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Impact of Direct Oral Anticoagulant Use on Endoscopic Presentation and In-Hospital Outcomes in Acute Upper Gastrointestinal Bleeding

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Title

Impact of Direct Oral Anticoagulant Use on Endoscopic Presentation and In-Hospital Outcomes in Acute Upper Gastrointestinal Bleeding

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ABSTRACT

Background:

Direct oral anticoagulants (DOACs) are widely used for thromboembolic disease, but their influence on endoscopic findings and short-term outcomes in acute upper gastrointestinal bleeding (UGIB) remains incompletely defined. This study evaluated whether DOAC use at presentation was associated with differences in endoscopic findings, hemostatic intervention, and in-hospital outcomes.

Methods:

We conducted a retrospective multicenter cohort study of adults undergoing upper gastrointestinal endoscopy for acute UGIB during 2024 at three UK hospitals. Patients receiving DOAC therapy at presentation were compared with contemporaneous patients not receiving DOAC therapy. Outcomes included endoscopic diagnoses, hemostatic interventions, blood transfusion, length of hospital stay, intensive treatment unit (ITU) admission, in-hospital mortality, and ITU admission or death. Analyses were based on available aggregate data and comprised unadjusted group-level comparisons.

Results:

Among 653 patients, 245 received DOAC therapy and 408 did not. Mean age was similar between groups (77.9 ± 10.2 vs 76.1 ± 8.5 years; $p = 0.12$), as was length of stay (11.4 ± 15.5 vs 11.2 ± 16.8 days; $p = 0.88$). Gastric ulceration was more frequent with DOAC use (12.2% vs 7.1%; $p = 0.034$), whereas esophageal varices were less frequent (2.9% vs 7.6%; $p = 0.015$). Other endoscopic findings and hemostatic interventions did not differ significantly. Mortality (9.0% vs 10.0%; $p = 0.65$), transfusion (16.7% vs 14.2%; $p = 0.39$), ITU admission (0.8% vs 2.0%; $p = 0.34$), and ITU admission or death (9.8% vs 12.0%; $p = 0.39$) were similar.

Conclusion:

DOAC use was not associated with statistically significant differences in measured short-term in-hospital outcomes. Selected differences in endoscopic diagnoses warrant cautious interpretation given the unadjusted analysis and limited patient-level data.

Keywords

Direct oral anticoagulants; DOAC; upper gastrointestinal bleeding; UGIB; endoscopy; hemostasis; transfusion; mortality; anticoagulation

Key messages

- DOAC-treated patients with acute UGIB did not have statistically significant differences in in-hospital mortality, transfusion requirement, ITU admission, or ITU admission/death compared with non-DOAC patients in this cohort.
- Endoscopic diagnoses and hemostatic interventions were broadly similar between DOAC and non-DOAC groups, although differences were observed for gastric ulceration and esophageal varices.
- The findings highlight the importance of individualized assessment of bleeding severity and clinical context when considering DOAC-associated UGIB and should not be interpreted as evidence that reversal therapy is unnecessary or universally indicated.

INTRODUCTION

Acute upper gastrointestinal bleeding (UGIB) remains a common gastrointestinal emergency associated with substantial hospital resource use, urgent endoscopy, transfusion, intensive care support, and mortality, particularly among older and comorbid populations [1–4]. Patient outcomes are determined by a complex interplay of factors, including the underlying bleeding aetiology, haemodynamic status, comorbidity burden, renal function, concurrent antithrombotic therapy, and the timeliness and effectiveness of resuscitation and endoscopic hemostasis.

Direct oral anticoagulants (DOACs), including factor Xa inhibitors and direct thrombin inhibitors, are widely used for stroke prevention in atrial fibrillation and for the treatment and prevention of venous thromboembolic disease. Compared with vitamin K antagonists (VKAs), DOACs have more predictable pharmacokinetics, fewer food and drug interactions, and generally do not require routine coagulation monitoring. However, gastrointestinal bleeding remains an important safety concern, particularly among older patients, those with renal impairment, and those receiving concomitant antiplatelet therapy or non-steroidal anti-inflammatory drugs (NSAIDs) [5].

Large randomized trials and meta-analyses have demonstrated that the risk of gastrointestinal bleeding varies between individual DOAC agents and doses, with some analyses suggesting a relatively favorable gastrointestinal safety profile for apixaban compared with selected alternative DOACs [5]. However, the clinical implications of DOAC exposure once an episode of acute UGIB has occurred remain less clear. An important clinical question is whether patients receiving DOAC therapy present with different endoscopic bleeding patterns, require more intensive hemostatic intervention, or experience worse short-term outcomes despite contemporary supportive and endoscopic management.

Clinical evidence regarding outcomes among patients with anticoagulant-associated UGIB remains heterogeneous. A prospective multicenter cohort study reported broadly comparable outcomes between patients receiving DOACs and those receiving VKAs, with no consistent evidence of increased rebleeding after multivariable adjustment [6]. Other retrospective studies have similarly reported comparable transfusion requirements, length of hospital stay, intensive care admission, and mortality among patients with oral-anticoagulant-associated UGIB, although differences in study populations, comparator groups, sample sizes, and analytical approaches limit direct comparison between studies [7–11].

The management of anticoagulation during acute UGIB may require consideration of temporary interruption and, in selected severe bleeding scenarios, pharmacological reversal. Specific reversal agents are available for individual DOACs, including idarucizumab for dabigatran and Andexanet

alfa for factor Xa inhibitors, while four-factor prothrombin complex concentrate (4F-PCC) may be used in selected circumstances when specific reversal is unavailable or unsuitable. However, decisions regarding reversal are influenced by bleeding severity, haemodynamic status, timing of the last DOAC dose, renal function, thrombotic risk, and the likelihood of achieving hemostasis through resuscitation and endoscopic treatment [12–16]. Importantly, the role of DOAC exposure itself in determining endoscopic presentation and short-term outcomes remains incompletely characterized.

The present study aimed to compare endoscopic findings, therapeutic endoscopic interventions, and selected in-hospital outcomes among patients with acute UGIB receiving DOAC therapy at presentation and those not receiving DOAC therapy. We evaluated transfusion requirement, length of hospital stay, intensive treatment unit (ITU) admission, in-hospital mortality, and the composite outcome of ITU admission or death.

METHODS

Study design and setting

Eligible patients were adults who underwent upper gastrointestinal endoscopy for suspected or confirmed acute UGIB during the study period. Patients receiving a DOAC at presentation were identified from medication records. The original study design sought to identify contemporaneous non-DOAC patients with similar age (within ±5 years) who underwent endoscopy within ±5 days of the DOAC-treated patient's procedure. Up to two non-DOAC patients could be selected for each DOAC-treated patient. Patients were excluded if endoscopy was performed for an elective non-bleeding indication, if the presentation was not consistent with acute UGIB, or if essential outcome data were unavailable.

Study population

Eligible participants were adults who underwent upper gastrointestinal endoscopy for suspected or confirmed acute UGIB. Patients receiving DOAC therapy at presentation were identified from medication records. The original study design sought to identify contemporaneous non-DOAC patients with similar age (within ±5 years) who underwent endoscopy within ±5 days of the DOAC-treated patient's procedure. Up to two non-DOAC patients could be selected for each DOAC-treated patient.

Patients were excluded if endoscopy was performed for an elective non-bleeding indication, if the clinical presentation was not consistent with acute UGIB, or if essential outcome data were unavailable.

Exposure definition

The primary exposure was documented DOAC use at presentation. DOAC therapy included factor Xa inhibitors and the direct thrombin inhibitor dabigatran. The available aggregate dataset did not permit complete patient-level assessment of DOAC agent, dose, timing of the last dose, renal function, concomitant antiplatelet or NSAID therapy, or reversal-agent use. These variables were therefore considered potential sources of residual confounding in the interpretation of the findings.

Data collection and outcomes

Data collected included age, sex, length of hospital stay, endoscopic diagnosis, therapeutic endoscopic intervention, blood transfusion requirement, intensive treatment unit (ITU) admission, in-hospital mortality, and the composite outcome of ITU admission or death.

Endoscopic findings included duodenal ulcer, gastric ulcer, oesophagitis, Oesophageal varices, gastric varices, gastric antral vascular ectasia (GAVE), and other lesions, including angioectasia, Dieulafoy lesion, malignancy, and portal hypertensive gastropathy.

Therapeutic endoscopic interventions included injection therapy, clip placement, hemostatic agents, heater probe therapy, argon plasma coagulation, and band ligation.

The primary clinical outcomes were in-hospital mortality, blood transfusion requirement, and ITU admission. The composite outcome of ITU admission or death was also assessed. Length of hospital stay and endoscopic findings and interventions were evaluated as additional outcomes.

Statistical analysis

Continuous variables were summarized as mean ± standard deviation (SD), and categorical variables as counts and percentages. Group-level comparisons were performed using independent-samples t-tests for continuous variables and chi-square or Fisher's exact tests for categorical variables, as appropriate. All statistical tests were two-sided, with $p < 0.05$ considered statistically significant.

The analyses reported in this manuscript were based on the available aggregate study data. No multivariable adjustment was performed; therefore, the reported associations should be interpreted as unadjusted comparisons and do not establish an independent effect of DOAC exposure on clinical outcomes**.**

RESULTS

Baseline characteristics

A total of 653 patients presenting with acute upper gastrointestinal bleeding (UGIB) were included in the study. Of these, 245 patients (37.5%) were receiving direct oral anticoagulant (DOAC) therapy at presentation, while 408 patients (62.5%) were not receiving DOAC therapy. Available baseline characteristics are presented in Table 1.

The mean age was 77.9 ± 10.2 years in the DOAC group and 76.1 ± 8.5 years in the non-DOAC group, with no statistically significant difference between groups (p = 0.12). Female sex was recorded in 47/245 (19.2%) patients in the DOAC group and 103/408 (25.2%) patients in the non-DOAC group (p = 0.09). Male sex was recorded in 81/245 (33.1%) and 169/408 (41.4%) patients, respectively. The reported male and female categories did not account for the entire study population, indicating incomplete recording of sex in the available dataset.

Table 1. Baseline characteristics according to DOAC status

Characteristic	DOAC group (n = 245)	Non-DOAC group (n = 408)	p value
Age at procedure, years, mean ± SD	77.9 ± 10.2	76.1 ± 8.5	0.12
Female sex, n (%)	47 (19.2)	103 (25.2)	0.09
Male sex, n (%)	81 (33.1)	169 (41.4)	—

Note: Values are presented as mean ± standard deviation (SD) or n (%). DOAC, direct oral anticoagulant. Percentages for sex were calculated using the full group denominator. The reported male and female categories do not sum to the total group size because sex data were incompletely recorded in the available dataset.

Endoscopic findings

Endoscopic findings are summarized in Table 2. Duodenal ulceration, gastric ulceration, and oesophagitis were among the commonly recorded findings in both groups.

Gastric ulceration was identified in 30 patients (12.2%) in the DOAC group compared with 29 patients (7.1%) in the non-DOAC group (p = 0.034). Oesophageal varices were identified in 7 patients (2.9%) receiving DOAC therapy and 31 patients (7.6%) not receiving DOAC therapy (p = 0.015).

Duodenal ulceration was recorded in 25 patients (10.2%) in the DOAC group and 35 patients (8.6%) in the non-DOAC group (p = 0.487), while oesophagitis was recorded in 33 patients (13.5%) and 43 patients (10.5%), respectively (p = 0.259). Gastric varices were recorded in 2 patients (0.8%) in the DOAC group and were not recorded in the non-DOAC group (p = 0.140). GAVE was recorded in 2 patients (0.8%) and 1 patient (0.2%), respectively (p = 0.560). Other lesions were identified in 10 patients (4.1%) in the DOAC group and 23 patients (5.6%) in the non-DOAC group (p = 0.462).

The observed differences in gastric ulceration and esophageal varices were based on unadjusted comparisons and should therefore be interpreted cautiously, particularly given the absence of complete patient-level clinical data.

Table 2. Endoscopic findings according to DOAC status

Endoscopic finding	DOAC group (n = 245), n (%)	Non-DOAC group (n = 408), n (%)	p value
Duodenal ulcer	25 (10.2)	35 (8.6)	0.487
Gastric ulcer	30 (12.2)	29 (7.1)	0.034
Oesophagitis	33 (13.5)	43 (10.5)	0.259
Oesophageal varices	7 (2.9)	31 (7.6)	0.015
Gastric varices	2 (0.8)	0 (0.0)	0.140
GAVE	2 (0.8)	1 (0.2)	0.560
Other lesions*	10 (4.1)	23 (5.6)	0.462

Note: Values are presented as n (%). DOAC, direct oral anticoagulant; GAVE, gastric antral vascular ectasia. *Other lesions included angioectasia, Dieulafoy lesion, malignancy, and portal hypertensive gastropathy. Endoscopic findings were not necessarily mutually exclusive, as individual patients could have more than one finding. P values represent unadjusted comparisons based on the reported aggregate counts.

Therapeutic endoscopic interventions

Therapeutic endoscopic interventions are presented in Table 3. Injection therapy was performed in 21 patients (8.6%) in the DOAC group and 41 patients (10.0%) in the non-DOAC group (p=0.583). Clip placement was performed in 18 patients (7.3%) and 27 patients (6.6%), respectively (p=0.751).

Hemostatic agents were used in 1.6% of DOAC-treated patients and 2.2% of non-DOAC patients (p=0.776). Heater probe therapy was performed in 2.0% and 2.9%, respectively (p=0.615), while argon plasma coagulation was used in 2.4% and 2.5% (p>0.999). Band ligation was performed in 0.8% of DOAC-treated patients compared with 2.7% of non-DOAC patients (p=0.146).

No statistically significant differences were observed between groups for the individual endoscopic intervention categories reported in Table 3.

Table 3. Therapeutic endoscopic interventions according to DOAC status

Endoscopic intervention	DOAC group (n=245), n (%)	Non-DOAC group (n=408), n (%)	p value
Injection therapy	21 (8.6)	41 (10.0)	0.583
Clips	18 (7.3)	27 (6.6)	0.751
Haemostatic agents	4 (1.6)	9 (2.2)	0.776
Heater probe	5 (2.0)	12 (2.9)	0.615
Argon plasma coagulation	6 (2.4)	10 (2.5)	>0.999
Band ligation	2 (0.8)	11 (2.7)	0.146

Note; Intervention counts are descriptive and may not be mutually exclusive because more than one hemostatic modality could be used during the same endoscopic procedure. P values are unadjusted exploratory Fisher exact tests based on aggregate intervention counts and group denominators.

Clinical outcomes

Clinical outcomes are detailed in Table 4. In-hospital mortality occurred in 22 DOAC-treated patients (9.0%) and 41 non-DOAC patients (10.0%; p = 0.65). Blood transfusion was required in 41 DOAC-treated patients (16.7%) and 58 non-DOAC patients (14.2%; p = 0.39). ITU admission occurred in 2 patients (0.8%) in the DOAC group and 8 patients (2.0%) in the non-DOAC group (p = 0.34). The composite outcome of ITU admission or death occurred in 24 DOAC-treated patients

(9.8%) and 49 non-DOAC patients (12.0%; p = 0.39). Mean length of hospital stay was also similar between groups (11.4 ± 15.5 vs 11.2 ± 16.8 days; p = 0.88).

No statistically significant differences were observed in the measured in-hospital outcomes between the DOAC and non-DOAC groups.

Table 4. In-hospital clinical outcomes according to DOAC status

Outcome	DOAC group (n = 245)	Non-DOAC group (n = 408)	p value
Length of hospital stay, days, mean ± SD	11.4 ± 15.5	11.2 ± 16.8	0.88
Blood transfusion required, n (%)	41 (16.7)	58 (14.2)	0.39
ITU admission, n (%)	2 (0.8)	8 (2.0)	0.34
In-hospital mortality, n (%)	22 (9.0)	41 (10.0)	0.65
ITU admission or death, n (%)	24 (9.8)	49 (12.0)	0.39
Medically managed (± transfusion), n (%)	174 (71.0)	301 (73.8)	—

Note: Values are presented as n (%) unless otherwise indicated. Continuous values are presented as mean ± standard deviation (SD). DOAC, direct oral anticoagulant; ITU, intensive treatment unit. P values represent the reported unadjusted aggregate analysis. The medically managed category is descriptive and was not used as a primary inferential endpoint.

DISCUSSION

Principal findings

In this multicenter retrospective cohort of 653 patients undergoing endoscopy for acute UGIB, 245 patients (37.5%) were receiving DOAC therapy at presentation and 408 (62.5%) were not. The principal finding was that DOAC exposure was not associated with statistically significant differences in the measured in-hospital outcomes. In-hospital mortality was 9.0% among DOAC-treated patients compared with 10.0% among non-DOAC patients (p=0.65), while blood transfusion was required in 16.7% and 14.2%, respectively (p=0.39). ITU admission occurred in 0.8% of DOAC-treated patients and 2.0% of non-DOAC patients (p=0.34), and the composite outcome of ITU admission or death occurred in 9.8% and 12.0%, respectively (p=0.39). Mean length of hospital stay was also similar between groups (11.4 ± 15.5 vs 11.2 ± 16.8 days; p=0.88).

These findings suggest that, within this cohort, DOAC treatment at presentation was not associated with a measurable increase in short-term adverse hospital outcomes. However, the absence of statistically significant differences should not be interpreted as demonstrating equivalence between the groups. Important determinants of bleeding severity and clinical outcome were not available for patient-level adjustment, and the findings therefore represent unadjusted associations.

The endoscopic findings showed a broadly similar distribution of common lesions between groups, although two statistically significant differences were observed. Gastric ulceration was more frequent among DOAC-treated patients than non-DOAC patients (12.2% vs 7.1%; p=0.034), whereas esophageal varices were less frequent (2.9% vs 7.6%; p=0.015). Other recorded lesions, including duodenal ulceration and oesophagitis, did not differ significantly. These findings indicate that DOAC exposure was associated with differences in the distribution of selected endoscopic diagnoses in this cohort, although the observational design does not establish that DOAC therapy caused these differences.

Therapeutic endoscopic intervention patterns were broadly comparable. Injection therapy was performed in 8.6% of DOAC-treated patients and 10.0% of non-DOAC patients (p=0.583), while clip placement was used in 7.3% and 6.6%, respectively (p=0.751). No statistically significant difference was observed for any individual hemostatic modality. These findings provide no evidence from this cohort of a substantially greater requirement for recorded endoscopic intervention among patients receiving DOAC therapy.

Comparison with previous literature

Our findings are broadly consistent with previous observational studies examining outcomes of UGIB among patients receiving oral anticoagulants. Gouriou et al. reported broadly comparable outcomes between patients receiving DOACs and those receiving VKAs, without a consistent increase in adverse outcomes following adjustment [6]. Similarly, other real-world studies have reported comparable transfusion requirements, intensive care utilization, length of hospital stay, and mortality among patients presenting with oral-anticoagulant-associated UGIB [7–11]. The absence of a statistically significant difference in mortality, transfusion requirement, ITU admission, and length of stay in the present cohort therefore adds further observational evidence that anticoagulant exposure alone may not determine short-term outcome after UGIB.

The present study also provides information regarding endoscopic presentation. Gastric ulceration was significantly more frequent in the DOAC group (12.2% vs 7.1%; p=0.034), whereas esophageal varices were significantly more frequent in the non-DOAC group (7.6% vs 2.9%; p=0.015). The latter finding is potentially relevant when interpreting overall clinical outcomes

because variceal bleeding represents a distinct clinical phenotype with different underlying disease mechanisms and management requirements. Nevertheless, the available data do not allow us to determine whether these differences reflect differences in underlying comorbidity, liver disease, medication exposure, or other patient-level characteristics rather than an effect of DOAC therapy itself.

The distinction between the risk of developing gastrointestinal bleeding and outcomes once bleeding has occurred is important. Previous evidence indicates that gastrointestinal bleeding risk varies between individual DOAC agents, with some analyses suggesting a relatively favorable gastrointestinal safety profile for apixaban compared with selected alternative agents [5]. In the present study, however, individual DOAC agents, doses, indications, and timing of the last dose were not available for analysis. Consequently, our findings should not be interpreted as demonstrating that all DOAC agents carry equivalent gastrointestinal risk or that individual DOACs have equivalent effects once bleeding occurs.

Endoscopic presentation and therapeutic management

The higher frequency of gastric ulceration among DOAC-treated patients represents one of the principal endoscopic findings of this study. Gastric ulceration was identified in 30 DOAC-treated patients (12.2%) compared with 29 non-DOAC patients (7.1%). Although statistically significant, this difference should be interpreted cautiously because the study was observational and the available data did not permit adjustment for factors that may influence ulcer development or presentation, including NSAID exposure, antiplatelet therapy, comorbidity, and gastroprotective medication use.

In contrast, esophageal varices were identified less frequently among DOAC-treated patients than among non-DOAC patients (2.9% vs 7.6%; p=0.015). This difference may indicate differences in the underlying clinical characteristics of the two groups. Because detailed information on liver disease, portal hypertension, and other comorbid conditions was not available for adjustment, it cannot be determined whether DOAC status itself contributed to the observed distribution.

The pattern of therapeutic intervention was broadly similar between groups. Injection therapy and clip placement were the most frequently recorded interventions, with no statistically significant difference between DOAC-treated and non-DOAC patients. Band ligation was numerically more frequent in the non-DOAC group (2.7% vs 0.8%), consistent with the greater frequency of esophageal varices in that group, although this difference was not statistically significant (p=0.146).

Taken together, the endoscopic findings and intervention data suggest that DOAC-treated patients in this cohort did not demonstrate a substantially different requirement for endoscopic hemostatic

therapy. However, because the dataset did not include immediate hemostatic success, rebleeding, repeat endoscopy, or subsequent radiological or surgical intervention, the degree to which DOAC exposure influences the difficulty or durability of hemostasis cannot be established.

Clinical outcomes and implications for anticoagulation management

The absence of statistically significant differences in mortality, transfusion requirement, ITU admission, or length of hospital stay is clinically relevant. Mortality was 9.0% among DOAC-treated patients compared with 10.0% among non-DOAC patients, while transfusion requirements were 16.7% and 14.2%, respectively. These findings are consistent with previous observational studies reporting broadly comparable short-term outcomes among anticoagulant-treated patients with UGIB [7–11].

However, these results should not be interpreted as evidence that DOAC therapy is without clinical consequences during acute UGIB. Bleeding severity is influenced by multiple factors, including the anatomical source of bleeding, haemodynamic status, baseline haemoglobin, renal and hepatic function, concomitant antithrombotic therapy, timing of endoscopy, and the effectiveness of hemostatic treatment. Several of these variables were not available in the present dataset. The observed similarity in outcomes may therefore reflect differences in these underlying characteristics rather than an absence of an effect of DOAC exposure.

The findings also have relevance to the clinical decision-making process surrounding DOAC interruption and reversal. Current guidance generally recommends that reversal strategies be considered selectively in severe or life-threatening bleeding rather than being administered routinely to every patient taking a DOAC [12–16]. The present study cannot directly evaluate this recommendation because reversal-agent administration, timing of the last DOAC dose, anticoagulant concentration, and hemostatic success were not available in the dataset. Therefore, our findings should not be interpreted as demonstrating that reversal is unnecessary or ineffective.

Instead, the results suggest that DOAC status alone should not be considered a sufficient measure of UGIB severity. Decisions regarding interruption or reversal should continue to incorporate the clinical severity of bleeding, haemodynamic stability, suspected bleeding source, timing of the last anticoagulant dose, renal function, individual thrombotic risk, and the availability of specific reversal therapy. This approach is consistent with the selective management strategy described in current guidance [12–16].

Anticoagulant resumption and longer-term management

Although the present study focused on outcomes during the index hospital admission, management of anticoagulation after UGIB remains an important clinical consideration. Previous evidence suggests that resumption of anticoagulation following gastrointestinal bleeding may reduce thromboembolic risk, although the timing of resumption requires balancing the risk of recurrent bleeding against the risk of thromboembolism [17].

The present dataset did not contain sufficient information to evaluate the timing or safety of DOAC resumption, recurrent bleeding, thromboembolic complications, or longer-term mortality. Accordingly, no conclusions regarding optimal anticoagulant resumption can be drawn from this study. Future management should remain individualized according to the indication for anticoagulation, thromboembolic risk, bleeding source, hemostatic control, and overall clinical status.

Strengths and limitations

The principal strengths of this study include its multicentre design, inclusion of a clinically relevant acute UGIB population, and assessment of both endoscopic findings and pragmatic in-hospital outcomes. The study included 653 patients across three UK hospital settings and examined clinically relevant outcomes including blood transfusion, ITU admission, mortality, and length of hospital stay.

Several limitations should be considered. First, the retrospective observational design limits causal inference and introduces the possibility of selection and information bias. Second, the study population comprised patients who underwent endoscopy and therefore may not be generalizable to all patients presenting with UGIB, including those managed without endoscopy.

Third, the available aggregate data did not permit comprehensive patient-level adjustment for potentially important confounders, including comorbidity burden, baseline haemoglobin, haemodynamic status, renal function, liver disease, concomitant antiplatelet or NSAID exposure, proton-pump inhibitor use, timing of endoscopy, and other markers of bleeding severity. Consequently, the reported comparisons were unadjusted and residual confounding cannot be excluded.

Fourth, individual DOAC agent, dose, indication, and timing of the last dose were not available for analysis. These factors may influence anticoagulant activity and bleeding risk. Similarly, vitamin K antagonist exposure within the non-DOAC group was not sufficiently characterized to permit a detailed distinction between patients receiving no anticoagulant therapy and those receiving alternative anticoagulation.

Fifth, information regarding reversal-agent administration and response to reversal was not available. The study therefore cannot assess the effectiveness, safety, or appropriateness of specific reversal strategies. The aggregate dataset also limited the ability to account fully for the original matching structure.

Finally, outcomes were restricted to the index hospital admission. Rebleeding, repeat endoscopy, thromboembolic complications, anticoagulant resumption, and 30- or 90-day mortality were not assessed. These limitations are particularly important when interpreting the absence of statistically significant differences between groups. Accordingly, the findings should be interpreted as unadjusted associations rather than evidence of a causal effect of DOAC therapy.

Future research

Future prospective multicenter studies should incorporate patient-level clinical and pharmacological data to better define the relationship between DOAC exposure and outcomes following acute UGIB. Important variables should include individual DOAC agent, dose, indication, timing of the last dose, renal and hepatic function, baseline haemoglobin, haemodynamic parameters, comorbidities, concomitant antiplatelet or NSAID therapy, and bleeding severity scores such as the Glasgow-Blatchford and Rockall scores.

Further studies should also capture timing of endoscopy, detailed endoscopic classification, hemostatic success, transfusion volume, reversal-agent administration, rebleeding, repeat endoscopy, radiological or surgical intervention, thromboembolic events, anticoagulant resumption, and longer-term mortality. Such data would permit appropriately adjusted analyses and help identify whether particular subgroups of DOAC-treated patients derive meaningful benefit from reversal or other treatment escalation.

Future research should additionally distinguish between individual DOAC agents and between variceal and non-variceal UGIB. This would help determine whether the broadly comparable outcomes observed in the present cohort apply consistently across different anticoagulant agents and different causes of UGIB.

CONCLUSION

In this multicenter retrospective cohort of patients undergoing endoscopy for acute upper gastrointestinal bleeding, DOAC use at presentation was not associated with statistically significant differences in in-hospital mortality, blood transfusion requirement, ITU admission, or the

composite outcome of ITU admission or death compared with non-DOAC status. Mean length of hospital stay was also similar between groups. Although differences were observed in selected endoscopic findings, particularly the higher frequency of gastric ulceration and lower frequency of esophageal varices among DOAC-treated patients, therapeutic endoscopic intervention patterns were broadly comparable.

These findings suggest that DOAC exposure alone may not be associated with worse short-term in-hospital outcomes among patients undergoing endoscopic assessment for acute UGIB. However, the observational design and limited availability of patient-level clinical, anticoagulant-specific, and bleeding-severity variables preclude causal inference. The findings should therefore be interpreted cautiously and should not be taken as evidence that DOAC therapy is equivalent to non-DOAC status or that reversal therapy is unnecessary. Clinical management should remain individualized according to bleeding severity, endoscopic findings, haemodynamic status, thrombotic risk, timing of the last anticoagulant dose, and other relevant patient factor

DECLARATIONS

Ethics approval and consent to participate

This retrospective study used routinely collected anonymized clinical data. Ethical approval was granted by the Sheffield Teaching Hospitals Ethical Review Committee (IRAS No. 326218; STH21991). Individual patient consent was not required because the study used anonymized routinely collected data and no identifiable patient-level information is reported.

Consent for publication

Not applicable. The manuscript contains no identifiable individual patient information.

Availability of data and materials

The anonymized aggregate data supporting the findings of this study are available from the corresponding author on reasonable request, subject to institutional governance and applicable data-sharing approvals. Patient-level data are not publicly available because they were derived from routine clinical records.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

NN, APS, SH, AH, SJ, SNA, SC, AG, KA1, EG, IK, TK, SAA, NW, KA2, HD, VA4, VA6, PL, MJ, GC, and MT contributed to the conceptualization, methodology, investigation, data curation, analysis, interpretation, and preparation and critical revision of the manuscript according to their respective roles in the study.

SJ additionally served as Audit Lead and was responsible for audit oversight, quality assurance, methodological governance, and verification of study processes. SNA served as the Corresponding Author and was responsible for manuscript coordination, communication with the journal and editorial office, management of revisions, and oversight of the submission process.

All authors reviewed and approved the final version of the manuscript and agree to be accountable for all aspects of the work.

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References

1. Gralnek IM, Stanley AJ, Morris AJ *et al.* Endoscopic diagnosis and management of nonvariceal upper gastrointestinal hemorrhage (NVUGIH): European Society of Gastrointestinal Endoscopy (ESGE) Guideline – Update 2021. *Endoscopy* 2021;**53**(03):300–32. https://doi.org/10.1055/a-1369-5274.

2. Barkun AN, Almadi M, Kuipers EJ *et al.* Management of Nonvariceal Upper Gastrointestinal Bleeding: Guideline Recommendations From the International Consensus Group. *Ann Intern Med* 2019;**171**(11):805–22. https://doi.org/10.7326/M19-1795.

3. Stanley AJ, Laine L. Management of acute upper gastrointestinal bleeding. *BMJ* 25 Mar. 2019:l536. https://doi.org/10.1136/bmj.l536.

4. Kamboj AK, Hoversten P, Leggett CL. Upper Gastrointestinal Bleeding: Etiologies and Management. *Mayo Clinic Proceedings* 2019;**94**(4):697–703. https://doi.org/10.1016/j.mayocp.2019.01.022.

5. Chen X, Wang L, Li H *et al.* Comparative differences in the risk of major gastrointestinal bleeding among different direct oral anticoagulants: An updated traditional and Bayesian network meta-analysis. *Front Pharmacol* 2023;**13**:1049283. https://doi.org/10.3389/fphar.2022.1049283.

6. Gouriou C, Bouguen G, Lahmek P *et al.* Outcomes of upper gastrointestinal bleeding are similar between direct oral anticoagulants and vitamin K antagonists. *Aliment Pharmacol Ther* 2021;**53**(6):688–95. https://doi.org/10.1111/apt.16236.

7. Xu Y, Schulman S, Dowlatshahi D *et al.* Direct Oral Anticoagulant- or Warfarin-Related Major Bleeding. *Chest* 2017;**152**(1):81–91. https://doi.org/10.1016/j.chest.2017.02.009.

8. Effect of Direct-acting Oral Anticoagulants and Warfarin on Hospital Outcomes in Upper Gastrointestinal Bleeding. *J Coll Physicians Surg Pak* 2022;**32**(10):1266–71. https://doi.org/10.29271/jcpsp.2022.10.1266.

9. Scibelli N, Mangano A, Raynor K *et al.* A Retrospective Review of Upper Gastrointestinal Bleed Outcomes During Hospital Admission While on Oral Anticoagulation. *Cureus* published online 16 May 2021. https://doi.org/10.7759/cureus.15061.

10. Brigida M, Di Caro S, Petruzziello C *et al.* Vitamin-K Antagonists vs. Direct Oral Anticoagulants on Severity of Upper Gastrointestinal Bleeding: A Retrospective Analysis of Italian and UK Data. *JCM* 2022;**11**(21):6382. https://doi.org/10.3390/jcm11216382.

11. Brodie MM, Newman JC, Smith T *et al.* Severity of Gastrointestinal Bleeding in Patients Treated with Direct-Acting Oral Anticoagulants. *The American Journal of Medicine* 2018;**131**(5):573.e9-573.e15. https://doi.org/10.1016/j.amjmed.2017.11.007.

12. Levy JH, Shaw JR, Castellucci LA *et al.* Reversal of direct oral anticoagulants: guidance from the SSC of the ISTH. *Journal of Thrombosis and Haemostasis* 2024;**22**(10):2889–99. https://doi.org/10.1016/j.jtha.2024.07.009.

13. Rodrigues A, Gonçalves LR, Gregório T *et al.* Urgent Reversal of Direct Oral Anticoagulants in Critical and Life-Threatening Bleeding: A Multidisciplinary Expert Consensus. *JCM* 2024;**13**(22):6842. https://doi.org/10.3390/jcm13226842.

14. Cormier S, Siegal DM. A framework for managing severe DOAC-related bleeding: Recognize, Reverse, Resume, Reduce. *Thrombosis Update* 2024;**15**:100165. https://doi.org/10.1016/j.tru.2024.100165.

15. Goldin M, Tsaftaridis N, Jnani J *et al.* Reversal of Direct Oral Anticoagulants (DOACs) for Critical Bleeding or Urgent Procedures. *JCM* 2025;**14**(3):1013. https://doi.org/10.3390/jcm14031013.

16. Chornenki NLJ, Odabashiain R, Lenteejens J *et al.* All-Cause Mortality after Major Gastrointestinal Bleeding Among Patients Receiving Direct Oral Anticoagulants: A Systematic Review and Meta-Analysis. *Blood* 2023;**142**(Supplement 1):4014–4014. https://doi.org/10.1182/blood-2023-174340.

17. Pálinkás D, Teutsch B, Gagyi EB *et al.* No Association between Gastrointestinal Rebleeding and DOAC Therapy Resumption: A Systematic Review and Meta-Analysis. *Biomedicines* 2023;**11**(2):554. https://doi.org/10.3390/biomedicines11020554.