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ORIGINAL ARTICLE

Outcomes and performance of risk scores in acute lower gastrointestinal bleeding

Aniwat Saleepol* and Uayporn Kaosombatwattana[†,‡]

*Internal Medicine Division, Jainad Narendra Hospital, Chai Nat, [†]Division of Gastroenterology, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University and [‡]Siriraj GI Endoscopy Center, Siriraj Hospital, Bangkok, Thailand

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Correspondence
Uayporn Kaosombatwattana, Division of Gastroenterology, Department of Medicine, Faculty of Medicine, Siriraj Hospital, Mahidol University, 2 Wanglang Road, Bangkoknoi, Bangkok 10700, Thailand.
Email: koigi214@gmail.com

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Abstract

Background and Aim: Treatment of acute lower gastrointestinal bleeding (LGIB) remains problematic, and clinical data is limited compared to that of upper GIB. This study aimed to describe the clinical outcomes and predictors of rebleeding and validate the performance of proposed scoring systems in patients with acute overt LGIB.
Methods: Patients with LGIB who underwent colonoscopies between 2013 and 2018 were retrospectively reviewed. Overt LGIB patients who presented within 72 h after bleeding onset were included. Demographics, comorbidities, initial management, endoscopic finding, and treatment outcomes were collected. Factors associated with rebleeding were explored, and the performance of Oakland, NOBLAD, and Strate scores regarding mortality and rebleeding were validated.
Results: A total of 537 patients from 3402 (age 72 years, 63–80) were included. Of this, 53% took antithrombotic agents and 59% required red cell transfusion, with a median of 4 red cell units. The most common diagnoses were diverticular bleeding (31.3%) and colorectal polyp/cancer (28.9%). The median time to colonoscopy was 2.3 days, and 80.3% of patients did not receive any hemostatic intervention. The 30-day mortality and rebleeding were 2.6% and 18.3%, respectively. Patients with radiation proctitis, angioectasia, diverticulosis and using dual antiplatelet drugs were associated with recurrent bleeding. The risk scores showed low performance in predicting recurrent bleeding and mortality.
Conclusion: Acute, overt LGIB was common among elders with comorbidities. The rebleeding risk was mostly linked to underlying lesions and the use of antiplatelet drugs. The performance of current risk stratification scores remains unsatisfactory and requires further development.

Introduction

Acute lower gastrointestinal bleeding (LGIB) accounts for 20% of gastrointestinal bleeding, and of this group, more than 50% require hospitalization.[1,2] Most patients are elderly and have multiple comorbidities, especially myocardial infarction, diabetes, and malignancies.[3] Although the majority of acute LGIB patients can be managed conservatively, most require in-patient intervention, including hospital admission and blood transfusion.[3,4] Data regarding treatment outcomes of LGIB in a randomized controlled design are scant compared to those of acute upper gastrointestinal bleeding (UGIB), leading to unclear clinical practices regarding risk stratification in LGIB patients, optimal time to endoscopy, appropriate hemoglobin levels, or choice of hemostatic intervention.

In the last two decades, several studies focusing on LGIB risk stratification systems have been published, including BLEED,[5] Strate,[6] Glasgow–Blatchford,[7] Newman,[8] NOBLADS,[9] and Oakland scores.[10] External validations of these scoring systems have revealed only modest performance, with the area under the receiver operating characteristic (AUROC) curve in the range of 0.72–0.95. Some scoring systems compromise detailed information, which is difficult to obtain in the emergency setting. Moreover, these scores have never been validated in Thailand.

The appropriate time for endoscopy is also an issue. Guidelines by the American College of Gastroenterology for treatment of acute gastrointestinal bleeding recommend that patients should undergo colonoscopy within 24 h.[11] Following an urgent colonoscopy, the length of stay can be reduced, probability of lesion detection improved,[12] and the homeostatic intervention rate increased.[13] However, early endoscopy does not reduce the mortality rate, rate of blood transfusion, or rate of surgery.[14,15] Moreover, the most recent randomized multicenter trial from Japan does not show any benefit of urgent colonoscopy in acute LGIB.[16] Conversely, the latest guideline from the American

College of Gastroenterology does not mention on the appropriate timing of colonoscopy, but also recommends to skip colonoscopy in selected patients if bleeding has subsided and the patient had high-quality colonoscopy done in the last 12 months.[17]

The objective of this study was to evaluate the characteristics of patients presenting acute LGIB and the therapeutic outcomes in a tertiary care center environment. Moreover, predictors of poor outcomes and the performance of risk stratification systems were also determined.

Methods

Patients. This retrospective study included patients above 18 years of age who presented acute, overt lower gastrointestinal hemorrhage and underwent colonoscopy at Siriraj Hospital, Bangkok, Thailand, between January 2013 and October 2018. The data were retrieved from the medical records at Siriraj Hospital and the endoscopic database of Siriraj GI endoscopic center. Regarding treatment for acute LGIB in this hospital, the timing for colonoscopy was based solely on the decision of the attending physician according to the clinical characteristics and bleeding severity. The indications for emergency colonoscopy usually include unstable hemodynamics and red blood hematochezia. Emergency colonoscopy can be performed by the on-call bleeding team on a 24/7 basis. If endoscopy fails, radiointervention and surgical treatment can be considered afterward. Only overt LGIB patients who presented within 72 h after bleeding onset were included. Demographics, comorbidities, initial management, endoscopic finding, and treatment outcomes were collected. Exclusion criteria were as follows: patients diagnosed with UGIB or mid-GIB, recurrent bleeding within 30 days, unable to present for follow-up within 30 days after discharge, and no definite diagnosis of the bleeding site. Unstable hemodynamics was defined as a systolic blood pressure <100 mmHg and/or heart rate (HR) >100 beats per minute.

Outcomes. The primary objective was to describe the patient characteristics and verify treatment outcomes in terms of mortality rate and recurrent bleeding rate within 30 days after index colonoscopy or after hospital discharge. The secondary objectives were to assess the rate of endoscopic intervention, surgical treatment, vascular occlusion therapy, blood transfusion, and hospitalization period. We also assessed the accuracy of the Strate score, NOBLAD score, and Oakland score regarding mortality and rebleeding prediction.

Predictor variables. We analyzed the impact of the following factors associated with rebleeding and death after acute LGIB: demographic data, clinical details at the time of diagnosis, laboratory findings at presentation of LGIB, initial management, endoscopic finding and intervention, diagnosis, post-endoscopic course, and complications.

Statistical analysis. Descriptive statistics of continuous data is presented as mean ± standard deviation or median and interquartile range (IQR) as appropriate. Categorical data are presented as frequency and percentage. Multiple logistic regression was used to identify factors associated with rebleeding and death. Univariate analysis was considered, with a *P*-value ≤0.1 to select the appropriate variable to include in the multivariable analysis. Then, multiple logistic regression was applied to assess the association between the independent variable and outcomes by the stepwise method with a statistically significant *P*-value ≤0.05.

The predicted probabilities of rebleeding and death according to the NOBLADS score, Oakland score, and Strate score were calculated. The accuracy of each score was analyzed and presented as an AUROC curve. Statistical analysis was performed using STATA version 14.

This study was approved by the Siriraj Institutional Review Board (approval no. Si 406/2019).

Table 1 Baseline characteristics of patients with acute LGIB

Factors	Total = 537 *N* (%)
Demographics	
Median age; year (IQR)	72 (63, 80)
Male gender	270 (50.3)
Comorbidities	
Diabetes	140 (26.1)
Hypertension	355 (66.1)
CAD	121 (22.5)
Cerebrovascular disease	86 (16)
Hematologic disease	46 (8.6)
Cirrhosis	28 (5.2)
Malignancy	
Gynecological	119 (22.2)
Colorectal	28 (5.2)
Prostate	18 (3.4)
Breast	11 (2.0)
Hepatopancreatobiliary	10 (1.9)
Medication used before LGIB	287 (53.4)
ASA	195 (36.3)
Clopidogrel	58 (10.8)
Warfarin	80 (14.9)
NSAIDs	7 (1.3)
NOACs	4 (0.7)
Previous history of LGIB	80 (14.9)
Hemodynamic unstable	149 (27.7)
SBP < 100 mmHg	79 (14.7)
HR > 100 bpm	113 (21)
Syncope	55 (10.2)

ASA, aspirin; bpm, beat per minute; CAD, coronary artery disease; CKD, chronic kidney disease; CVD, cerebrovascular disease; HR, heart rate; IQR, interquartile range; LGIB, lower gastrointestinal bleeding; NOACs, non-vitamin K antagonist oral anticoagulants; NSAIDs, nonsteroidal anti-inflammatory drugs; SBP, systolic blood pressure.

Results

Patient characteristics. A total of 537 patients out of 3402 were retrospectively reviewed. The median age was 72 years (IQR 63–80), with similar numbers for males and females. Sixty-seven percent of the patients were hospitalized for treatment of LGIB. A Charlson Comorbidity Index ≥1 was found in 73% of patients. Cardiovascular disease risks included hypertension, hypercholesterolemia, diabetes mellitus, and atrial fibrillation as common comorbidities (Table 1). Malignancy was

Table 2 Treatment outcomes of acute LGIB

Outcome	Total = 537 *N* (%)
PRC transfusion during admission, unit (IQR)	
1–4 units	265 (49.4)
5–10 units	45 (8.4)
>10 units	6 (1.1)
Vasopressor	8 (1.5)
Timing of endoscopy [h]; median (IQR)	54 (28–112)
<24	94 (17.5)
24–48	132 (24.6)
48–72	95 (17.7)
>72	216 (40.2)
Diagnosis	
Diverticular bleeding	168 (31.3)
Presumed	131 (24.4)
Definite	37 (6.9)
Colorectal polyp/cancer	155 (28.9)
Radiation proctitis	35 (12)
Stercoral ulcer	49 (9.1)
Hemorrhoid	33 (6.1)
Ischemic colitis	18 (3.4)
Dieulafoy's lesion	18 (3.4)
Post polypectomy	17 (3.2)
Intervention	
None	431 (80.3)
Hemoclip	61 (11.4)
APC	38 (7.1)
Rescue therapy	
Surgery	19 (3.5)
Embolization	7 (1.3)
Recurrent bleeding	97 (18.3)
Dead at discharge	9 (1.7)
Dead at 30 days	14 (2.6)
Cause of death	
Bleeding	1 (0.2)
Infection	5 (0.9)
Malignancy	5 (0.9)
CVD	2 (0.4)
Other	1 (0.2)
Length of stay, days	6 (4–10)

APC, argon plasma coagulation; CAD, coronary artery disease; CKD, chronic kidney disease; CVD, cerebrovascular disease; h, hour; IQR, interquartile range; PRC, packed red cell.

noted in 22.2% of patients, with gynecologic cancer (30.3%), colorectal cancer (23.5%), and prostate cancer (15.1%) being the three most common.

Fifteen percent of patients had a previous history of LGIB, and 53% took antithrombotic agents. Aspirin use was the most prevalent at 67.9%, while warfarin and clopidogrel use was reported by 27.9% and 20.2% of patients, respectively. Only 1.4% of patients took non-vitamin K antagonist oral anticoagulants (NOACs) at the time of data collection. The percentage of hospitalized patients who used more than one antithrombotic drug was higher than that of non-hospitalized patients (18.5% *vs* 3.1%). At the time of presentation, coagulopathy was not prevalent, as the mean INR (International Normalized Ratio) was 1.24. (Table 1).

Table 3 Factors associated with 30-day rebleeding

Factors (*N* = 97)	Odds ratio (95% CI)	*P*-value
Radiation proctitis	5.31 (2.40–11.74)	<0.001
Angioectasia	2.77 (1.04–7.39)	0.041
Diverticulosis	1.51 (1.03–2.22)	0.036
Antiplatelet		
Single	1.22 (0.72–2.09)	0.461
Dual	2.77 (1.22–6.29)	0.015

Clinical presentation and intervention. Forty-nine percent of patients passed maroon colored stool, while 27.7% had unstable hemodynamics. Abdominal pain (14%), syncope (10.2%), and alteration of mental status (3.2%) were uncommon. At the time of presentation, vasopressors were required in 1.5% of patients, and 58.9% of the cohort required red blood cell transfusion (median 4 units).

Endoscopic services were available mostly during normal working hours (518/537, 96.5%) with only 57% (306/537) of all procedures achieving good bowel preparation. The median time from bleeding onset to colonoscopy was 2.3 days (54 h, IQR 28–112 h), and 60% of patients underwent colonoscopy within 72 h.

In endoscopic diagnosis, diverticular bleeding, colorectal polyp/cancer, and radiation proctitis were the most common findings (Table 2). Hemoclips (57.5%) and argon plasma coagulation (35.8%) were commonly used in endoscopic hemostasis; however, 80.3% of patients did not receive hemostatic intervention. Rescue therapy, including surgery and embolization, was required in 3.5% and 1.3% of all cases, respectively.

Regarding post-endoscopic complications, fever was identified in 15.1%. Of these, 8.2% were diagnosed as due to an infection. The urinary tract and lung were the most common sites of infection.

Treatment outcomes. The median length of hospital stay was 6 days (4–10). In-hospital mortality was 1.7%, and 30-day mortality was 2.6% (Table 2). The leading causes of death were associated with infection and malignancy. A total of 10% of patients rebled during admission and 18.3% rebled within 28 days.

Given the low mortality, we were unable to measure the factors associated with this outcome. Afterward, we evaluated the factors associated with recurrent bleeding, which were radiation proctitis (OR 5.31, 95%CI: 2.40–11.74), angioectasia (OR 2.77, 95%CI: 1.04–7.39), diverticulosis (OR 1.51, 95% CI: 1.03–2.22), and the use of dual antiplatelet drugs (OR 2.77, 95% CI: 1.22–6.29) (Table 3).

The performance of proposed LGIB clinical risk scores are shown in AUROC curves. For 30-day rebleeding and mortality prediction, the Oakland score seems to show better performance than the Strate and NOBLAD scores. However, the overall performance was only fair (Fig. 1).

Discussion

This is the first study to evaluate the treatment outcome of patients presenting with acute LGIB in a tertiary hospital in Thailand. The condition is common in elderly patients with

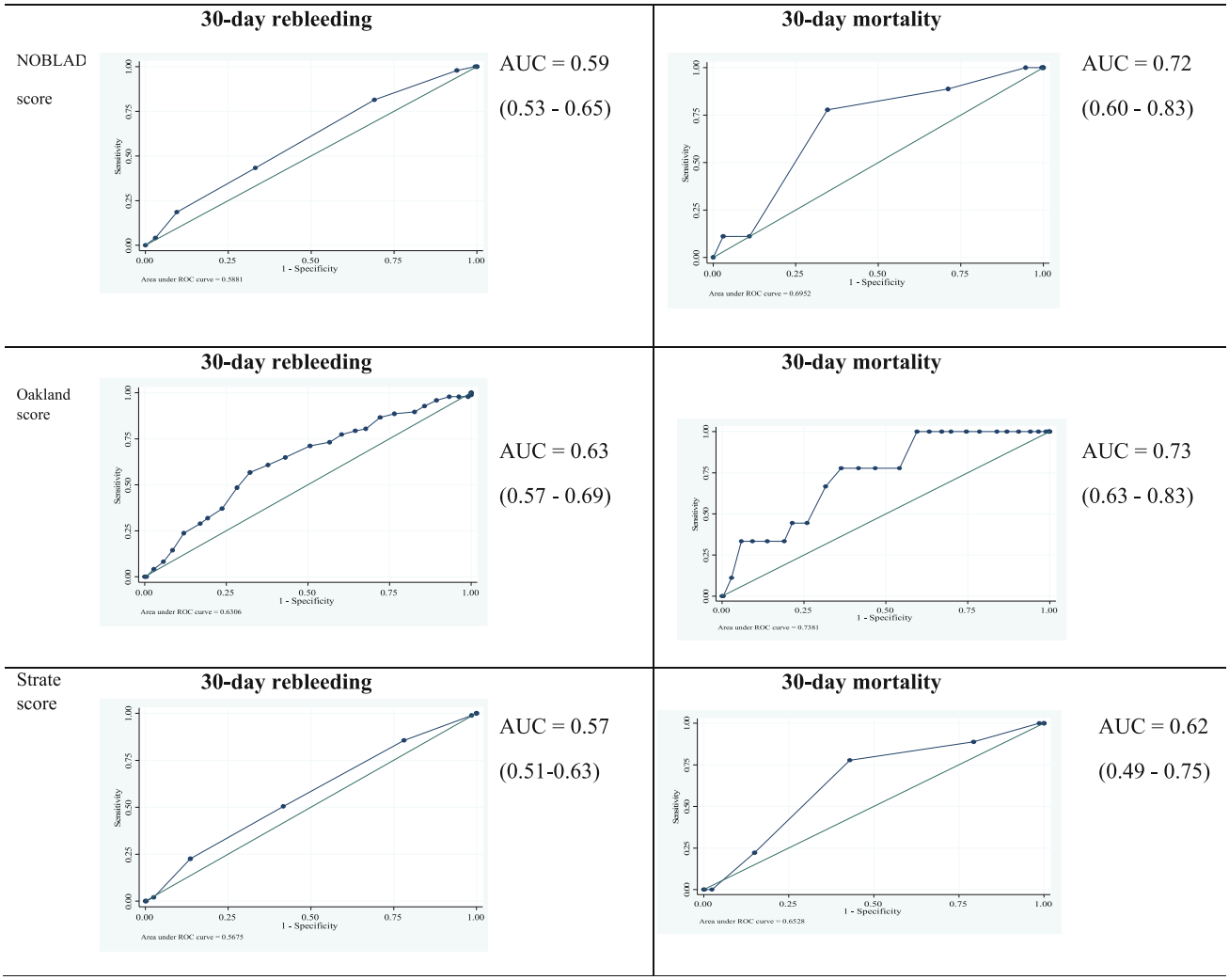

Figure 1 Areas under receiver operating characteristics curves of NOBLADS, Oakland, and Strate scores for predicting rebleeding and mortality.

multiple comorbidities, especially atherosclerotic diseases, malignancy, and the use of antithrombotic agents, which is in agreement with studies from the United Kingdom[3] and Australia.[2] Although 28% of patients had an unstable hemodynamic status, most cases were limited to tachycardia with normal blood pressure, and only 10% experienced syncope. The median hemoglobin level at presentation was 9.5 g/dL; however, blood transfusions were required in more than half of all patients, which is higher than the number reported in the UK study (only 26.3%).[3] This might be the result of a worrisome fragility of patient status, overestimation of bleeding due to a lack of effective tools to monitor bleeding status compared to the nasogastric tube in UGIB, and a lack of precise guidelines for transfusion in LGIB cases.

This study shows that mortality rates following acute LGIB are low and that the major causes of death are not bleeding-related. The considerably low fatality rate is comparable with that in an Australian study[2] and considerably lower than that reported from other population-based studies.[3,18–20] The treatment outcomes of a single tertiary care center with the full facility of endoscopy services, radiologic intervention, and surgery may be better. The rate of rebleeding in this study was 8.5%, mostly due to underlying lesions and the use of dual antiplatelet drugs. These risk factors conform to those noted in a study from Japan.[20] The most common etiology of LGIB in this cohort was diverticular bleeding. However, the majority of those cases were presumed to be diverticular bleeding, but only one-fourth were counted as definite diverticular bleeding. The intermittent and self-limiting nature of diverticular bleeding is the most likely cause of rebleeding. Unfortunately, recommendations for the optimal timing of endoscopy in acute LGIB are excluded, probably because of discordance in the outcome among the studies.[12,13,16] According to the American College of Gastroenterology guideline,[11] endoscopy within 24 h after the first presentation is recommended in high-risk patients or patients with ongoing bleeding to improve diagnostic and therapeutic yields. Conversely, the latest guideline does not mention the appropriate timing of colonoscopy, but recommends to skip colonoscopy in selected patients if bleeding has subsided and the patient had high-quality colonoscopy within the previous

12 months.[17] Nevertheless, the majority of our cohort underwent colonoscopy within 72 h, and most of them could be managed conservatively as hemostatic interventions were required only in 20% of cases.

Several risk prediction tools have been proposed for acute LGIB. However, currently no risk stratification scores can precisely predict the treatment outcomes. The Oakland score performed best in terms of rebleeding and mortality prediction. Our external validation for these scores shows a comparable performance with those of studies performed in the United Kingdom and Japan.[21]

This study has some limitations. We collected the data only for patients who underwent colonoscopy. Patients with severe, life-threatening bleeding who initially proceeded to surgery or embolization were not included. Moreover, patients who were lost to follow-up within 30 days were excluded. These exclusions might affect the lower mortality in our study. Lastly, this single, tertiary center study might not represent the treatment outcome for the overall patient population in Thailand. Although this is a retrospective study, it has several strengths: the number of patients was large, significant outcomes were described, and, last but not least, the rebleeding risk and performance of the risk stratification score were evaluated.

Conclusions

Acute LGIB was common among elderly patients with comorbidities, malignancy, and antithrombotic agent usage. The mortality rate was low compared with that of acute UGIB. Rebleeding risk was mainly related to underlying lesions and the use of dual antiplatelet drugs. Novel risk stratification scores with higher performance are required for better outcome prediction.

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