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Retrospective Study

In-hospital acute upper gastrointestinal bleeding: What is the scope of the problem?

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Abstract

BACKGROUND

Acute upper gastrointestinal bleeding (AUGIB) is a frequently encountered condition in the Gastroenterology field with a mortality rate of 10-14%. Despite recent newer innovations and advancements in endoscopic techniques and available medications, the mortality rate associated with AUGIB remained persistently elevated.

AIM

To explore mortality, characteristics and outcome differences between hospitalized patients who develop AUGIB while in-hospital, and patients who initially present with AUGIB.

METHODS

This is a retrospective of patients who presented to Northwell Health Staten Island University Hospital from October 2012 to October 2016 with AUGIB that was confirmed endoscopically. Patients were divided in two groups: Group 1 comprised patients who developed AUGIB during their hospital stay; group 2 consisted of patients who initially presented with AUGIB as their main complaint. Patient characteristics, time to endoscopy, endoscopy findings and

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interventions, and clinical outcomes were collected and compared between groups.

RESULTS

A total of 336 patients were included. Group 1 consisted of 139 patients and group 2 of 196 patients. Mortality was significantly higher in the 1st group compared to the 2nd (20% *vs* 3.1%, $P \leq 0.05$). Increased length of stay (LOS) was noted in the 1st group (13 *vs* 6, $P \leq 0.05$). LOS post-endoscopy, vasopressor use, number of packed red blood cell units and patients requiring fresh frozen plasma were higher in group 1. Inpatients were more likely to be on corticosteroids, antiplatelets and anticoagulants. Conversely, the mean time from bleeding to undergoing upper endoscopy was significantly lower in group 1 compared to group 2.

CONCLUSION

In-hospital AUGIB is associated with high mortality and morbidity despite a shorter time to endoscopy. Larger scale studies assessing the role of increased comorbidities and antithrombotic use in this setting are warranted.

Key words: Upper gastrointestinal bleeding; Melena; Hematemesis; Variceal bleeding; Non-variceal bleeding; Mortality; Length of stay

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Core tip: This is a retrospective study to evaluate acute upper gastrointestinal bleeding (AUGIB). We compared characteristics and outcomes between patients who develop AUGIB while in-hospital and patients who initially present with AUGIB. In-hospital patients had elevated mortality and morbidity, with higher vasopressor use and extended length of stay. Antithrombotic use constituted a robust risk factor for in-hospital AUGIB. Interestingly, the shorter time to endoscopy in inpatients did not offset their worse outcomes. To determine whether this observation is related to increased comorbidities and antithrombotic use in in-hospital bleeders, larger scale studies are warranted to shed more light on this important matter.

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INTRODUCTION

Acute Upper Gastrointestinal Bleeding (AUGIB) is a common medical problem defined as bleeding from the gastrointestinal (GI) tract proximal to the ligament of Treitz^[1,2]. According to previous reports, the annual incidence of AUGIB was estimated to be between 36-172 cases per 100,000 adults^[3-19], with a decline to 90-108 cases per 100,000 adults during the last decade^[14,15,20]. This decline has been predominantly described in patients from developed countries^[12,14,15,19], and has been attributed to advances in ulcer prevention and treatment, such as prophylactic proton pump inhibitors in targeted subgroups of patients on non-steroidal anti-inflammatory drugs (NSAIDs), as well as the decreased incidence of *Helicobacter pylori* (*H. pylori*) infection^[6,13-15]. The leading cause of AUGIB continues to be peptic ulcer disease (PUD)^[6,9,11-13,15-18,20-23], particularly duodenal ulcers^[23].

Patients with AUGIB may present with bloody vomiting, passage of tarry black stools and/or passage of bright red blood per rectum^[1]. Patients with slow bleeding usually present with non-specific symptoms like shortness of breath and generalized fatigue, while patients with active bleeding have more dramatic presentations^[1]. Laboratory findings are usually significant for microcytic anemia, low ferritin levels, and high reticulocyte counts^[1]. The initial management of patients presenting with AUGIB depends on stratification into low or high risk^[24,25]. Multiple classification scores have been studied based on clinical, laboratory and endoscopic findings, but

the most commonly used scores are the Glasgow-Blatchford score and Rockall score^[26,27].

The Glasgow-Blatchford score is calculated before endoscopy by adding up the score value for each of the following components: Blood urea, hemoglobin, systolic blood pressure, heart rate, presence of melena, syncope, liver disease, and cardiac failure. A Glasgow-Blatchford score > 0 requires endoscopic intervention. Rockall score consists of a clinical initial score before the endoscopy and a full post-endoscopy score. The clinical (pre-endoscopic) Rockall score is calculated by adding the age, shock status, and comorbidity scores, whereas a full (post-endoscopic) Rockall score is based on the addition of the diagnosis and the evidence of bleeding scores to the initial clinical Rockall score. A clinical Rockall score of 0 and a full Rockall score of 0-2 indicate a low risk of bleeding or death^[26,27].

Patients identified as low risk do not need emergency endoscopy and can be treated as outpatients^[1]. Hemodynamically unstable patients require intensive care unit (ICU) monitoring before endoscopic intervention^[1]. Forrest classification and specific endoscopic findings such as localization and type of bleeding can further predict the risk of re-bleeding^[28]. Management is case- and cause-dependent, and includes hemodynamic stabilization, close monitoring, blood transfusions, holding medications that might worsen bleeding, medical and endoscopic therapy^[1].

Despite major progress in Gastroenterology and Critical Care, notably the use of acid-suppressing medications to promote bleeding cessation and ulcer healing and major advances in endoscopic techniques, the mortality of AUGIB has remained unchanged over the last few decades, ranging between 10-14%^[6,29]. Although previous studies noted an all-cause mortality at 30 d of 9-14%^[6,9-11,15,18,21], mortality directly attributed to bleeding was lower^[14,2]. In addition, multiple reports suggested higher mortality and worse outcomes associated with AUGIB occurring in patients already admitted to the hospital [inpatients (Ips)] compared with patients presenting with AUGIB [outpatients (Ops)]^[30-35]. To date, the etiology of these findings has not been adequately elucidated. Limited reports comparing Ips to Ops indicate that Ips tend to be older with multiple comorbidities, are more likely to be on antithrombotics, and tend to have more severe bleeding as well^[30].

Based on these observations, we conducted an observational study to compare AUGIB occurring in Ips *vs* Ops. We evaluated and compared the mortality, characteristics, and risk factors of patients with acute upper GI bleeding among patients already admitted (group 1 or Ips) and patients presenting with GI bleeding to Staten Island University Hospital (group 2 or Ops).

MATERIALS AND METHODS

This is a retrospective case control study that uses electronic medical records and discharge registries from Northwell Health Staten Island University Hospital (SIUH) in Staten Island, New York as a database. Records of individuals who were admitted to the medical wards in SIUH between October 2012 and October 2016 were reviewed. The final international classification of disease code diagnosis at discharge was used to select patients who had potential acute upper GI bleeding, manifested as hematemesis, melena, and hematochezia. All included patients have undergone an upper endoscopy, which confirmed the upper GI source of bleeding defined as bleeding in the GI tract originating proximally to the ligament of Treitz in the distal duodenum. A total of 1,274 patients were screened, out of which 938 patients were excluded. The remaining 336 patients qualified as having endoscopically-proven acute upper GI bleeding and met the inclusion criteria. Included patients were placed into two groups: A first group of patients admitted to SIUH that developed overt acute upper GI bleeding during their admission, which was confirmed by upper endoscopy in the inpatient setting (group 1 or Ips); and a second group of patients presenting to SIUH with overt acute upper GI bleeding confirmed by upper endoscopy (group 2 or Ops). Exclusion criteria included patients aged 18 years or less, patients with indeterminate source of bleeding and patients with bleeding from outside the upper GI tract. Patient charts were retrospectively evaluated in order to collect patient demographics and baseline characteristics, clinical and endoscopic features of bleeding, in addition to major outcomes, namely mortality and morbidity.

Medical records for both groups were reviewed. Study data were managed using research electronic data capture (REDCap) tools hosted at the Feinstein Institutes for Medical Research at Northwell Health System. REDCap is a secure web-based software platform designed to support data capture for research studies. Collected data included: Demographics, week day of admission, gender, social history, hospitalization within the last 6 mo, history of GI bleed, history of PUD, medication

history, nasogastric lavage result, bleeding type, mortality, cause of death, length of stay (LOS), LOS post-endoscopy, blood product transfusion, ICU transfer, vasopressor use, intubation, bleeding to endoscopy time, complications, interventions, endoscopic diagnosis, Glasgow-Blatchford score, Rockall score, and Child Pugh score in patients with cirrhosis.

The primary objective of this study is to determine the mortality associated with acute upper GI bleeding among patients already admitted (Ips) and patients presenting with bleeding to Staten Island University Hospital (Ops), and to compare the characteristics and risks for AUGIB of both groups. Patients were risk-stratified through Glasgow-Blatchford and Rockall scores. The LOS, timing of endoscopy and endoscopic findings, and treatments were compared.

The Institutional Review Board at North Shore Long Island Jewish Hospital and Staten Island University Hospital approved the study protocol. All researchers involved in this study adhered to the confidentiality of patient health information.

Statistical analysis

Patient demographics and clinical characteristics were summarized by study groups. Continuous data were presented as medians and interquartile ranges. Frequency distribution and percentages were provided for categorical variables. Differences between study groups in continuous variables were estimated with nonparametric Mann-Whitney *U* tests. The association between categorical variables with study groups was evaluated using Chi-squared tests or Fisher's exact tests as appropriate.

The primary analysis tests the null hypotheses that there is no difference in mortality between the study groups. Multiple logistic regression analysis using in-hospital mortality as an outcome was used to identify independent risk factors. All statistical tests of significance were two-sided and conducted at the < 0.05 level of significance. All statistical analyses were conducted using SAS (statistical analysis system) Version 9.3.

In order to define an adequate sample size, existing data from prior studies were reviewed. Based on available literature, assuming a mortality rate of 14%, and using an acceptable error of $\alpha = 0.05$ powered at 80%, the calculated sample size was around 300 patients.

RESULTS

Population demographics

A total of 335 patients were included. The study population was divided into 139 patients who developed in-hospital GI bleed and were included in the first group, and 196 patients who initially presented with GI bleed were included in the second group.

Gender proportion was equal in both groups, with 59% males and 41% females. Around 40% of patients in both groups were smokers. Ops had significantly more alcohol use than Ips (29.6% *vs* 16.6%, $P < 0.05$).

The majority of patients in both groups were aged between 60-79 years. In group 1, 51.1% were 60-79 years of age, 28.1% were more than 80, and 20.2% were less than 60. In group 2, 43.4% were 60-79 years of age, 31.6% were less than 60, and 25% were more than 80. Group 2 had a significantly higher number of patients who were less than 60 years of age ($P < 0.05$).

Patients were hospitalized 6 mo prior to presentation (44.6% *vs* 39.8%), had a prior history of upper GI Bleed (13% *vs* 25.5%), a prior history of lower GI bleed (2.2% *vs* 3.1%), and a prior history of PUD (18% *vs* 19.4%) at similar rates in group 1 and 2, respectively.

Patients in both groups were on similar medications prior to presentation, including: Proton pump inhibitors (PPIs) (36.7% *vs* 32.7%), H2-blockers (7.9% *vs* 7.1%), and NSAIDs for more than 5 d (7.9% *vs* 4.6%, respectively). Interestingly, a higher proportion of patients who developed inpatient GI bleed were on anticoagulants and antiplatelets (80.6%) and steroids (27.3%) than patients who presented with GI bleed (33.2%, $P = 0.01$ and 11.7%, $P < 0.05$, respectively).

Ips received significantly more aspirin and clopidogrel (48.2% *vs* 33.2%, $P < 0.05$ and 25.9% *vs* 13.3%, $P < 0.05$, respectively). Similarly, Ips received more heparin, low molecular weight heparin and warfarin (39.6% *vs* 2.6%, $P < 0.05$, 18% *vs* 2.6%, $P < 0.05$, and 20.9% *vs* 11.2%, $P < 0.05$, respectively). Both groups received novel anticoagulants (NOACs) at similar rates (6.1% *vs* 2.9%), however more Ips received apixaban, whereas more Ops received rivaroxaban (2.2% *vs* none, $P < 0.05$ and 0.7% *vs* 4.6%, $P < 0.05$, respectively) (Table 1).

Patients' presentation and esophagogastroduodenoscopy indication

Table 1 Demographics and baseline characteristics

	In-hospital GI bleed (<i>n</i> = 139)	GI bleed on presentation (<i>n</i> = 196)	<i>P</i> value
Baseline characteristics, <i>n</i> (%)			
Sex			
Male	82 (59)	116 (59.2)	0.93
Female	57 (41)	80 (40.8)	
Age			
< 60	28 (20.2)	62 (31.6)	0.05
60-79	71 (51.1)	85 (43.4)	> 0.05
> 80	39 (28.1)	49 (25)	> 0.05
Smoking	56 (40.3)	76 (38.8)	0.78
Alcohol use	23 (16.6)	58 (29.6)	0.01
Hospitalization within last 6 mo	62 (44.6)	78 (39.8)	0.35
Prior history of upper GI bleed	18 (13)	50 (25.5)	0.66
Prior history of lower GI bleed	3 (2.2)	6 (3.1)	
Prior history of PUD	25 (18)	38 (19.4)	0.8
Medication use prior to bleeding			
Proton pump inhibitors	51 (36.7)	64 (32.7)	0.44
H2-blockers	11 (7.9)	14 (7.1)	0.79
NSAIDs for > 5 d	11 (7.9)	9 (4.6)	0.21
Steroid	38 (27.3)	23 (11.7)	0.01
Antiplatelets or anticoagulants	112 (80.6)	65 (33.2)	0.01
Aspirin	67 (48.2)	65 (33.2)	0.01
Clopidogrel	36 (25.9)	26 (13.3)	0.01
Prasugrel	0	2 (1)	0.23
Cilostazol	1 (0.7)	0	0.23
Dipyridamole	1 (0.7)	0	0.23
Heparin	55 (39.6)	5 (2.6)	0.01
Low molecular weight heparin	25 (18)	5 (2.6)	0.01
Warfarin	29 (20.9)	22 (11.2)	0.02
Eptifibatide	2 (1.4)	0	0.92
Novel anticoagulants	4 (2.9)	12 (6.1)	0.18
Apixaban	3 (2.2)	0	0.04
Rivaroxaban	1 (0.7)	9 (4.6)	0.04
Dabigatran	0	3 (1.5)	0.14

GI: Gastrointestinal; PUD: Peptic ulcer disease; NSAIDs: Non-steroidal anti-inflammatory drugs.

In both groups, the most common GI bleed presentation was melena (58% *vs* 68%), followed by hematemesis (41% *vs* 37.8%) and hematochezia (13% *vs* 15.3%). When nasogastric lavage was performed, more coffee ground material was noted in Ips compared to Ops (15.8% *vs* 5.1%, $P < 0.05$), however bright red blood was seen similarly in both groups (3.6% *vs* 3.1%).

The most common indications for esophagogastroduodenoscopy (EGD) in both groups were: GI bleed (44.6% *vs* 45.4%), anemia (34.5% *vs* 34.7%), melena (28.1% *vs* 25%), and hematemesis (24.5% *vs* 20.4%) (Table 2).

Diagnosis on esophagogastroduodenoscopy

In group 1, the most common diagnosis was chronic gastritis (59%) followed by esophagitis (41%) and PUD (33%). In group 2, the most common diagnosis was chronic gastritis (67%) followed by PUD (47.9%). Ops had significantly more duodenal ulcers and esophageal varices (20.4% *vs* 12%, $P = 0.05$ and 12.8% *vs* 4.3%, $P < 0.05$, respectively), whereas Ips had significantly more esophagitis (41% *vs* 24.5%, $P < 0.05$). Both groups had similar diagnoses of gastric ulcers (20.1% in Ips *vs* 27% in Ops) (Table 2).

Outcomes

More Ips received fresh frozen plasma (FFP) than Ops (23% *vs* 12.8%; $P = 0.05$), but

Table 2 Bleeding characteristics

	In-hospital GI bleed (n = 139)	GI bleed on presentation (n = 196)	P value
Bleeding type, n (%)			
Melena	81 (58.3)	133 (67.9)	0.07
Hematemesis	57 (41)	74 (37.8)	0.55
Hematochezia	18 (13)	30 (15.3)	0.54
Nasogastric lavage finding			
Bright red blood	5 (3.6)	6 (3.1)	0.79
Ground coffee	22 (15.8)	10 (5.1)	0.01
EGD indication			
GI bleed	62 (44.6)	89 (45.4)	0.88
Anemia	48 (34.5)	68 (34.7)	0.98
Melena	39 (28.1)	49 (25)	0.53
Hematemesis	34 (24.5)	40 (20.4)	0.38
Hematochezia	6 (4.3)	6 (3.1)	0.54
Maroon stools	3 (2.2)	-	0.04
Fecal occult blood positive	5 (3.6)	8 (4.1)	0.82
Abdominal pain	6 (4.3)	4 (2)	0.23
Dysphagia	1 (0.7)	2 (1)	0.77
NSAIDs use	1 (0.7)	1 (0.5)	0.81
Vomiting	2 (1.4)	3 (1.5)	0.95
Diarrhea	-	1 (0.5)	0.4
Nausea	-	1 (0.5)	0.4
Weight loss	-	1 (0.5)	0.4
Other	8 (5.8)	22 (11.2)	0.08
Diagnosis			
Chronic gastritis	82 (59)	131 (66.8)	0.14
Esophagitis	57 (41)	48 (24.5)	0.01
Other	39 (28.1)	50 (25.5)	0.6
Duodenitis	33 (23.7)	37 (18.9)	0.54
Gastric ulcer	28 (20.1)	53 (27)	0.15
Duodenal ulcer	17 (12.2)	40 (20.4)	0.05
Peptic ulcer	1 (0.7)	1 (0.5)	0.81
Acute gastritis	15 (10.8)	13 (6.6)	0.18
Angiodysplasia of stomach and duodenum	7 (5)	19 (9.7)	0.12
Ulcer of esophagus	7 (5)	8 (4.1)	0.68
Esophageal varices	6 (4.3)	25 (12.8)	0.01
Alcoholic gastritis	1 (0.7)	1 (0.5)	0.81
Gastritis and duodenitis	2 (1.4)	3 (1.5)	0.95
Gastroduodenitis, unspecified	1 (0.7)	0	0.23
Malignant neoplasm of duodenum	1 (0.7)	0	0.23
Malignant neoplasm of esophagus	2 (1.4)	2 (1)	0.73
Malignant neoplasm of stomach	2 (1.4)	2 (1)	0.73

GI: Gastrointestinal; EGD: Esophagogastroduodenoscopy; NSAIDs: Non-steroidal anti-inflammatory drugs.

both groups required packed red blood cell (PRBCs) transfusions in a similar proportion (76.3% *vs* 67.3%).

The median number of PRBCs that Ips received was higher compared to Ops (3 *vs* 2; $P < 0.05$, respectively), whereas the median number of FFP was similar (3 *vs* 2, respectively).

Both the median Rockall score and Glasgow-Blatchford score were equally elevated in both groups (5 *vs* 5 and 12 *vs* 13, respectively). Patients with liver cirrhosis had similar Child-Pugh scores in both groups (8 *vs* 8).

Patients in both groups required intensive care unit admission (41% *vs* 44.9%) and intubation (15.8% *vs* 9.2%) comparably. However, more Ips required vasopressors

compared to Ops (12.2% *vs* 4.1%; $P < 0.05$).

The mean duration of bleed was higher in Ips compared to Ops (58 h *vs* 41 h, $P < 0.05$). Bleed to EGD time was significantly shorter in Ips compared to Ops (mean \pm CI: 40.9 \pm 8.9 *vs* 57.9 \pm 8.7 h, $P < 0.05$). Ips had higher American Society of Anesthesiologists scores and lower platelet counts compared to Ops (3.7 *vs* 3.4, $P < 0.05$ and 230.3 *vs* 261.5, $P < 0.05$, respectively).

The main complication in both groups was re-bleeding occurring in similar rates (2.2% of Ips and 3.1% of Ops). Ops required more interventions after EGD ($P < 0.05$). Surgical approach was mostly used in Ops (13.7% of Ips *vs* 26.5% of Ops, $P < 0.05$) rather than interventional radiology-guided control of bleed, which was equally used in both groups (2.9% *vs* 2.6%, respectively).

The median total LOS and the length of hospitalization post-endoscopy were statistically higher in Ips compared to Ops (13 *vs* 6 d; $P < 0.05$ and 7 *vs* 4 d; $P < 0.05$) (Table 3).

Primary outcome: Mortality

The mortality rate was 6-fold higher in Ips compared to Ops (20% *vs* 3.1%, $P < 0.05$). Interestingly, the main cause of mortality was cardiovascular in Ips (10.8%), followed by sepsis (5%), multi-organ failure (4.3%), and GI bleed (2.9%). In Ops, however, the main cause of death was cardiovascular (2%), followed equally by GI bleed, sepsis, multi-organ failure, and thromboembolic events (0.5% each) (Table 3).

Multiple logistic regression analysis showed that independent predictors of mortality were in-hospital patient status [Odds ratio (OR) = 15.6, 95% confidence interval (CI): 3.2-76.6, $P = 0.01$], hematemesis type of bleeding (OR = 9.1, 95% CI: 2.7-30.4, $P = 0.01$), endoscopic finding of duodenal ulcers (OR = 4.1, 95% CI: 1.1-16.9, $P = 0.05$) and number of PRBC transfusions (OR = 1.2, 95% CI: 1.1-1.4, $P = 0.01$).

DISCUSSION

Differences in outcomes between inpatient and outpatient GI bleeders has been a topic of interest. On one hand, identifying modifiable factors that impact the outcome and prevent mortality is needed. On the other hand, as available resources are becoming scarce, limiting costs by cutting unnecessary interventions is also needed to optimize cost-effectiveness.

In our study, we aimed to compare the different characteristics of inpatient *vs* outpatient GI bleeders, and to identify any difference in the received care that could have affected the outcomes. Significantly more inpatient GI bleeders were on warfarin, anti-platelets, and steroids than outpatient bleeders. This observation was also noted in previous published studies^[30,31,35]. However, both Ips and Ops were equally on NOACs. This finding could be related to the presence of conditions that affected some Ips more than Ops, and constituted a contraindication precluding them from being on NOACs (Table 4).

In both groups, the endoscopic diagnosis revealed acid-related conditions, with chronic gastritis, PUD and esophagitis being the most common diagnoses of AUGIB. Remarkably, the chronic PPI intake prior to admission was comparable in both groups.

There was no difference in the predictive scores of re-bleeding and mortality between both groups in our study. This correlated with comparable rates of re-bleeding between Ips and Ops, which was consistent with most of the previously reported findings in the literature^[31,32,35]. However, the English study by Jairath *et al.*^[30] was the only study to show a more than twofold increased odds of re-bleeding in Ips compared to Ops, which translated into higher surgery and embolization needs for Ips that was not the case in all the other studies^[31,32,35], including ours (Table 4).

In our study, Ips were scoped earlier than Ops presenting with GI bleed. This finding is unique to our study when compared to previous ones, where time to endoscopy was equal between Ips and Ops^[30,32,35] or longer^[31]. This could have been the result of the effect of the healthcare setting and availability of resources. However, despite having an earlier endoscopic intervention, Ips experienced a six-fold increased mortality after GI bleed when compared to Ops. This rate is comparable to the fivefold increase in crude mortality in Ips compared to Ops^[30], and to that reported by the Canadian registry study of threefold greater mortality in Ips and from studies in Europe^[32,35], with five-fold greater mortality in Ips (Table 4).

Interestingly, the shorter time from bleeding to endoscopic treatment in in-hospital bleeders did not seem to counterweight their higher mortality and morbidity when compared to Ops. Both Ips and Ops died mostly from cardiovascular events in our study. The lack of correlation between the time to endoscopy and rate of mortality

Table 3 Complications and outcomes

	In-hospital GI bleed (n = 139)	GI bleed on presentation (n = 196)	P value
Transfusion, n (%)	30 (21.6)	61 (31.1)	0.05
Patients requiring PRBC	106 (76.3)	132 (67.3)	0.08
Patients requiring FFP	32 (23)	25 (12.8)	0.01
Number of PRBC median [Interquartile range] (Units)	3 [2-5]	2 [2-4]	< 0.05
Number of FFP (Units)	3 [2-5.5]	2 [2-5]	0.54
Rockall score at endoscopy	5 [4-6]	5 [3-6]	0.45
Glasgow- Blatchford score	12 [9-14]	13 [9-14.5]	0.22
Child-Pugh score in cirrhotics	8 [7-12]	8 [6-9]	0.22
Platelets at bleeding (mean +/-SD)	230.3 +/-9.9	261.5 +/-8.7	0.02
Creatinine at bleeding	1.8 +/-0.1	1.7 +/-0.1	0.77
ASA score	3.7 +/-0.05	3.4 +/-0.05	0.01
Days till bleeding in inpatients	7.2 +/-7.9		
Day of admission			
Mon-Fri	99 (71.2)	144 (73.5)	> 0.05
Sat-Sun	38 (27.3)	52 (26.5)	
Time of EGD			
Before 5 pm	119 (86.9)	166 (84.7)	> 0.05
After 5 pm	18 (13.1)	30 (15.3)	
ICU admission	57 (41)	88 (44.9)	0.51
Intubation	22 (15.8)	18 (9.2)	0.06
Vasopressors use	17 (12.2)	8 (4.1)	0.01
Complications			
Re-bleeding	3 (2.2)	6 (3.1)	0.62
Aspiration	0	0	
Perforation	0	0	
Obstruction	1 (0.7)	0	0.23
Other	4 (2.9)	11 (5.6)	0.23
Intervention after EGD			0.02
Interventional radiology guided	4 (2.9)	5 (2.6)	0.87
Surgical	19 (13.7)	52 (26.5)	0.01
Mean duration of bleed (hours)	41	58	< 0.05
Bleed to EGD time (h)	40.9 +/-4.2	57.9 +/-5.7	0.02
LOS post endoscopy (d)	7 [4-11]	4 [2-8]	< 0.05
Length of hospitalization (d)	13 [9-22]	6 [4-11]	< 0.05
Mortality	25 (20)	6 (3.1)	0.01
Cause of mortality			
Cardiovascular	15 (10.8)	4 (2)	0.01
GI bleed	4 (2.9)	1 (0.5)	0.08
Malignancy	0	0	
Multiorgan failure	6 (4.3)	1 (0.5)	0.02
Sepsis	7 (5)	1 (0.5)	0.01
Thromboembolic	0	1 (0.5)	0.4
Other	11 (7.9)	3 (1.5)	0.01

GI: Gastrointestinal; PRBCs: Packed red blood cells; FFP: Fresh frozen plasma; EGD: Esophagogastroduodenoscopy; ASA: American society of anesthesiologists; LOS: Length of stay; ICU: Intensive care unit; SD: Standard deviation.

could be possibly explained by the higher comorbidities that Ips carry.

Ips required more vasopressor use and FFP transfusions. In addition, they had a longer total LOS and length of hospitalization post-endoscopy compared to Ops, which conform with the findings of previous studies^[31,32,35]. Moreover, Ips required a higher number of PRBC transfusions.

Multiple logistic regression analysis was performed to evaluate for independent predictors of mortality. Our data showed that in-hospital patient status, hematemesis

Table 4 Comparison of current findings with previous studies

	Jairath <i>et al</i> ^[30] , 2014	Marmo <i>et al</i> ^[35] , 2014	Müller <i>et al</i> ^[31] , 2009	Klebl <i>et al</i> ^[32] , 2005	Our study
Medications at time of bleeding	Ips > Ops were taking antiplatelet agents	Ips > Ops were taking steroids and heparin Ips = Ops taking antiplatelets and anticoagulant	Ips > Ops were taking aspirin, steroids and heparin	Ips > Ops were taking proton pump inhibitors	Ips > Ops were taking heparin, antiplatelets and steroids
PRBC transfusion requirements	Ips = Ops	Ips > Ops	Ips = Ops	Ips > Ops	Ips = Ops
Hemodynamic instability	Ips > Ops	Ips > Ops	Ips = Ops	Ips = Ops regarding systolic blood pressure Ips had lower diastolic blood pressure	Ips > Ops manifested by higher pressure support requirement
Rockall score	Ips > Ops	-	-	Ips = Ops	Ips = Ops
Time to endoscopy	Ips = Ops	Ips = Ops	Ips waited longer for upper endoscopy	Ips = Ops in terms of time to endoscopy	Ips waited less for upper endoscopy
Diagnosis	Ips > Ops had more PUD Ops > Ips had variceal bleed	Ips > Ops had active bleeding lesions Ips > Ops had more gastric and duodenal ulcers	Ips = Ops had ulcers and erosions predominately	Ips = Ops had predominantly PUD	Ips = Ops had predominantly acid related conditions
ICU admissions	-	Ips > Ops	Ips > Ops	Ips = Ops	Ips = Ops
Alternative treatments	Ips > Ops required more surgical and/or radiological interventions	Ips = Ops in terms of surgery requirement	Ips = Ops in terms of surgery requirement	Ips = Ops in terms of surgery requirement	Ops > Ips required surgical interventions
Re-bleeding	Ips > Ops	Ips > Ops (slight)	Ips = Ops	Ips = Ops	Ips = Ops
LOS	Ips > Ops (x2)	Ips > Ops	Ips > Ops	-	Ips > Ops
Mortality	Ips > Ops	Ips > Ops	Ips > Ops	Ips > Ops	Ips > Ops
Death secondary to GI bleeding	-	Ips > Ops	-	Ips > Ops	Ips = Ops

Ips: Inpatients; Ops: Outpatients; ICU: Intensive care unit; PRBC: Packed red blood cell; LOS: Length of stay; PUD: Peptic ulcer disease.

type of bleeding, endoscopic finding of duodenal ulcer, and number of PRBC transfusions independently predicted mortality in our study population. Our results confirm the findings of prior studies. Additional predictors of mortality suggested by previous reports include advanced age, hemodynamic instability at presentation, red blood in nasogastric aspiration, and occurrence of re-bleeding^[36].

Many findings in this study confirm the previous studies, even though it represents the most recent study performed in a teaching hospital in the United States, and thus the latest guidelines regarding management of upper GI bleed would have been applied on our population. All previous studies concurred on Ips carrying more comorbidities than Ops.

An important limitation of our study is that comorbidities were not reported in each group, however comorbidities are considered non-modifiable factors that are inherent to the patient's characteristics. Similarly, *H. pylori* carriage rate could not always be defined. The retrospective design was also a limitation, introducing recall bias and limiting our control on the gathered data from the charts.

In conclusion, in-hospital AUGIB is associated with a significantly higher mortality and morbidity, as shown by prolonged total LOS, higher pressure support requirement, number of patients requiring FFP units, and mean number of PRBCs units used. Antithrombotic use was noted to be a prominent risk factor for in-hospital AUGIB. Remarkably, the shorter time from bleeding to endoscopic treatment in in-hospital bleeders did not seem to counterbalance their higher mortality and morbidity when compared to Ops. Larger scale studies are warranted to help discern whether this observation is related to increased comorbidities and antithrombotic use in in-hospital bleeders, and to confirm the interesting findings of our study.

ARTICLE HIGHLIGHTS

Research background

Acute upper gastrointestinal bleeding (AUGIB) is a common medical problem encountered in

the Gastroenterology field.

Research motivation

Despite major advances in medical and endoscopic therapy over the last few decades, AUGIB is still associated with high mortality and morbidity.

Research objectives

The aim of this retrospective study was to explore mortality, characteristics and outcome differences between hospitalized patients who develop AUGIB while in-hospital, and patients who initially present with AUGIB.

Research methods

This is a retrospective observational study of endoscopy-confirmed AUGIB patients who presented to Staten Island University Hospital from October 2012 to October 2016. They were divided in two groups: Group 1 comprised patients who developed AUGIB during their hospital stay; group 2 consisted of patients who initially presented with AUGIB as their main complaint. Patient characteristics, time to endoscopy, endoscopy findings and interventions, and clinical outcomes were collected and compared between groups.

Research results

A total of 336 patients were included. Group 1 consisted of 139 patients and group 2 of 196 patients. Mortality was significantly higher in the 1st group compared to the 2nd (20% *vs* 3.1%, $P \leq 0.05$). Increased length of stay (LOS) was noted in the 1st group (13 *vs* 6, $P \leq 0.05$). LOS post-endoscopy, vasopressor use, patients requiring fresh frozen plasma, and mean number of packed red blood cells units were higher in the 1st group. Group 1 patients were more likely to be on antiplatelets, anticoagulants, and corticosteroids. On the other hand, the mean time from the recognition of bleed to upper endoscopy was significantly lower in the in-hospital bleeders compared to those who initially presented with AUGIB.

Research conclusions

In-hospital AUGIB is associated with a notably higher mortality and morbidity, as shown by higher rates of vasopressor use and extended LOS. Use of antiplatelets and/or anticoagulants obviously constituted a robust risk factor for in-hospital AUGIB. Interestingly, the shorter time to endoscopic therapy in inpatient bleeders did not seem to offset the higher morbidity and mortality noted in this group.

Research perspectives

To determine whether the above observation is related to increased comorbidities and antithrombotic use in in-hospital bleeders, larger scale studies are warranted to help confirm the intriguing findings of our study and shed more light on this important matter.

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