

Admission Creatinine, Not Anticoagulant Class, Predicts In-Hospital Mortality in Anticoagulated Patients With Upper Gastrointestinal Bleeding

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Abstract

Background

Direct oral anticoagulants (DOACs) have largely replaced vitamin K antagonists and are associated with modestly higher rates of gastrointestinal-specific bleeding than warfarin. Whether the class of anticoagulant influences the in-hospital trajectory of an established upper gastrointestinal bleeding (UGIB) hospitalization, after adjustment for patient-level prognostic factors, remains poorly characterized. We compared in-hospital outcomes across anticoagulant classes and sought independent predictors of in-hospital mortality.

Methods

We conducted a retrospective multicenter cohort study of adults aged 18–89 years admitted with UGIB across the Northwell Health system from January 2019 through January 2024. UGIB was identified by ICD-10 codes with chart confirmation of a bleeding source proximal to the ligament of Treitz. The exposure was outpatient anticoagulant class at admission (DOAC, heparin product, or warfarin). The primary outcome was in-hospital all-cause mortality; secondary outcomes were intensive care unit (ICU) admission, length of stay (LOS), therapeutic endoscopic intervention, and 30-day all-cause readmission. Continuous variables were compared with the Kruskal–Wallis test and categorical variables with chi-square or Fisher exact tests. Univariable predictors of mortality were screened at $p < 0.10$, and a multivariable logistic regression was constrained to two predictors per the events-per-variable rule, with anticoagulant class forced into the model. Analyses used SAS 9.4.

Results

Of 2,009 UGIB admissions, 303 (15.1%) had documented outpatient anticoagulant exposure: 240 (79.2%) DOAC, 40 (13.2%) heparin product, and 23 (7.6%) warfarin. The groups were elderly and comparable in age, sex, and comorbidity burden. In-hospital mortality occurred in 22 patients (7.3%) and did not differ by class (DOAC 7.5%, heparin 5.0%, warfarin 8.7%; $p = 0.83$). ICU admission ($p = 0.27$), LOS ($p = 0.14$), endoscopic intervention ($p = 0.66$), and 30-day readmission ($p = 1.00$) were similarly distributed. In the multivariable model, anticoagulant class was not associated with mortality ($p = 0.92$), whereas each 1 mg/dL increment in admission serum creatinine was associated with a 50% relative increase in the odds of in-hospital death (adjusted odds ratio 1.50, 95% confidence interval 1.02–2.20; $p = 0.041$). The model demonstrated acceptable discrimination (c-statistic 0.62) and calibration (Hosmer–Lemeshow $p = 0.82$).

Conclusion

Among anticoagulated patients hospitalized with UGIB, anticoagulant class did not independently predict any in-hospital outcome, whereas admission creatinine independently predicted mortality. Renal function on admission may be a more clinically actionable prognostic marker than the specific anticoagulant class and warrants prospective validation within UGIB risk-stratification frameworks.

Introduction

Direct oral anticoagulants (DOACs) have largely supplanted vitamin K antagonists for stroke prophylaxis in atrial fibrillation and for the treatment of venous thromboembolism. Pivotal randomized trials and large pharmacoepidemiologic cohorts have established that DOAC use carries modestly higher rates of gastrointestinal-specific bleeding than warfarin, with apixaban demonstrating the most favorable profile and rivaroxaban and high-dose dabigatran the least favorable.^{1,2} These data describe the incidence of bleeding while on therapy and are used to inform agent selection in primary prevention.

Far less is known about what happens once a clinically significant upper gastrointestinal bleeding (UGIB) event has occurred and the patient has been hospitalized. Whether the pharmacologic class of the implicated anticoagulant shapes the subsequent in-hospital course — mortality, intensive care utilization, length of stay, the need for therapeutic endoscopy, and early readmission — after accounting for patient-level acuity has not been well characterized outside the randomized trial setting. Most comparative data derive from analyses of bleeding incidence rather than from cohorts of patients hospitalized with an established bleed.

We therefore conducted a multicenter cohort study comparing in-hospital outcomes across DOAC, heparin, and warfarin exposure groups in patients admitted with UGIB, and sought to identify patient-level factors that independently predict in-hospital mortality in this population.

Methods

Design and setting. We performed a retrospective multicenter cohort study of adults admitted with UGIB across the Northwell Health system from January 2019 through January 2024. The protocol was approved by the Northwell Health Institutional Review Board with a waiver of informed consent.

Cohort. Eligible patients were aged 18–89 years. UGIB was identified by ICD-10 diagnosis codes consistent with hematemesis, melena, gastric or duodenal ulcer with hemorrhage, esophageal or gastric variceal hemorrhage, or hemorrhagic gastritis, with chart confirmation of a bleeding source proximal to the ligament of Treitz. The analytic cohort comprised patients with documented outpatient anticoagulant exposure at the time of admission.

Exposure. The exposure of interest was outpatient anticoagulant class at admission, classified as DOAC (apixaban, rivaroxaban, dabigatran, or edoxaban), heparin product (therapeutic-dose enoxaparin, dalteparin, or fondaparinux), or warfarin.

Outcomes. The primary outcome was in-hospital all-cause mortality. Secondary outcomes were ICU admission, length of stay (LOS), therapeutic endoscopic intervention, and 30-day all-cause readmission.

Statistical analysis. Continuous variables were compared across anticoagulant groups with the Kruskal–Wallis test and are reported as median (interquartile range [IQR]); categorical variables were compared with chi-square or Fisher exact tests, as appropriate. Univariable predictors of mortality were screened by logistic regression at an exploratory threshold of $p < 0.10$. Because only 22 mortality events were observed, the final multivariable logistic regression model was constrained to two predictors in accordance with the events-per-variable rule. Anticoagulant class was forced into the model as the exposure of primary interest, and the second predictor was selected from the screened candidates on the basis of statistical significance and model fit. Model performance was assessed by the c-statistic (discrimination) and the Hosmer–Lemeshow goodness-of-fit test (calibration). All analyses were performed in SAS 9.4 (SAS Institute, Cary, NC).

Results

Cohort characteristics. Of 2,009 UGIB admissions during the study period, 303 (15.1%) had documented outpatient anticoagulant exposure: 240 (79.2%) on a DOAC, 40 (13.2%) on a heparin product, and 23 (7.6%) on warfarin. The cohort was elderly (median age 77, 73.5, and 75 years for the DOAC, heparin, and warfarin groups, respectively; $p = 0.12$), and baseline demographics and comorbidities — including female sex, disseminated malignancy, liver cirrhosis, acute kidney injury, sepsis, and shock — did not differ across groups (Table 1).

Primary and secondary outcomes. In-hospital mortality occurred in 22 patients (7.3%) and did not differ significantly by anticoagulant class (DOAC 7.5%, heparin 5.0%, warfarin 8.7%; $p = 0.83$). ICU admission (DOAC 25.4%, heparin 35.0%, warfarin 17.4%; $p = 0.27$), LOS (median 6.79, 9.85, and 6.62 days, respectively; $p = 0.14$), endoscopic intervention (29.2%, 32.5%, 21.7%; $p = 0.66$), and 30-day readmission (3.3%, 2.5%, 0.0%; $p = 1.00$) were similarly distributed across groups.

Predictors of in-hospital mortality. On univariable screening, admission serum creatinine ($p = 0.034$) and age ($p = 0.062$) met the $p < 0.10$ threshold for consideration; admission creatinine was selected as the second model predictor on the basis of its significance and superior model fit. In the constrained multivariable model, anticoagulant class was not associated with mortality (overall $p = 0.92$; heparin vs DOAC adjusted odds ratio [OR] 0.79, 95% confidence interval [CI] 0.17–3.62; warfarin vs DOAC adjusted OR 1.22, 95% CI 0.26–5.70). Admission serum creatinine remained an independent predictor: each 1 mg/dL increment was associated with a 50% relative increase in the odds of in-hospital death (adjusted OR 1.50, 95% CI 1.02–2.20; $p = 0.041$). The model demonstrated acceptable discrimination (c-statistic 0.62) and calibration (Hosmer–Lemeshow $p = 0.82$).

Discussion

Two findings warrant emphasis. First, no significant outcome differences emerged across the DOAC, heparin, and warfarin exposure groups. This is consistent with the hypothesis that, once a clinically significant bleed has occurred, the acute hospital course is dominated by hemodynamic status, bleeding severity, and comorbid burden rather than by the pharmacologic class of the implicated agent. Second, admission serum creatinine independently predicted in-hospital mortality after adjustment for anticoagulant class.

This second finding aligns with the integration of renal physiology into existing UGIB risk-stratification frameworks. The Glasgow-Blatchford score uses elevated blood urea nitrogen as a marker of upper gastrointestinal blood load and prerenal physiology,³ the AIMS65 score incorporates albumin and altered mental status as proxies for systemic illness,⁴ and current American College of Gastroenterology guidelines emphasize early hemodynamic and laboratory assessment to triage UGIB severity.⁵ Admission creatinine integrates several pathophysiologically relevant signals: chronic kidney disease that limits anticoagulant clearance and amplifies drug exposure (particularly relevant for the renally cleared agent dabigatran), acute kidney injury from hypovolemia related to ongoing blood loss, and the hepatorenal physiology that may complicate cirrhotic UGIB.

The heparin subgroup deserves cautious interpretation. Outpatient heparin use is most often driven by cancer-associated venous thromboembolism, perioperative bridging, or recent thromboembolic events, and these patients carry a clinically distinct illness burden. The numerically longer median LOS (9.85 days) and higher ICU utilization (35.0%) in this group most plausibly reflect confounding by indication rather than an effect of heparin pharmacology. An earlier interim analysis of this cohort identified a statistically significant LOS difference,⁶ with cohort expansion and additional follow-up, this signal no longer persists, which supports the interpretation of confounding rather than a true treatment effect.

Limitations. Several limitations should be noted. The study was retrospective and drawn from a single health system, which may limit generalizability. We lacked granular data on bleeding severity, transfusion volume, time to endoscopy, lesion source, and reversal-agent use (idarucizumab, andexanet alfa, four-factor prothrombin complex concentrate). Decisions on anticoagulation interruption and resumption, which influence both rebleeding and thromboembolic risk,^{7,8} were not captured at the granularity required for adjustment. The small heparin (n = 40) and warfarin (n = 23) subgroups produced wide confidence intervals around between-class effect estimates, and clinically meaningful differences cannot be excluded with the available statistical power. Finally, with only 22 mortality events, the multivariable model had limited events-per-variable capacity and was necessarily constrained to two predictors, which precludes more extensive adjustment.

Conclusion

Among anticoagulated patients hospitalized with UGIB, anticoagulant class did not independently predict in-hospital mortality, ICU admission, length of stay, endoscopic intervention, or 30-day readmission. Anticoagulant class alone should therefore not drive triage decisions or anticipated

severity assessment in this setting. Admission renal function — a laboratory value typically available within the first hour of presentation — provides independent prognostic information and warrants incorporation into early risk-stratification frameworks alongside established scores. Prospective work using propensity-score matching and incorporating bleeding-source and reversal-agent data is needed to validate admission creatinine as a stratifier in this population.

Declarations

Ethics approval and consent to participate:

This retrospective study was approved by the Northwell Health Institutional Review Board, which granted a waiver of informed consent because the analysis used pre-existing, de-identified patient data and posed no more than minimal risk to participants. All procedures were conducted in accordance with the Declaration of Helsinki.

Consent for publication:

Not applicable. The manuscript contains no individually identifiable patient data.

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None. **Conflicts of interest:** The authors declare no relevant conflicts of interest.

Author Contribution

A.S. conceptualized the study, performed the data analysis, and wrote the main manuscript text. U.S.A.V., B.G., M.A.B., and J.M. performed data collection, chart review, and assisted in drafting the manuscript. L.D. supervised the research and critically revised the manuscript for important intellectual content. All authors reviewed the manuscript.

Data Availability

The datasets generated and analyzed during the current study are not publicly available due to patient privacy restrictions and regulations governing Protected Health Information (PHI) under the approved Institutional Review Board protocol. De-identified datasets used for the analysis are available from the corresponding author upon reasonable request.

References

1. Holster IL, Valkhoff VE, Kuipers EJ, et al. New oral anticoagulants increase risk for gastrointestinal bleeding: a systematic review and meta-analysis. *Gastroenterology*. 2013;145:105–12.
2. Abraham NS, Noseworthy PA, Yao X, et al. Gastrointestinal safety of direct oral anticoagulants: a large population-based study. *Gastroenterology*. 2017;152:1014–22.
3. Blatchford O, Murray WR, Blatchford M. A risk score to predict need for treatment for upper-gastrointestinal haemorrhage. *Lancet*. 2000;356:1318–21.
4. Saltzman JR, Tabak YP, Hyett BH, et al. A simple risk score accurately predicts in-hospital mortality, length of stay, and cost in acute upper GI bleeding. *Gastrointest Endosc*. 2011;74:1215–24.
5. Laine L, Barkun AN, Saltzman JR, et al. ACG Clinical Guideline: upper gastrointestinal and ulcer bleeding. *Am J Gastroenterol*. 2021;116:899–917.
6. Sohail A, Javor J, et al. Impact of anticoagulant class on clinical outcomes in upper gastrointestinal bleeding: a multi-center analysis [abstract]. *Digestive Disease Week*; 2026.
7. Sengupta N, Feuerstein JD, Patwardhan VR, et al. The risks of thromboembolism vs. recurrent gastrointestinal bleeding after interruption of systemic anticoagulation in hospitalized inpatients with gastrointestinal bleeding: a prospective study. *Am J Gastroenterol*. 2015;110:328–35.
8. Radaelli F, Dentali F, Repici A, et al. Management of anticoagulation in patients with acute gastrointestinal bleeding. *Dig Liver Dis*. 2015;47:621–7.

Table 1

Table 1

Baseline characteristics, in-hospital outcomes, and multivariable predictors of in-hospital mortality among 303 anticoagulated patients admitted with upper gastrointestinal bleeding.

Variable	DOAC (n = 240)	Heparin (n = 40)	Warfarin (n = 23)	p-value
Baseline characteristics				
Age, years, median (IQR)	77 (70–83)	73.5 (63–83)	75 (67–83)	0.12*
Female sex, n (%)	121 (50.4)	16 (40.0)	9 (39.1)	0.32†
Disseminated malignancy, n (%)	20 (8.3)	4 (10.0)	2 (8.7)	0.87‡
Liver cirrhosis, n (%)	6 (2.5)	1 (2.5)	0 (0.0)	1.00‡
Acute kidney injury, n (%)	89 (37.1)	13 (32.5)	7 (30.4)	0.72†
Sepsis, n (%)	43 (17.9)	10 (25.0)	3 (13.0)	0.44†
Shock, n (%)	26 (10.8)	7 (17.5)	2 (8.7)	0.42‡
In-hospital outcomes				
In-hospital mortality, n (%)	18 (7.5)	2 (5.0)	2 (8.7)	0.83‡
ICU admission, n (%)	61 (25.4)	14 (35.0)	4 (17.4)	0.27‡
LOS, days, median (IQR)	6.79 (3.89–11.70)	9.85 (4.50–18.65)	6.62 (4.67–13.11)	0.14*
Endoscopic intervention, n (%)	70 (29.2)	13 (32.5)	5 (21.7)	0.66†
30-day readmission, n (%)	8 (3.3)	1 (2.5)	0 (0.0)	1.00‡
Multivariable logistic regression for in-hospital mortality (22 events)				
Predictor	Adjusted OR	95% CI	p-value	
Anticoagulant class (overall)	—	—	0.92	
Heparin vs DOAC	0.79	0.17–3.62	0.69	
Warfarin vs DOAC	1.22	0.26–5.70	0.70	
Admission creatinine, per 1 mg/dL	1.50	1.02–2.20	0.041	

DOAC, direct oral anticoagulant; ICU, intensive care unit; IQR, interquartile range; LOS, length of stay; OR, odds ratio. *Kruskal–Wallis test; †chi-square test; ‡Fisher exact test. Multivariable model: c-statistic 0.62; Hosmer–Lemeshow goodness-of-fit $p = 0.82$.