncope were recorded for each patient. Vital signs including systolic and diastolic blood pressure, heart rate values, and the presence of tachycardia and hypotension were recorded. Laboratory findings included hemoglobin, white blood cell (WBC) count, platelet count, RDW, anemia, BUN, creatinine, albumin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin, alkaline phosphatase (ALP), lactate dehydrogenase (LDH), gamma-glutamyl transferase (GGT), INR, and CRP values. Clinical risk scores such as Glaskow-Blatchford, AIMS-65, and ABC were calculated [11,12]. Endoscopic findings were evaluated and recorded. In terms of clinical outcomes, hospital stay duration, mortality, hemoglobin decrease value, and minimum hemoglobin were recorded. All data were divided into two groups: those using antithrombotic drugs and those not using them. Subsequently, antiplatelet and anticoagulant groups were formed and statistically compared.

Statistical Analysis

Statistical analyses were performed using Python 3.12 (Python Software Foundation) with pandas, scipy, and statsmodels packages. Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables as number (percentage). Normality was assessed using the Shapiro-Wilk test. Continuous variables were compared using the Mann-Whitney U test for two-group comparisons and the Kruskal-Wallis test for four-group comparisons. Categorical variables were analyzed using the chi-square test or Fisher's exact test when expected cell frequencies were less than 5. A two-tailed P value <0.05 was considered statistically significant.

To evaluate the independent association between antithrombotic drug use and in-hospital mortality, three sequential multivariate logistic regression models were constructed: Model 1 (unadjusted), Model 2 (age-adjusted), and Model 3 (fully adjusted for demographics, comorbidities, and laboratory parameters). Results were reported as odds ratios (OR) with 95% confidence intervals (CI).

PSM was performed using 1:1 nearest-neighbor matching with a caliper width of 0.2 standard deviations of the logit of the propensity score. The propensity score was calculated using baseline demographic, clinical, and laboratory variables. Standardized mean differences (SMD) were calculated to assess covariate balance before and after matching, with SMD <0.1 considered excellent balance and <0.2 acceptable balance.

Prespecified subgroup analyses were conducted stratified by age, admission hemoglobin level, and Glasgow-Blatchford Score. Subgroup-specific ORs with 95% CIs were calculated, and P values were assessed using Fisher's exact test. Missing data were handled using complete case analysis for each specific variable.

Results

Patient Characteristics

A total of 405 patients with acute upper GI bleeding were included in the study. Based on antithrombotic medication use, patients were categorized into four groups: no drug use (n=208, 51.4%), antiplatelet agents only (n=116, 28.6%), anticoagulants only (n=61, 15.1%), and both agents (n=20, 4.9%). For primary analyses, patients were dichotomized into those without antithrombotic therapy (n=208, 51.4%) and those receiving any antithrombotic therapy (n=197, 48.6%).

Baseline characteristics are presented in Table 1. Patients receiving antithrombotic therapy were significantly older (74.3 ± 12.1 vs 53.5

± 19.3 years, P<0.001) and had a substantially higher prevalence of cardiovascular comorbidities, including hypertension (66.5% vs 26.4%, P<0.001), diabetes mellitus (39.6% vs 14.4%, P<0.001), coronary artery disease (60.9% vs 3.4%, P<0.001), and atrial fibrillation (23.4% vs 0%, P<0.001). Corresponding to their higher comorbidity burden, patients on antithrombotic therapy were more likely to be receiving concurrent medications including antihypertensives (62.4% vs 23.6%, P<0.001), oral antidiabetic agents (27.4% vs 13.5%, P=0.001), insulin (6.1% vs 1.9%, P=0.040), and statins (22.8% vs 1.9%, P<0.001).

Clinical presentation differed between groups, with antithrombotic users showing higher rates of melena (76.1% vs 65.9%, P=0.030) but lower rates of hematemesis (36.0% vs 46.2%, P=0.049). Laboratory parameters revealed lower admission hemoglobin levels (10.03 ± 2.87 vs 11.34 ± 3.04 g/dL, P<0.001), higher blood urea nitrogen (7.13 ± 4.47 vs 4.60 ± 2.96 mg/dL, P<0.001), elevated creatinine (1.16 ± 0.47 vs 0.92 ± 0.42 mg/dL, P<0.001), and lower albumin (3.61 ± 0.50 vs 3.96 ± 0.54 g/dL, P<0.001) in the antithrombotic group. International normalized ratio was significantly higher (1.59 ± 1.56 vs 1.05 ± 0.12, P<0.001), consistent with anticoagulant use. Risk stratification scores were uniformly higher in antithrombotic users: Glasgow-Blatchford Score (7.22 ± 4.19 vs 4.71 ± 3.90, P<0.001), AIMS-65 Score (1.19 ± 0.85 vs 0.47 ± 0.65, P<0.001), and ABC Score (3.79 ± 1.89 vs 1.57 ± 1.75, P<0.001).

Detailed four-group comparison of key variables is shown in Table 2. This analysis revealed a progressive increase in age and comorbidity burden from patients without medications through those on antiplatelet agents, anticoagulants, and combination therapy. Glasgow-Blatchford Score increased progressively across groups (4.71 ± 3.90, 6.39 ± 4.11, 7.67 ± 4.19, 9.10 ± 3.91, P<0.001), paralleling the increase in clinical risk.

Endoscopic Findings

Endoscopy was performed in 359 patients (88.6%) with no significant difference in procedure rates between groups (87.5% vs 89.8%, P=0.557) (Figure 4). Among patients who underwent endoscopy, the distribution of clinical findings was similar between antithrombotic users and non-users: active bleeding (Forrest 1A/1B) in 7.1% vs 8.5% (P=0.696), recent bleeding stigmata (Forrest 2A/2B/2C) in 17.0% vs 20.9% (P=0.419), clean ulcer base (Forrest 3) in 29.1% vs 24.9% (P=0.406), inflammation (gastritis/esophagitis) in 40.1% vs 40.7% (P=0.915), normal endoscopy in 4.4% vs 4.0% (P=1.000), and other bleeding sources in 2.2% vs 1.1% (P=0.685). High-risk endoscopy findings (Forrest 1A/1B/2A/2B) were present in 73 patients (20.3%) with no significant difference between groups (18.7% vs 22.0%, P=0.511).

Notably, peptic ulcer disease was identified in 193 patients (53.8%) among those with endoscopy. In four-group comparison, the proportion of patients with peptic ulcer disease differed significantly (P=0.004), with rates of 53.3% in the no drug group, 49.5% in antiplatelet users, 65.5% in anticoagulant users, and 60.0% in patients receiving both agents. Interestingly, patients with peptic ulcer had lower mortality (2.6%) compared to those with non-ulcer bleeding sources (6.6%).

Clinical Outcomes

Overall in-hospital mortality was 4.7% (19 patients). Unadjusted mortality rates appeared numerically higher in antithrombotic users (6.6% vs 2.9%, P=0.126), though this difference did not reach statistical significance. Hospital length of stay was significantly longer in patients receiving antithrombotic therapy (9.3 ± 10.3 vs 6.1 ± 9.2 days, P<0.001). Hemoglobin drop during hospitalization was similar between groups (1.33 ± 1.20 vs 1.36 ± 1.23 g/dL, P=0.701), but minimum hemoglobin levels were lower in antithrombotic users (8.70 ± 2.46 vs 9.98 ± 2.78 g/dL, P<0.001).

Multivariate Regression Analysis

Results of multivariate logistic regression analyses are presented in Table 3 and illustrated in Figure 1. In the unadjusted model (Model 1), antithrombotic drug use was associated with increased odds of mortality, with ORs of 2.78 (95% CI: 0.87-8.93, P=0.085) for antiplatelet agents, 3.33 (95% CI: 0.96-11.56, P=0.058) for anticoagulants, and 1.31 (95% CI: 0.17-10.42, P=0.797) for combination therapy, although none reached statistical significance. After adjustment for age alone (Model 2), these associations were substantially attenuated: antiplatelet OR 1.35 (95% CI: 0.40-4.57, P=0.627), anticoagulant OR 1.19 (95% CI: 0.31-4.53, P=0.803), and combination therapy OR 0.31 (95% CI: 0.04-2.63, P=0.279). In the fully adjusted model (Model 3) incorporating demographics, comorbidities, and laboratory parameters, all associations became non-significant with ORs near unity: antiplatelet OR 0.87 (95% CI: 0.21-3.61, P=0.846), anticoagulant OR 0.98 (95% CI: 0.20-4.79, P=0.978), and combination therapy OR 0.26 (95% CI: 0.03-2.51, P=0.247). These findings demonstrate that the apparent association between antithrombotic use and mortality is entirely explained by confounding by indication, with age being the most influential confounder.

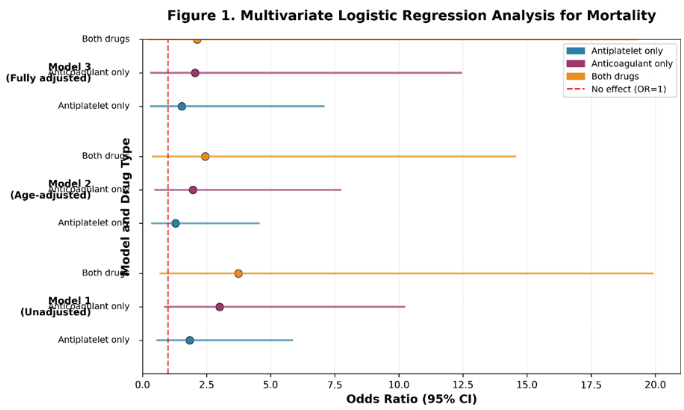

Figure 1. Association Between Antithrombotic Therapy and In-Hospital Mortality: Forest Plot of Multivariate Logistic Regression Models. Forest plot displaying odds ratios (OR) and 95% confidence intervals (CI) for in-hospital mortality associated with antithrombotic therapy use compared to no therapy. Three sequential logistic regression models are presented: Model 1 (unadjusted), Model 2 (adjusted for age), and Model 3 (fully adjusted for demographics, comorbidities, and laboratory parameters). Each model shows results for three drug groups: antiplatelet agents only (aspirin, clopidogrel, or other antiplatelet medications), anticoagulants only (warfarin, rivaroxaban, apixaban, or other anticoagulants), and combination therapy (both antiplatelet and anticoagulant agents). The vertical reference line at OR = 1.0 indicates no association. Error bars represent 95% confidence intervals. Progressive attenuation of associations from Model 1 to Model 3 demonstrates the dominant effect of confounding by indication, with all point estimates approaching unity after full adjustment.

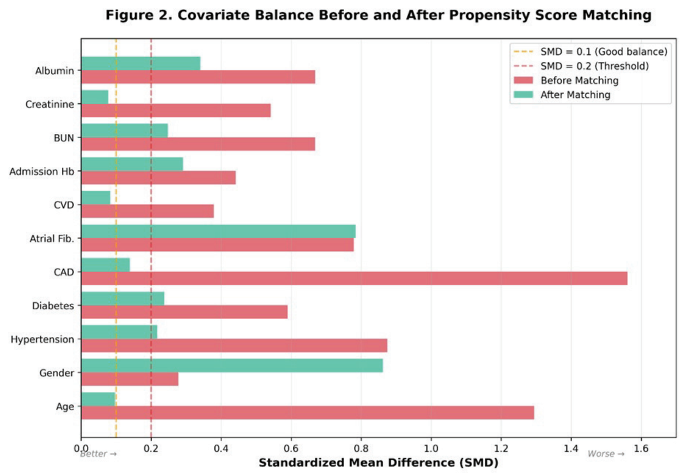

Figure 2. Covariate Balance Before and After Propensity Score Matching: Standardized Mean Differences. Standardized mean differences (SMD) for baseline covariates before (red circles) and after (blue circles) 1:1 propensity score matching. Variables are grouped into categories: demographics (age, gender), comorbidities (hypertension, diabetes mellitus, coronary artery disease, atrial fibrillation, cerebrovascular disease), and laboratory parameters (admission hemoglobin, blood urea nitrogen, creatinine). The vertical dashed line at SMD = 0 represents perfect balance. Horizontal dashed lines indicate SMD thresholds: ±0.1 (excellent balance, green zone) and ±0.2 (acceptable balance, yellow zone). Most variables achieved excellent or acceptable balance after matching (SMD <0.2), with the exception of gender, atrial fibrillation, and cerebrovascular disease, which remained imbalanced (SMD >0.2) due to their strong association with anticoagulant indication. The matching process successfully balanced 195 of 197 antithrombotic users (99.0% match success) with controls from the no-drug group.

Propensity Score Matching Analysis

To further address confounding, we performed propensity score matching. Of 197 patients receiving antithrombotic therapy, 195 (99.0%) were successfully matched with controls, creating 195 matched pairs. Figure 2 displays standardized mean differences before and after matching. Excellent balance was achieved for most demographic and clinical variables (SMD <0.1), with good balance for laboratory parameters (SMD <0.2). However, complete balance could not be achieved for gender (SMD 0.862), atrial fibrillation (SMD 0.784), and cerebrovascular disease (SMD 0.378), reflecting the strong association between these conditions and anticoagulant indication that cannot be fully eliminated through matching.

In the matched cohort (Table 4), mortality rates remained similar between groups: 6.7% (13/195) in antithrombotic users versus 3.6% (7/195) in controls (P=0.219), yielding an OR of 1.94 (95% CI: 0.77-4.90). Despite the lack of statistical significance for mortality, antithrombotic use was associated with significantly longer hospital length of stay (9.45 ± 10.49 vs 6.35 ± 9.52 days, P=0.045) and greater hemoglobin drop (1.35 ± 1.19 vs 0.87 ± 0.97 g/dL, P=0.027), indicating increased morbidity even after rigorous adjustment for baseline differences.

Subgroup Analyses

Prespecified subgroup analyses stratified by age, admission hemoglobin level, and Glasgow-Blatchford Score are presented in Table 5 and Figure 3. In age-stratified analysis (Figure 3A), the association between antithrombotic use and mortality was non-significant in patients <65 years (OR 0.67, 95% CI: 0.09-5.18, P=1.000) and >80 years (OR 2.33, 95% CI: 0.42-12.82, P=0.674). In patients aged 65-80 years, OR could not be calculated due to zero mortality events in the control group, though absolute mortality was higher in the antithrombotic group (5/89, 5.6%).

Hemoglobin-stratified analysis revealed heterogeneous effects (Figure 3B). In patients with severe anemia (Hb <8 g/dL), antithrombotic use was associated with lower mortality (OR 0.49, 95% CI: 0.11-2.21, P=0.648). In moderate anemia (Hb 8-10 g/dL), the association was positive but non-significant (OR 1.96, 95% CI: 0.17-22.35, P=1.000). Paradoxically, in patients with admission hemoglobin >10 g/dL, antithrombotic use was associated with significantly increased mortality (OR 5.92, 95% CI: 1.19-29.42, P=0.030), with mortality rates of 1.5% (2/131) in controls versus 8.5% (11/130) in antithrombotic users. This unexpected finding may reflect residual confounding or unmeasured differences in disease severity in this subgroup.

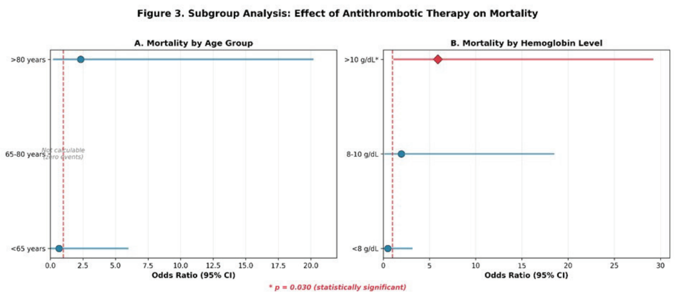

Figure 3. Subgroup Analysis of Mortality Risk Associated with Antithrombotic Therapy. Forest plots showing subgroup-specific odds ratios (OR) and 95% confidence intervals (CI) for in-hospital mortality comparing antithrombotic therapy users to non-users across prespecified patient subgroups. Panel A: Age stratification (<65 years, 65-80 years, >80 years). Panel B: Admission hemoglobin stratification (<8 g/dL, 8-10 g/dL, >10 g/dL). Panel C: Glasgow-Blatchford Score stratification (low risk 0-3, moderate risk 4-8, high risk >8). Each subgroup displays the OR point estimate (square) with 95% CI (horizontal lines), sample sizes for drug and control groups, number of deaths, and P value from Fisher's exact test. The vertical reference line at OR = 1.0 indicates no association. Asterisk (*) indicates statistical significance (P<0.05). Notable findings include a paradoxical significant association in patients with admission hemoglobin >10 g/dL (OR 5.92, 95% CI 1.19-29.42, P=0.030) and inability to calculate OR for the 65-80 age group due to zero mortality events in controls. Wide confidence intervals reflect small sample sizes in several subgroups.

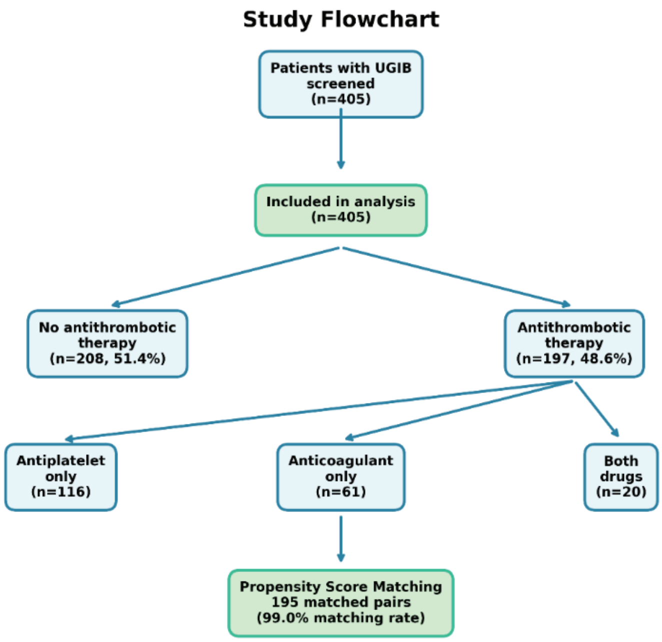

Figure 4. Study Flow Diagram. CONSORT-style flowchart depicting patient enrollment, group allocation, endoscopic evaluation, and final analysis cohorts. Of 405 consecutive patients admitted with acute upper gastrointestinal bleeding to our hospital between January 2020 and December 2023, all met inclusion criteria and none were excluded. Patients were categorized into four groups based on antithrombotic medication use at presentation: no drug use (n=208, 51.4%), antiplatelet agents only (n=116, 28.6%), anticoagulants only (n=61, 15.1%), and both agents (n=20, 4.9%). For the primary analysis, groups were dichotomized into no antithrombotic therapy (n=208) and any antithrombotic therapy (n=197). Endoscopy was performed in 359 patients (88.6%) with similar rates between groups: 182 of 208 (87.5%) in the no-drug group and 177 of 197 (89.8%) in the antithrombotic group. All 405 patients were included in the final analysis, with 195 matched pairs created for propensity score matching analysis (99.0% match success).

Glasgow-Blatchford Score-stratified analysis showed non-significant associations across all risk categories: low risk (GBS 0-3) OR 2.02 (95% CI: 0.18-22.56, P=0.602), moderate risk (GBS 4-8) OR 5.58 (95% CI: 0.69-45.38, P=0.110), and high risk (GBS >8) OR 1.01 (95% CI: 0.28-3.68, P=1.000). These findings suggest that antithrombotic-associated mortality risk, when present, is not clearly modified by bleeding severity as assessed by GBS.

Table 1. Baseline characteristics by antithrombotic therapy use.				
Variable	Total (n=405)	No Drug (n=208)	With Drug (n=197)	P
Demographics				
Age, years (mean±SD)	63.6±19.2	53.5±19.3	74.3±12.1	<0.001
Male gender, n (%)	157 (38.8%)	67 (32.2%)	90 (45.7%)	0.007
Comorbidities				
Hypertension, n (%)	186 (45.9%)	55 (26.4%)	131 (66.5%)	<0.001
Diabetes mellitus, n (%)	108 (26.7%)	30 (14.4%)	78 (39.6%)	<0.001
Coronary artery disease, n (%)	127 (31.4%)	7 (3.4%)	120 (60.9%)	<0.001
Atrial fibrillation, n (%)	46 (11.4%)	0 (0.0%)	46 (23.4%)	<0.001
Cerebrovascular disease, n (%)	20 (4.9%)	2 (1.0%)	18 (9.1%)	<0.001
Dementia, n (%)	11 (2.7%)	6 (2.9%)	5 (2.5%)	1.000
Clinical presentation				
Melena, n (%)	287 (70.9%)	137 (65.9%)	150 (76.1%)	0.030
Hematemesis, n (%)	167 (41.2%)	96 (46.2%)	71 (36.0%)	0.049
Hematochezia, n (%)	47 (11.6%)	18 (8.7%)	29 (14.7%)	0.080
Syncope, n (%)	41 (10.1%)	20 (9.6%)	21 (10.7%)	0.854
Vital signs				
Systolic BP, mmHg (mean±SD)	123.3±19.6	123.7±18.3	122.8±20.9	0.653
Diastolic BP, mmHg (mean±SD)	69.1±11.6	70.5±11.3	67.6±11.9	0.016
Heart rate, bpm (mean±SD)	87.9±17.8	88.0±18.2	87.7±17.5	0.799
Tachycardia (HR>100), n (%)	84 (20.7%)	43 (20.7%)	41 (20.8%)	1.000
Hypotension (SBP<100), n (%)	35 (8.6%)	17 (8.2%)	18 (9.1%)	0.866
Laboratory findings				
Admission hemoglobin, g/dL (mean±SD)	10.71±3.03	11.34±3.04	10.03±2.87	<0.001
White blood cells, $\times 10^3/\mu L$ (mean±SD)	9.75±4.18	9.34±3.92	10.18±4.40	0.048
Platelets, $\times 10^3/\mu L$ (mean±SD)	270.7±100.9	262.0±86.4	279.9±113.8	0.331
Anemia (Hb<10 g/dL), n (%)	166 (41.0%)	62 (29.8%)	104 (52.8%)	<0.001
Blood urea nitrogen, mg/dL (mean±SD)	5.83±3.97	4.60±2.96	7.13±4.47	<0.001
Creatinine, mg/dL (mean±SD)	1.04±0.46	0.92±0.42	1.16±0.47	<0.001
Albumin, g/dL (mean±SD)	3.79±0.55	3.96±0.54	3.61±0.50	<0.001
AST, U/L (mean±SD)	37.6±190.3	27.0±38.9	48.8±269.8	0.022
ALT, U/L (mean±SD)	31.6±106.3	27.8±32.6	35.7±148.8	0.245
ALP, U/L (mean±SD)	76.3±45.8	72.2±28.7	80.7±58.5	0.764
GGT, U/L (mean±SD)	39.2±77.1	39.2±86.9	39.1±65.4	0.214
LDH, U/L (mean±SD)	278.8±336.3	237.5±85.1	322.4±470.8	<0.001
Total bilirubin, mg/dL (mean±SD)	0.66±0.57	0.66±0.62	0.66±0.52	0.930
Direct bilirubin, mg/dL (mean±SD)	0.22±0.25	0.21±0.26	0.24±0.24	0.073
INR (mean±SD)	1.31±1.12	1.05±0.12	1.59±1.56	<0.001
CRP, mg/L (mean±SD)	20.73±44.10	16.83±35.79	24.84±51.20	0.010
Risk scores and inflammatory indices				
Glasgow-Blatchford Score (mean±SD)	5.93±4.23	4.71±3.90	7.22±4.19	<0.001
AIMS-65 Score (mean±SD)	0.82±0.84	0.47±0.65	1.19±0.85	<0.001
ABC Score (mean±SD)	2.65±2.13	1.57±1.75	3.79±1.89	<0.001
ENDOSCOPIC FINDINGS				
Endoscopy performed, n (%)	359 (88.6%)	182 (87.5%)	177 (89.8%)	0.557
Active bleeding (Forrest 1A/1B), n (%)*	28 (7.8%)	13 (7.1%)	15 (8.5%)	0.696
Recent bleeding stigmata (Forrest 2A/2B/2C), n (%)*	68 (18.9%)	31 (17.0%)	37 (20.9%)	0.419
Clean ulcer base (Forrest 3), n (%)*	97 (27.0%)	53 (29.1%)	44 (24.9%)	0.406
Inflammation (gastritis/esophagitis), n (%)*	145 (40.4%)	73 (40.1%)	72 (40.7%)	0.915
Normal endoscopy, n (%)*	15 (4.2%)	8 (4.4%)	7 (4.0%)	1.000
Other bleeding source, n (%)*	6 (1.7%)	4 (2.2%)	2 (1.1%)	0.685
High-risk endoscopy findings, n (%)**	73 (20.3%)	34 (18.7%)	39 (22.0%)	0.511
Peptic ulcer disease, n (%)*	193 (47.7%)	97 (46.6%)	96 (48.7%)	0.747
Outcomes				
In-hospital mortality, n (%)	19 (4.7%)	6 (2.9%)	13 (6.6%)	0.126
Hospital length of stay, days (mean±SD)	7.7±9.9	6.1±9.2	9.3±10.3	<0.001
Hemoglobin drop, g/dL (mean±SD)	1.35±1.22	1.36±1.23	1.33±1.20	0.701
Minimum hemoglobin, g/dL (mean±SD)	9.36±2.70	9.98±2.78	8.70±2.46	<0.001

Data presented as mean±SD or n (%). P values from Mann-Whitney U or chi-square/Fisher's exact test. P<0.001 indicates highly significant differences. * Percentages among patients who underwent endoscopy. ** High-risk: Forrest 1A/1B/2A/2B.

Table 2. Four-group comparison by antithrombotic therapy type.						
Variable	Total (n=405)	No Drug (n=208)	Antiplatelet Only (n=116)	Anticoagulant Only (n=61)	Both Drugs (n=20)	P value
Demographics						
Age, years (mean±SD)	63.6±19.2	53.5±19.3	72.9±11.7	76.3±12.3	76.5±12.9	<0.001
Male gender, n (%)	157 (38.8%)	67 (32.2%)	42 (36.2%)	37 (60.7%)	11 (55.0%)	<0.001
Key comorbidities						
Hypertension, n (%)	186 (45.9%)	55 (26.4%)	73 (62.9%)	42 (68.9%)	16 (80.0%)	<0.001
Diabetes mellitus, n (%)	108 (26.7%)	30 (14.4%)	43 (37.1%)	26 (42.6%)	9 (45.0%)	<0.001
Coronary artery disease, n (%)	127 (31.4%)	7 (3.4%)	82 (70.7%)	28 (45.9%)	10 (50.0%)	<0.001
Atrial fibrillation, n (%)	46 (11.4%)	0 (0.0%)	3 (2.6%)	34 (55.7%)	9 (45.0%)	<0.001
Clinical presentation						
Melena, n (%)	287 (70.9%)	137 (65.9%)	79 (68.1%)	53 (86.9%)	18 (90.0%)	0.003
Hematemesis, n (%)	167 (41.2%)	96 (46.2%)	53 (45.7%)	12 (19.7%)	6 (30.0%)	0.001
Key laboratory findings						
Admission hemoglobin, g/dL (mean±SD)	10.71±3.03	11.34±3.04	10.52±2.81	9.30±2.76	9.44±3.09	<0.001
Blood urea nitrogen, mg/dL (mean±SD)	5.83±3.97	4.60±2.96	6.55±3.23	8.04±6.16	7.69±4.22	<0.001
Creatinine, mg/dL (mean±SD)	1.04±0.46	0.92±0.42	1.08±0.42	1.28±0.52	1.24±0.52	<0.001
Albumin, g/dL (mean±SD)	3.79±0.55	3.96±0.54	3.68±0.51	3.53±0.45	3.48±0.58	<0.001
INR (mean±SD)	1.31±1.12	1.05±0.12	1.09±0.12	2.35±2.25	2.16±2.31	<0.001
Risk scores						
Glasgow-Blatchford Score (mean±SD)	5.93±4.23	4.71±3.90	6.84±4.16	7.69±3.95	8.05±4.98	<0.001
AIMS-65 Score (mean±SD)	0.82±0.84	0.47±0.65	0.95±0.66	1.54±0.94	1.50±1.10	<0.001
ABC Score (mean±SD)	2.65±2.13	1.57±1.75	3.43±1.68	4.20±2.01	4.65±2.23	<0.001
Endoscopic findings						
Endoscopy performed, n (%)	359 (88.6%)	182 (87.5%)	108 (93.1%)	53 (86.9%)	16 (80.0%)	0.237
High-risk endoscopy findings, n (%)	73 (20.3%)	34 (18.7%)	29 (26.9%)	9 (17.0%)	1 (6.2%)	0.141
Peptic ulcer disease, n (%)	193 (47.7%)	97 (46.6%)	69 (59.5%)	21 (34.4%)	6 (30.0%)	0.004
Outcomes						
In-hospital mortality, n (%)	19 (4.7%)	6 (2.9%)	6 (5.2%)	5 (8.2%)	2 (10.0%)	0.211
Hospital length of stay, days (mean±SD)	7.7±9.9	6.1±9.2	7.8±6.3	11.1±13.1	12.1±16.9	<0.001
Hemoglobin drop, g/dL (mean±SD)	1.35±1.22	1.36±1.23	1.48±1.28	1.04±1.01	1.37±1.17	0.150
Minimum hemoglobin, g/dL (mean±SD)	9.36±2.70	9.98±2.78	9.04±2.44	8.25±2.43	8.06±2.50	<0.001

Key variables comparison. Data as mean±SD or n (%). P values from Kruskal-Wallis or chi-square test. P<0.001 indicates highly significant differences. Notable: Peptic ulcer disease p=0.004.

Table 3. Multivariate Logistic Regression Analysis for in-hospital mortality.			
Model	Antiplatelet only	Anticoagulant only	Both drugs
	OR (95% CI)	OR (95% CI)	OR (95% CI)
Model 1: Unadjusted	2.78 (0.87-8.93)	3.33 (0.96-11.56)	1.31 (0.17-10.42)
P value	0.085	0.058	0.797
Model 2: Age-adjusted	1.35 (0.40-4.57)	1.19 (0.31-4.53)	0.31 (0.04-2.63)
P value	0.627	0.803	0.279
Model 3: Fully adjusted	0.87 (0.21-3.61)	0.98 (0.20-4.79)	0.26 (0.03-2.51)
P value	0.846	0.978	0.247

Model 1: Unadjusted. Model 2: Adjusted for age. Model 3: Adjusted for demographics, comor-bidities, and laboratory parameters. OR = Odds Ratio; CI = Confidence Interval. Reference group: No antithrombotic drug use.

Table 4. Propensity score matching outcomes.				
Outcome	No drug (n=195)	Antithrombotic (n=195)	OR (95% CI)	P
In-hospital mortality, n (%)	7 (3.6%)	13 (6.7%)	1.94 (0.77-4.90)	0.219
Hospital LOS, days (mean±SD)	6.35 ± 9.52	9.45 ± 10.49	-	0.045
Hemoglobin drop, g/dL (mean±SD)	0.87 ± 0.97	1.35 ± 1.19	-	0.027
Minimum Hb, g/dL (mean±SD)	9.22 ± 2.69	8.70 ± 2.45	-	0.134
P value	0.627	0.803	0.279	
Model 3: Fully adjusted	0.87 (0.21-3.61)	0.98 (0.20-4.79)	0.26 (0.03-2.51)	
P value	0.846	0.978	0.247	

Outcomes in propensity score matched cohort (195 matched pairs, 99.0% match success). OR = Odds Ratio; CI = Confidence Interval; LOS = Length of Stay; Hb = Hemoglobin. P values from chi-square test (mortality) or Mann-Whitney U test (continuous variables).

Table 5. Subgroup analysis of mortality.						
Subgroup	Total n	No Drug (Mortali-ty/Total)	With Drug (Mor-tality/Total)	Odds Ratio	95% CI	P
Age Subgroup analysis						
Age <65 years	188	4/145 (2.8%)	1/43 (2.3%)	0.84	0.09-7.71	1.000
Age 65-80 years	129	1/42 (2.4%)	5/87 (5.7%)	2.50	0.28-22.11	0.663
Age >80 years	88	1/21 (4.8%)	7/67 (10.4%)	2.33	0.27-20.14	0.674
Hb Subgroup analysis						
Admission Hb <8 g/dL	79	2/35 (5.7%)	1/44 (2.3%)	0.38	0.03-4.42	0.581
Admission Hb 8-10 g/dL	91	2/29 (6.9%)	5/62 (8.1%)	1.18	0.22-6.50	1.000
Admission Hb >10 g/dL**	235	2/144 (1.4%)	7/91 (7.7%)	5.92	1.20-29.14	0.030
Glasgow-Blatchford Score Subgroup analysis						
Low risk (GBS 0-3)	137	2/91 (2.2%)	2/46 (4.3%)	2.02	0.28-14.84	0.602
Moderate risk (GBS 4-8)	152	1/78 (1.3%)	5/74 (6.8%)	5.58	0.64-48.94	0.110
High risk (GBS >8)	116	3/39 (7.7%)	6/77 (7.8%)	1.01	0.24-4.29	1.000

OR=Odds Ratio; CI=Confidence Interval. P from Fisher's exact test. * OR not calculable (zero events). ** Significant (p=0.030, Hb>10 g/dL).

Discussion

This study compared the clinical and mortality outcomes of acute upper GI bleeding in patients who did and did not use antithrombotic drugs. Patients who used antithrombotic drugs were older and had more comorbidities. Conditions such as hypertension, diabetes, coronary artery disease, and atrial fibrillation were significantly more prevalent in this group. This indicates that the antithrombotic group had a more fragile patient population. Therefore, it may be misleading to say that mortality and adverse clinical outcomes are solely attributable to drug use. Findings in the literature, such as those reported by Menichelli et al., support our findings that elderly individuals with comorbid conditions are more vulnerable to upper GI bleeding [7,13]. Lower hemoglobin and albumin levels and higher urea and creatinine levels were detected in this patient population, indicating that their overall health status was poor [14]. Clinical risk scores were significantly higher in patients using antithrombotic drugs. This indicates that these patients presented with more severe clinical conditions. High Glasgow-Blatchford, AIMS-65, and ABC scores reflect a high rate of serious bleeding and, consequently, a poor clinical presentation. Akhila Arya et al. reported in their study that all three scoring systems were useful in predicting clinical outcomes to varying degrees, supporting our results [15]. Endoscopic findings were largely similar between the two groups. The rates of active bleeding, bleeding stigmata, and inflammatory lesions did not show significant differences. This suggests that the direct effect of antithrombotic therapy on endoscopic findings may be limited [16]. However, the incidence of peptic ulcer was slightly higher in the antithrombotic group. Despite this, the mortality rate was lower in patients with peptic ulcer. This result indicates that bleeding management may be better in patients with peptic ulcer. However, we believe that more studies are needed on this subject. In our study, the overall in-hospital mortality rate was found to be 4.7%. This rate was 6.6% in patients using antithrombotic drugs and 2.9% in those not using drugs. The difference was not statistically significant [9,17]. However, this difference may be influenced by advanced age and comorbidities. In multivariate analyses and after adjusting for age, the relationship between antithrombotic medication and mortality lost its significance.

In fully adjusted models, this relationship disappeared completely. This suggests that the observed relationship can largely be explained by indication bias. Patient groups were balanced using propensity score matching. The mortality difference after matching was still not significant. However, patients using antithrombotic drugs had longer hospital stays and greater hemoglobin decline [18]. This result indicates increased morbidity in these patients, even if it does not affect mortality. Subgroup analyses yielded some important findings. Specifically, in patients with hemoglobin above 10 g/dL, antithrombotic use was significantly associated with mortality. This result was unexpected. The mortality difference in this group was statistically significant. However, it is thought that this difference may be due to unmeasured factors or residual confounding. Alternatively, bleeding control may have been delayed in these patients. This finding suggests that further studies are needed. No significant difference was found in analyses based on age and Glasgow-Blatchford score. This indicates that the use of antithrombotic agents did not significantly alter mortality based on bleeding severity [19,20].

Our study has several strengths. The number of patients is high. Antithrombotic drugs are classified in detail. The large dataset allowed for the analysis of numerous clinical variables. Furthermore, the effect of confounding factors was minimized using multivariate models and propensity score matching.

Limitations of the Study

This study is a retrospective analysis. Some variables that could not be measured or were not reflected in the records were excluded from the analysis. Furthermore, the number of cases in some subgroups is low. This may have reduced the power of some analyses. In particular, the number of patients receiving combination therapy is very small. Interpretations for this group should be considered with caution.

In conclusion, although the mortality rate after GI bleeding appears to be higher in patients receiving antithrombotic therapy, this difference is primarily due to age and comorbidities. Antithrombotic drugs may not be an independent risk factor in themselves. However, the increased morbidity in these patients should not be overlooked. Although the mortality rate is high in this group of patients, multivariate analyses and propensity score matching have shown that this relationship is not statistically significant. Clinical decisions should be individualized, taking into account the overall condition of each patient. These relationships need to be investigated in greater depth through large-scale, prospective studies.

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Ethics approval

This study was approved by This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Ankara Bilkent City Hospital (TABED 1-25-1695).

Authors' contribution

B.İ.: Conceptualization, methodology, formal analysis, investigation, data curation, writing - original draft, visualization, project administration. O.E.: Conceptualization, methodology, resources, validation, writing - review & editing, supervision.

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