A Clinical Predictive Model for Risk Stratification of Patients with Severe Acute Lower Gastrointestinal Bleeding

Manraj Singh (✉ Upstart.manraj@gmail.com)  
Singapore General Hospital  https://orcid.org/0000-0003-0928-257X

Jayne Chiang  
Singapore General Hospital

Andre Seah  
Singapore General Hospital

Nan Liu  
SingHealth Duke-NUS Academic Medical Centre

Ronnie Mathew  
Singapore General Hospital

Sachin Mathur  
Singapore General Hospital

Research article

Keywords: Lower gastrointestinal bleeding, predictive model

DOI: https://doi.org/10.21203/rs.3.rs-768939/v1

License: ☺ ☑ This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License
Abstract

**Background:** Lower Gastro-Intestinal Bleeding (LGIB) is a common presentation of surgical admissions, imposing a significant burden on healthcare costs and resources. There is a paucity of standardised clinical predictive tools available for the initial assessment and risk stratification of patients with LGIB. We propose a simple clinical scoring model to prognosticate patients at risk of severe LGIB and an algorithm to guide management of such patients.

**Methods:** A retrospective cohort study was conducted, identifying consecutive patients admitted to our institution for LGIB over a 1-year period. Baseline demographics, clinical parameters at initial presentation and treatment interventions were recorded. Severe LGIB was the primary outcome measure. Multivariate logistic regression was performed to identify factors predictive of severe LGIB. A clinical management algorithm was developed to discriminate between patients requiring admission, and to guide endoscopic, angiographic and/or surgical intervention.

**Results:** 226/649 (34.8%) patients had severe LGIB. Six variables were entered into a clinical predictive model for risk stratification of LGIB: Tachycardia (HR\(\geq 100\)), hypotension (SBP\(<90\text{mmHg}\)), anemia (Hb\(<9\text{g/dL}\)), metabolic acidosis, use of antiplatelet/anticoagulants, and active per-rectal bleeding. The optimum cut-off score of \(\geq 1\) had a sensitivity of 91.9%, specificity of 39.8%, and Positive and Negative Predictive Values of 45% and 90.2% respectively for predicting severe LGIB. The Area Under Curve (AUC) was 0.77.B

**Conclusion:** Early diagnosis and management of severe LGIB remains a challenge for the acute care surgeon. The predictive model described comprises objective clinical parameters routinely obtained at initial triage to guide risk stratification, disposition and inpatient management of patients.

**Background**

Lower Gastrointestinal Bleeding (LGIB), defined as bleeding distal to the ligament of Treitz, remains a common presenting symptom for emergency general surgical patients. The annual incidence (20–30 cases per 100,000 adults) rises 200-fold between the 3rd and 9th decade of life. (1, 2) Amongst the elderly, the morbidity secondary to LGIB is exacerbated due to the interplay of multiple comorbidities, use of antiplatelet and/or anticoagulants and poor functional reserves. (3)

The complexity in management of patients with LGIB relates to the wide spectrum of aetiologies, spanning benign and malignant disease, affecting the small and large intestine as well as anal canal. The presentation varies widely between stable hemorrhoidal bleeding requiring outpatient management to exsanguinating colonic bleeding that may require a colectomy. For these presentations and everything in between, a well-developed diagnostic, investigative and therapeutic strategy is required to resuscitate, localise and then treat the underlying pathology. As there is no ‘one size fits all’, LGIB management remains difficult to protocolise.
Timely recognition of severe LGIB is crucial in implementing effective management pathways. However, few clinical predictive tools for prognostication of LGIB exist in the literature. Furthermore, none have been validated in Asian populations. (4) In this study, we aim to identify predictors of severe LGIB and develop a predictive model. Furthermore, we aim to develop an algorithm for the management of patients with LGIB.

**Materials And Methods**

A retrospective cohort study was conducted of adult (≥ 21-years-old) patients admitted via the Emergency Department (ED) to our institution over a 12-month period from July 2016 to June 2017. Patients with an ICD coding of “lower gastrointestinal bleeding” (LGIB) or “per-rectal bleeding” from the ED database and inpatient discharge summaries were identified.

LGIB was defined as gastrointestinal bleeding originating distal to the ligament of Treitz confirmed via digital per-rectal examination and / or endoscopy. Our definition of severe LGIB was modified from Strate’s: Presence of bleeding necessitating 2 or more units of packed red blood cell transfusion within the first 24-hours of admission, re-bleeding after 24-hours of clinical stability and/or the need for additional transfusion beyond 24-hours. (5) Those with UGIB (upper gastrointestinal bleeding), as defined by the presence of hematemesis, melena and with endoscopic confirmation of a bleeding source proximal to the ligament of Treitz were excluded. The study protocol was approved by the local Institutional Review Board.

**Statistical Analysis**

Patient demographics, clinical parameters and biochemistry on admission were presented as dichotomised variables. Categorical variables were analysed with the Pearson X² or Fisher exact test, while continuous variables were analysed with a paired T-test or Mann-Whitney U. Severe and non-severe LGIB were used to stratify the aetiology of bleeding, therapeutic intervention as well as severity outcome measures such as mortality and ICU admission.

Univariate predictors of severe LGIB were determined and those that were statistically significant entered into a multivariate logistic regression model using backward selection. Odds ratios (OR) were generated for the effect of individual variables with 95% confidence intervals. Factors significant on multivariable analysis were incorporated into a 6-point clinical predictive model. The sensitivity, specificity, positive (PPV) and negative predictive values (PPV) were calculated based on the cumulative increase in score of the model. A Receiver Operating Statistics (ROC) curve was plotted and the Area Under Curve (AUC) calculated to assess the performance of the model in predicting severe LGIB.

P-values less than 0.05 were considered statistically significant. All statistical analysis was performed using SPSS Statistics for Windows v25.0 (Armonk, NY: IBM Corp)
Results

There were 649 patients admitted with acute LGIB during the study period, of which 226 (34.8%) were designated severe and 423 (65.2%) non-severe. The demographics and clinical parameters are described in Table 1. Most patients (n = 469/649, 72.3%) were above 60 years of age [mean 67(± SD15)]. The M:F ratio was 54:46 respectively and the majority were of Chinese ethnicity (n = 576/649, 88.8%). Almost two-thirds of patients had a Charlson Comorbidity (CCM) (6) score of 2 or more, which had higher incidence in those with severe LGIB (71.2% vs 64.3%, \( P = 0.07 \)). The use of antiplatelet or anticoagulant medications was higher in the severe LGIB cohort (38.1% vs 29.1%, \( P = 0.02 \)).
| Variable                        | Total Cohort | Severe Bleed | Non-Severe Bleed n = 423 (%) | P-Value |
|--------------------------------|--------------|--------------|------------------------------|---------|
|                                | n = 649 (%)  | n = 226 (%)  |                              |         |
| Mean Age, y (± SD)             | 67.3 (15.2)  | 68.3 (15.0)  | 66.7 (15.3)                  | 0.65    |
| < 60                           | 180 (27.7)   | 59 (26.1)    | 121 (28.6)                   | 0.50    |
| ≥ 60                           | 469 (72.3)   | 167 (73.9)   | 302 (71.4)                   |         |
| Gender                         |              |              |                              |         |
| Male                           | 351 (54.1)   | 121 (53.5)   | 230 (54.4)                   | 0.84    |
| Female                         | 298 (45.9)   | 105 (46.5)   | 193 (45.6)                   |         |
| Race                           |              |              |                              | 0.053   |
| Chinese                        | 576 (88.8)   | 203 (89.8)   | 373 (88.2)                   |         |
| Malay                          | 40 (6.2)     | 18 (8.0)     | 22 (5.2)                     |         |
| Indian                         | 16 (2.5)     | 3 (1.3)      | 13 (3.1)                     |         |
| Others                         | 17 (2.6)     | 2 (0.9)      | 15 (3.5)                     |         |
| CCM<a Score                    |              |              |                              | 0.074   |
| ≤ 2                            | 216 (33.3)   | 65 (28.8)    | 151 (35.7)                   |         |
| > 2                            | 433 (66.7)   | 161 (71.2)   | 272 (64.3)                   |         |
| CKD<b                          |              |              |                              | 0.009   |
| Recent NSAID<sup>c</sup> Use   | 67 (10.3)    | 33 (14.6)    | 34 (8.0)                     |         |
| Antiplatelet/                  |              |              |                              | 0.02    |
| coagulant use                  | 209 (32.2)   | 86 (38.1)    | 123 (29.1)                   |         |
| Median duration of bleeding,   |              |              |                              | 0.65    |
| days (IQR<sup>d</sup>)        | 1 (1–4)      | 1 (1–3)      | 2 (1–4)                      |         |

<sup>a</sup>CCM: Charlson Comorbidity; <sup>b</sup>CKD: Chronic Kidney Disease; <sup>c</sup>NSAID: Non-steroidal anti-inflammatory drugs; <sup>d</sup>IQR: Inter-Quartile Range

At initial presentation in ED, patients in the severe LGIB cohort were more likely to have active per-rectal bleeding (43.8% vs 30.3%, P = 0.001, Table 2), tachycardia (HR ≥ 100, 22.6% vs 9.5%, P< 0.001), hypotension (SBP < 90mmHg, 6.2% vs 0.5%, P< 0.001) and anemia (Hb < 9g/dL, 46.9% vs 5.0%, P< 0.001). Acute Kidney Injury (AKI) was seen in a third of patients, with 45.1% in the severe cohort vs 27.0%
in the non-severe group ($P < 0.001$). Metabolic acidosis, as reflected by a low serum bicarbonate, was seen more frequently in the severe LGIB cohort (12.8% vs 3.8%, $P < 0.001$). Two patients (0.3%) presented with cardiovascular collapse secondary to ongoing rapid haemorrhage.
| Variable                  | Total Cohort n = 649 (%) | Severe Bleed n = 226 (%) | Non-Severe Bleed n = 423 (%) | P Value |
|---------------------------|--------------------------|--------------------------|------------------------------|---------|
| HRa (SD)                  | 83 (16)                  | 86 (17)                  | 81 (15)                      | 0.009   |
| ≥ 100                     | 91 (14.0)                | 51 (22.6)                | 40 (9.5)                     | < 0.001 |
| < 100                     | 558 (86.0)               | 175 (77.4)               | 383 (90.5)                   |         |
| SBPb, mmHg (SD)           | 134.8 (25.3)             | 126 (27)                 | 140 (23)                     | 0.002   |
| < 90                      | 16 (2.5)                 | 14 (6.2)                 | 2 (0.5)                      | < 0.001 |
| ≥ 90                      | 633 (97.5)               | 212 (93.8)               | 421 (99.5)                   |         |
| DBPc, mmHg (SD)           | 72 (13)                  | 66 (13)                  | 75 (12)                      | 0.001   |
| MAPd, mmHg (SD)           | 93 (16)                  | 86 (16)                  | 96 (14)                      | 0.48    |
| < 65                      | 14 (2.2)                 | 11 (4.9)                 | 3 (0.7)                      | 0.001   |
| ≥ 65                      | 632 (97.4)               | 212 (93.8)               | 420 (99.3)                   |         |
| Hb e, g/dL (SD)           | 11.3 (2.8)               | 9.1 (2.6)                | 12.5 (2.1)                   | < 0.001 |
| < 9                       | 127 (19.6)               | 106 (46.9)               | 21 (5.0)                     | < 0.001 |
| ≥ 9                       | 521 (80.3)               | 120 (53.1)               | 401 (94.8)                   |         |
| Hctf, % (SD)              | 34.4 (7.7)               | 28.5 (7.4)               | 37.6 (5.8)                   | < 0.001 |
| > 35                      | 344 (53.0)               | 46 (20.4)                | 298 (70.4)                   | < 0.001 |
| ≤ 35                      | 304 (46.8)               | 180 (79.6)               | 124 (29.3)                   |         |
| AKIg                      | 216 (33.3)               | 102 (45.1)               | 114 (27.0)                   | < 0.001 |
| Coagulopathy, INR h ≥ 1.5 | 27 (4.2)                 | 14 (6.2)                 | 13 (3.1)                     | 0.08    |
| HCO3, mEq/L (SD)          | 23.9 (3.0)               | 22.8 (3.3)               | 24.5 (2.6)                   | 0.003   |
| ≤ 19                      | 45 (6.9)                 | 29 (12.8)                | 16 (3.8)                     | < 0.001 |
| > 19                      | 594 (91.5)               | 193 (85.4)               | 401 (94.8)                   |         |

aHR: Heart rate; bSBP: Systolic blood pressure; cDBP: Diastolic blood pressure; dMAP: Mean arterial pressure; eHb: Hemoglobin; fHct: Hematocrit; gAKI: Acute kidney injury; hINR: International Normalised Ratio; iHCO3: Bicarbonate (acidosis)
| Variable                  | Total Cohort n = 649 (%) | Severe Bleed n = 226 (%) | Non-Severe Bleed n = 423 (%) | P Value |
|--------------------------|--------------------------|--------------------------|-----------------------------|---------|
| Active PR Bleed          | 227 (35.0)               | 99 (43.8)                | 128 (30.3)                  | 0.001   |
| Cardiovascular Collapse  | 2 (0.3)                  | 2 (0.9)                  | 0 (0)                       | 0.12    |

aN: Heart rate; bSBP: Systolic blood pressure; cDBP: Diastolic blood pressure; dMAP: Mean arterial pressure; eHb: Hemoglobin; fHct: Hematocrit; gAKI: Acute kidney injury; hINR: International Normalised Ratio; iHCO3: Bicarbonate (acidosis)

The distribution of aetiologies for LGIB is described in Table 3. The majority of patients had bleeding secondary to haemorrhoids (36.4%), diverticular disease (32.5%) and colorectal cancer (15.1%). Less frequent causes included colitis and proctitis (9.2%), post-polypectomy or haemorrhoidectomy bleeding (1.4%), solitary rectal ulcers (SRUS, 1.7%) and small bowel bleed (0.3%). There was a higher incidence of diverticular bleeding in the severe LGIB group (46.9% vs 24.8%). The majority of non-severe LGIB were due to haemorrhoids (42.6%). Sixteen (2.4%) patients had inconclusive investigations, or declined workup due to age or financial concerns. We postulate that a number of these were AVMs (Arteriovenous Malformation).
Table 3

Etiology of LGIB

|                      | Total Cohort n = 649 (%) | Severe Bleed n = 226 (%) | Non-Severe Bleed n = 423 (%) |
|----------------------|--------------------------|--------------------------|-----------------------------|
| Hemorrhoids          | 236 (36.4)               | 56 (24.8)                | 180 (42.6)                  |
| Diverticular Disease | 211 (32.5)               | 106 (46.9)               | 105 (24.8)                  |
| Colorectal Malignancy| 98 (15.1)                | 32 (7.6)                 | 66 (15.6)                   |
| Colitis              | 39 (6.0)                 | 7 (3.1)                  | 32 (7.6)                    |
| Radiation Proctitis  | 21 (3.2)                 | 6 (2.7)                  | 15 (3.5)                    |
| SRUS<sup>a</sup>     | 11 (1.7)                 | 5 (2.2)                  | 6 (1.4)                     |
| Postoperative bleeding<sup>b</sup> | 9 (1.4) | 3 (1.3) | 6 (1.4) |
| Perianal disease<sup>c</sup> | 4 (0.6) | 1 (0.4) | 3 (0.7) |
| Rectal Prolapse      | 1 (0.1)                  | 0 (0)                    | 1 (0.2)                     |
| Abernathy Lesion     | 1 (0.1)                  | 1 (0.4)                  | 0 (0)                       |
| Small bowel bleed    | 2 (0.3)                  | 2 (0.9)                  | 0 (0)                       |
| Unknown (includes AVM<sup>d</sup>) | 16 (2.4) | 7 (3.1) | 9 (2.1) |

<sup>a</sup> SRUS: Solitary rectal ulcer syndrome; <sup>b</sup> Post-op bleeding (post-polypectomy, hemorrhoidectomy); <sup>c</sup> Perianal fissure, hematoma or fistula; <sup>d</sup> AVM: Arteriovenous Malformation

Table 4 outlines the differences in therapeutic intervention and clinical outcomes between severe and non-severe LGIB patients. More than a third of patients required packed cells transfusion (n = 212/649, 36.7%), with 89.1% (n = 212/238) receiving their first transfusion within 24-hours, and 65.9% (n = 149/226) of those with severe LGIB receiving 2 or more units. Overall, 362 patients (55.8%) underwent endoscopic evaluation during the admission of which 123 (19%) were performed within 24-hours (24H). More patients in the severe LGIB group underwent endoscopic evaluation (65.5% vs 50.6%, P<0.001). There was no significant difference in the incidence of early endoscopy within 24-hours between both strata. Eleven patients (1.7%) underwent angio-embolisation, all of whom were from the severe LGIB cohort – 2 received it within 24-hours of admission.

Five patients (0.8%) required admission to the Intensive Care Unit (ICU). The 72-hour mortality rate was 0.2% (1 patient) and 30-day mortality was 0.5% (3 patients); all were from the severe LGIB group. The median length of stay was significantly longer in the severe LGIB group (5 vs 3 days, P<0.001).
| Variable                              | Total Cohort (n = 649) | Severe Bleed (n = 226) | Non-Severe Bleed (n = 423) | P Value |
|---------------------------------------|------------------------|------------------------|---------------------------|---------|
| Rebleeding during admission          | 106 (16.3)             | 106 (46.9)             | 0 (0)                     | < 0.001 |
| Required blood transfusion            | 238 (36.7)             | 204 (90.3)             | 34 (8.0)                  | < 0.001 |
| Blood transfusion within 24H          | 212 (32.7)             | 178 (78.8)             | 34 (8.0)                  | < 0.001 |
| ≥ 2 PCT<sup>a</sup>                   | 149 (23.0)             | 149 (65.9)             | 0 (0)                     | < 0.001 |
| Median PCT (IQR)                      | 0 (0–2)                | 2 (2–4)                | 0 (0)                     | < 0.001 |
| Endoscopy                             | 362 (55.8)             | 148 (65.5)             | 214 (50.6)                | < 0.001 |
| OGD                                   | 190 (29.3)             | 107 (47.3)             | 83 (19.6)                 | < 0.001 |
| Colonoscopy                           | 314 (48.4)             | 121 (53.5)             | 193 (45.6)                | 0.06    |
| Sigmoidoscopy                         | 42 (6.5)               | 21 (9.3)               | 21 (5.0)                  | 0.033   |
| Endoscopy < 24H                       | 123 (19.0)             | 42 (18.6)              | 81 (19.1)                 | 0.86    |
| Surgery                               | 48 (7.4)               | 23 (10.2)              | 25 (5.9)                  | 0.048   |
| Surgery < 24H                         | 12 (1.8)               | 3 (1.3)                | 9 (2.1)                   | 0.56    |
| Angioembolisation                     | 11 (1.7)               | 11 (4.9)               | 0 (0)                     | < 0.001 |
| Angioembolisation < 24H               | 2 (0.3)                | 2 (0.9)                | 0 (0)                     | 0.12    |
| ICU stay < 24H                        | 5 (0.8)                | 5 (2.2)                | 0 (0)                     | 0.005   |
| Median length of stay (IQR)           | 3 (2–5)                | 5 (3–7)                | 3 (2–4)                   | < 0.001 |
| 72H Mortality                         | 1 (0.2)                | 1 (0.4)                | 0 (0)                     | 0.35    |
| 30 Day Mortality                      | 3 (0.5)                | 3 (1.3)                | 0 (0)                     | 0.042   |

<sup>a</sup>PCT: Packed Red Blood Cell Transfusion, in units. Values in parentheses are percentages

Forty-eight patients (7.4%) required surgical intervention during the index admission, with a larger proportion from the severe LGIB group (10.2% vs 5.9%, Table 5). There was no statistically significant difference in incidence of emergency surgery within 24-hours between both strata. The most common operative procedures in our cohort were haemorrhoidectomy (n = 24/48, 50%, Table 5) and colectomy (n = 11/48, 22.9%). Most patients who required early surgery within 24-hours had profound haemorrhoidal bleeding requiring haemorrhoidectomy and haemostasis (n = 8/12, 75%). One underwent a right
hemicolectomy for massive bleeding from right-sided diverticula, and two underwent colostomy creation with haemostasis for large ulcerated and obstructing rectal tumours.

Table 5
Surgical Intervention across the cohort and within 24H of admission

| Surgical Intervention                                      | n (%) |
|------------------------------------------------------------|-------|
| Emergency Surgery during admission (total cohort)          | 48 (7.4) |
| Hemorrhoidectomy                                           | 24 (3.7) |
| Colectomy                                                  | 11 (1.7) |
| Colostomy                                                  | 10 (1.5) |
| Small bowel resection                                      | 3 (0.5) |
| Emergency Surgery within 24H of admission                  | 12 (1.8) |
| Hemorrhoidectomy, EUA and hemostasis                       | 8 (1.2) |
| Colostomy                                                  | 2 (0.3) |
| Laparotomy, enterotomy, endoscopic clipping of jejunal AVM | 1 (0.2) |
| Right hemicolecotomy                                       | 1 (0.2) |

aEUA: Examination Under Anesthesia; bAVM: Arteriovenous Malformation

Logistic Regression

Table 6 shows the univariate predictors of severe LGIB. Significant predictors (P < 0.05) included: tachycardia (HR ≥ 100), hypotension (SBP < 90 mmHg or MAP < 65 mmHg), anaemia (Hb < 9 g/dL), low haematocrit (< 35%), metabolic acidosis (serum bicarbonate ≤ 19 mEq/dL), antiplatelet and/or anticoagulant use, active per-rectal bleeding, and acute kidney injury.

These variables were entered into a multivariate logistic regression model – only tachycardia, hypotension, anaemia, active per-rectal bleeding, antiplatelet and/or anticoagulant use and metabolic acidosis were statistically significant in predicting severe LGIB (Table 6). These 6 variables were used to construct a prognostic scoring model, with 1 point allocated for each risk factor (Table 7). The optimum cut-off was defined as ≥ 1 point, where sensitivity was 91.9%, specificity 39.8%, positive predictive value (PPV) 45.0% and negative predictive value (NPV) 90.2% in predicting severe LGIB (Table 8). The AUC (Fig. 1) of the model was 0.77 (P < 0.001, 95% CI 0.73–0.81).
### Table 6
Univariable and multivariable logistic regression analysis for predictive factors of severe LGIB

| Variable                        | Univariate Analysis | Multivariable analysis |
|--------------------------------|---------------------|------------------------|
|                                | Odds Ratio (95% CI) | P-value | Odds Ratio (95% CI) | P-value |
| Age > 60                       | 1.13 (0.79–1.63)    | 0.5      | -                   |
| Gender, Male                   | 1.03 (0.75–1.43)    | 0.84     | -                   |
| CCM\(^a\) >2                  | 1.38 (0.97–1.95)    | 0.075    | -                   |
| CKD\(^b\)                      | 1.96 (1.18–3.26)    | 0.01     | -                   |
| Antiplatelet/ anticoagulant    | 1.50 (1.07–2.11)    | 0.02     | 1.93 (1.26–2.94)    | 0.002   |
| Active PRB\(^c\)              | 1.80 (1.29–2.51)    | 0.001    | 2.36 (1.55–3.59)    | < 0.001 |
| HR\(^d\) ≥ 100                | 2.79 (1.78–4.38)    | < 0.001  | 3.74 (2.17–6.46)    | < 0.001 |
| SBP\(^e\) < 90                | 13.91 (3.13–61.73)  | 0.001    | 15.46 (3.12–76.73)  | < 0.001 |
| MAP\(^f\) < 65                | 7.26 (2.01–26.32)   | 0.003    | -                   |
| Hb\(^g\) < 9                  | 16.87 (10.12–28.11) | < 0.001  | 20.74 (11.89–36.17) | < 0.001 |
| Hct\(^h\) < 35%               | 9.40 (6.40–13.83)   | < 0.001  | -                   |
| AKI/AOCKD\(^i\)               | 2.22 (1.58–3.12)    | < 0.001  | -                   |
| INR\(^i\) ≥ 1.5               | 1.97 (0.91–4.28)    | 0.085    | -                   |
| HCO3\(^k\) ≤ 19               | 3.77 (2.00–7.10)    | < 0.001  | 3.69 (1.65–8.22)    | 0.001   |

\(^a\) CCM: Charlson Comorbidity Index; \(^b\) CKD: Chronic kidney disease; \(^c\) PRB: PR bleeding; \(^d\) HR: Heart rate; \(^e\) SBP: Systolic blood pressure; \(^f\) MAP: Mean arterial pressure; \(^g\) Hb: Hemoglobin; \(^h\) Hct: Hematocrit; \(^i\) AKI: Acute kidney injury, AOCKD: Acute on chronic kidney disease; \(^j\) INR: International Normalised Ratio; \(^k\) HCO3: Bicarbonate (acidosis)
Table 7
Prognostic factors for severe LGIB for inclusion in our clinical predictive model

| Clinical Predictive Risk Factor          | Score (Points) |
|------------------------------------------|----------------|
| Tachycardia HR ≥ 100                     | 1              |
| Hypotension SBP < 90 mmHg                | 1              |
| Anemia Hb < 9g / dL                      | 1              |
| Active PR bleeding                       | 1              |
| Antiplatelet/ Anticoagulant use          | 1              |
| Metabolic Acidosis HCO3 ≤ 19             | 1              |

Table 8
Clinical predictive model for severe LGIB with sensitivity, specificity, PPV and NPV

| Score | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) |
|-------|-----------------|-----------------|---------|---------|
| ≥ 1   | 91.9            | 39.8            | 45      | 90.2    |
| ≥ 2   | 57              | 83.9            | 65.5    | 78.5    |
| ≥ 3   | 18.8            | 97.8            | 82.4    | 69.3    |
| ≥ 4   | 3.1             | 100             | 100     | 65.9    |
| ≥ 5   | 0.4             | 100             | 100     | 65.3    |

*No patient had a maximum score of 6

Algorithm For Management Of LGIB

Figure 2 shows our proposed algorithm for managing patients with LGIB. Patients with 0 points derived from the multivariate model may be categorised into a non-severe LGIB, lower risk group. These patients may be either discharged with plans for early outpatient endoscopic evaluation after a period of observation, or may be admitted for endoscopic evaluation if 1 predictive factor is met. Patients with ≥ 1 point (severe LGIB) should be admitted, with hemodynamically stable patients proceeding for early endoscopic evaluation. Hemodynamically unstable patients should undergo urgent CT mesenteric angiogram (CTMA) and if indicated, angioembolisation. Once adequately resuscitated, an esophagogastroduodenoscopy (OGD) is useful to rule out an upper gastrointestinal source; early colonoscopy can be performed in the same setting. Patients with severe LGIB that recurs or is refractory to angioembolisation and/or endoscopic intervention must be considered for colectomy.
Discussion

Admissions for acute LGIB represent a wide spectrum of presentations from a minor bleed in hemodynamically stable patients to massive haemorrhage complicated by hypovolemic shock. Most cases of LGIB may resolve spontaneously in up to 85% of patients, allowing for potential discharge with outpatient follow up. (7) Overall prognosis is favourable, with mortality rates ranging from 2 to 10%. (2, 8) For the acute care surgeon, early dichotomisation of patients into severe versus non-severe LGIB categories may assist with timely investigations and management after initial resuscitation. In this study we have shown that our predictive model stratifies patients with severe LGIB utilising six objective variables obtained at initial presentation: active per-rectal bleed, use of antiplatelets and/or anticoagulants, tachycardia, hypotension, anaemia and/or metabolic acidosis.

Whereas multiple risk stratification systems have been validated for patients with upper gastrointestinal bleeding (UGIB), few predictive models for patients with severe LGIB currently exist. Heterogeneous resource availability and varied clinician experience worldwide has led to a lack of standardized international protocols for LGIB management. Furthermore, none have been validated in Asian populations. (9) The clinical predictive model described in the current study utilises real world and easily obtainable parameters, where the statistical likelihood of severe LGIB increases with each cumulative factor added (Table 8). Those scoring ≥ 1 point comprise a higher risk group for severe LGIB, while those scoring 0 points could potentially be managed in the outpatient setting (Fig. 2). In general, there was strong concordance of risk factors in the existing literature with the findings from our study. (10)

Previous attempts have been made to risk stratify LGIB patients utilising re-bleeding, intervention rates and mortality as the end-points. In the BLEED study, re-bleeding was validated as a predictive tool for poor prognosis. Kollef et al cited active bleed, hypotension, altered mental status and an elevated prothrombin time as predictive factors, however the tool was deemed too complex for practical use in an acute setting. (11–13) Das et al constructed an Artificial Neural Network (ANN) model that outperformed the BLEED criteria in predicting mortality, recurrent bleed and need for intervention. This model used non-endoscopic data made available at triage, including low haematocrit and known history of diverticular disease or arteriovenous malformation. (14) Strate et al prospectively validated a predictive model for severe LGIB requiring 3 of 7 clinical risk factors to be satisfied – tachycardia, low systolic blood pressure, syncope, non-tender abdominal examination, per-rectal bleed in the first 4-hours of medical assessment, aspirin use and more than 2 active comorbid diseases. (15) Each of these models report heterogeneous primary and secondary outcomes, limiting parallel comparisons of their performance. (16) Furthermore, some incorporated factors that may not be readily available or investigated upfront in the acute setting, such as undiagnosed diverticular disease or prothrombin time.

Thirty-day mortality was investigated as an endpoint by Sengupta et al. Advanced age, CKD, hypoalbuminemia, low haematocrit, chronic obstructive pulmonary disease, anticoagulant use, cognitive
Impairment and metastatic cancer were identified as independent negative prognostic factors. (17) In the current study, we found that age and CCM scores (as a surrogate marker of significant medical comorbidities) were not independently predictive of severe LGIB. Only CKD was positively correlated on multivariable analysis. Hypoalbuminemia (defined by serum albumin < 30g/dL) was also incorporated into the HAKA score developed by Chong et al and is generally a marker of poor nutrition and overall poor health status. (18) Its role as prognosticator for mortality has been well documented in predictive risk models for UGIB, including the Blatchford and AIMS-65. (19, 20) However, as serum albumin is not a routine investigation for patients acutely presenting with LGIB, its role in predicting severity remains to be further elucidated.

The incidence of LGIB increases with age and associated comorbidities, presumably due to higher prevalence of diverticulosis and underlying vascular pathology. (21) The mean age in our cohort was 67, with two-thirds having 2 or more comorbidities. The higher use of anticoagulant/antiplatelet medications in this cohort (30%) may suggest why they were over-represented in the severe LGIB group. Antithrombotic therapy is associated with an increased risk of LGIB leading to bleeding from latent lesions such as colonic diverticula or arteriovenous malformations. Management of such agents should form an initial step in the treatment of LGIB. Though these medications are typically withheld following acute admission, the platelet and coagulation factor dysfunction is not easily reversed. Although warfarin reversal is well established, patients on novel anticoagulants (NOACs) remain a challenge due to the potency of these drugs and lack of a complete reversal agent. (22–24) In managing these patients, a haematologist should be consulted and fresh frozen plasma, prothrombin complex concentrate (or specific reversal agent) must be considered in cases of ongoing severe haemorrhage.

The differential diagnosis for acute LGIB can vary widely, and are well published in Western literature, with the most common being diverticulosis (47.5%), colorectal polyps (20.4%) and hemorrhoids (16.9%). (25, 26) The prevalence of colonic diverticulosis increases with age, and can result in massive and recurrent bleeding between 14–38% of patients. In contrast to the Western population where most of the disease burden is on the left side, amongst Asians, diverticula are predominantly located in the right colon. Between 50–90% of all diverticular bleeding originates from the right side, which is in line with the high incidence of diverticular bleeding in our cohort, comprising almost 50% of all severe LGIB. (27) Bai et al, in a systematic analysis of 53951 patients in the Chinese literature, reported a higher incidence of LGIB secondary to underlying colorectal malignancy (24.4%) and polyps (24.1%), with the remainder attributed to colitis (16.8%), anorectal disease (9.8%) and inflammatory bowel disease (9.5%). (28) In the current study, we reported a higher incidence of haemorrhoidal bleeding (36.4%), of which the majority were non-severe LGIB. The higher incidence of haemorrhoidal bleeding may account for the shorter median length of stay of 3 days which in turn may result from selection bias in our local context with easier access to tertiary healthcare, as compared to other jurisdictions. Small bowel bleeding remains relatively uncommon (0.3%) but may be as high as 2–9% of LGIB in the literature, with angiodysplastic lesions being most prominent. (29, 30) It is an important differential to consider in LGIB patients with normal endoscopic findings necessitating further investigation with video capsule endoscopy or double balloon enteroscopy.
The algorithm described represents an evidence-based approach to LGIB management (Fig. 2). Colonoscopic evaluation is widely accepted as an initial modality for evaluation of LGIB. In our cohort, 55% underwent colonoscopy/flexible sigmoidoscopy, of which 39.8% were performed within 24-hours. As most LGIB resolves spontaneously, colonoscopy can be performed semi-electively – by waiting for 24-hours or more following admission, a patient may be optimised with blood transfusions and formal bowel preparation. Ghassemi et al reported that urgent colonoscopy for LGIB after cleansing with bowel purge is more cost effective and associated with shorter length of stay (LOS) and higher diagnostic yield. (31) The downside however, is that it can often be difficult to pinpoint a source after cessation of bleeding, particularly in the face of multiple co-existing pathologies such as haemorrhoids and diverticula in the elderly patient.

In our algorithm, mesenteric angiography with embolization is reserved for hemodynamically unstable patients with refractory bleeding, and in whom there is inadequate time to await formal bowel preparation. Angiography can detect bleeding rates down to 0.5-1.0ml/min, and location of bleeding of angiography before successful embolization is associated with a reduced risk of re-bleeding. (32) Where amenable, super-selective angioembolisation has become more widely advocated for its greater safety profile, with lower rates of ischemic complications and bowel infarction. However, this is a technically demanding procedure that requires specialist expertise, and is not necessarily first-line intervention in many institutions. An urgent OGD should also be considered to rule out a brisk bleeding source proximal to the ligament of Treitz.

Patients requiring urgent colectomy for LGIB have decreased significantly over the years due to advances in endoscopic haemostasis and angio-embolisation techniques. Surgery is undertaken in our institution for patients with recurrent or refractory bleeding, unsuccessful endoscopic haemostasis or obscure LGIB without an identifiable source and those who are unstable despite resuscitation and medical optimisation. None of our patients required a blind subtotal colectomy, which may be performed in cases where massive LGIB is attributed to an unidentifiable colonic source, for example in a patient with pan-diverticulosis. However, this procedure is historically associated with high morbidity and mortality rates and generally serves as a last resort. (33, 34)

There are limitations to our retrospective analysis. The cohort is derived from a single tertiary institution involving patients admitted to surgical services. Those discharged directly from ED were not captured and may have contributed to a selection bias. The counter argument is that patients deemed fit for discharge from ED were likely at inherent “low risk” for severe LGIB, and may not have had a significant impact on our predictive model. The model was constructed from a derivative cohort and needs to be externally validated in a prospective cohort, limiting the generalisability of our findings. Finally, the predictive factors studied are non-exhaustive, and confounders of prognostic significance may exist, which have yet to be identified.

Overall, our study contributes to the existing literature by evaluating real world and easily accessible clinical and pre-endoscopic factors for risk-stratification of patients with LGIB. To our knowledge, it
remains the first Asian study to do so. The ROC curve reflected high predictive accuracy and in those patients with a threshold of $\geq 1$ point(s), the model showed high sensitivity and NPV. Hence, the model was strongest for “ruling out” a severe bleed, which can guide potential discharge of a low-risk patient. The proposed model can be easily implemented to aid in clinical decision making, allowing for early identification of severe LGIB patients who require aggressive resuscitation, admission to a monitored bed and consideration of endoscopic or surgical intervention.

**Conclusion**

Timely diagnosis and management of severe LGIB remains a challenge. The acute care surgeon needs to recognise this clinical entity early and determine the need for urgent endoscopic evaluation and/or angio-embolisation and surgery. The clinical predictive model for severe LGIB described utilises objective clinical parameters routinely obtained at initial evaluation. Further studies are needed to externally validate this model in a prospective cohort.

**List Of Abbreviations**

LGIB Lower Gastro-Intestinal Bleed

AUC Area Under Curve

ED Emergency Department

UGIB Upper Gastro-Intestinal Bleed

OR Odds Ratio

PPV Positive Predictive Value

NPV Negative Predictive Value

ROC Receiver Operating Characteristics

AUC Area Under Curve

CCM Charlson Comorbidity Index

CKD Chronic Kidney Disease

NSAID Non-Steroidal Anti-Inflammatory Drug

HR Heart Rate

SBP Systolic Blood Pressure
DBP Diastolic Blood Pressure
MAP Mean Arterial Pressure
HB Haemoglobin
HCT Haematocrit
AKI Acute Kidney Injury
INR International Normalised Ratio
HCO3 Serum Bicarbonate
SRUS Solitary Rectal Ulcer Syndrome
AVM Arteriovenous Malformation
PCT Packed Cell Transfusion
OGD Oesophago Gastro Duodenoscopy
IQR Interquartile Range
ICU Intensive Care Unit
EUA Examination Under Anaesthesia
NOAC Novel Oral Anticoagulant
LOS Length of Stay

**Declarations**

Neither the manuscript nor any part of its content is currently under consideration or published in another journal.

Ethics Approval and consent to participate - The study protocol was approved by the Singhealth Institutional Review Board

Consent for publication - Not applicable

Availability of data and materials - The datasets during and/or analysed during the current study available from the corresponding author on reasonable request.

Competing interest - The authors declare that they have no competing interests
Funding - No funding was sought

Authors’ contributions - S.M conceived the study design. J.C, M.S and A.S were involved in data retrieval and database creation. M.S, J.C and N.L performed the analysis. M.S, J.C and S.M were involved in interpretation of the analysis. M.S, J.C, R.M and S.M were major contributors in writing the manuscript. All authors read and approved the final manuscript.

Acknowledgements - None

References

1. Laine L, Yang H, Chang S-C, Datto C. Trends for Incidence of Hospitalization and Death Due to GI Complications in the United States From 2001 to 2009. Am J Gastroenterol. 2012 Aug;107(8):1190–5.

2. Longstreth GF. Epidemiology and outcome of patients hospitalized with acute lower gastrointestinal hemorrhage: a population-based study. Am J Gastroenterol. 1997 Mar;92(3):419–24.

3. Chait MM. Lower gastrointestinal bleeding in the elderly. World J Gastrointest Endosc. 2010;2(5):147.

4. Arroja B, Cremers I, Ramos R, Cardoso C, Rego AC, Caldeira A, et al. Acute lower gastrointestinal bleeding management in Portugal. Eur J Gastroenterol Hepatol. 2011 Apr;23(4):317–22.

5. Strate LL, Orav EJ, Syngal S. Early predictors of severity in acute lower intestinal tract bleeding. Arch Intern Med. 2003.

6. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. J Chronic Dis. 1987 Jan;40(5):373–83.

7. Raphaeli T, Menon R. Current treatment of lower gastrointestinal hemorrhage. Clin Colon Rectal Surg. 2012;25(4):219–27.

8. Hreinsson JP, Gumundsson S, Kalaitzakis E, Björnsson ES. Lower gastrointestinal bleeding. Eur J Gastroenterol Hepatol. 2013 Jan;25(1):37–43.

9. Stanley AJ, Laine L, Dalton HR, Ngu JH, Schultz M, Abazi R, et al. Comparison of risk scoring systems for patients presenting with upper gastrointestinal bleeding: international multicentre prospective study. BMJ. 2017 Jan 4;i6432.

10. Tapaskar N, Jones B, Mei S, Sengupta N. Comparison of clinical prediction tools and identification of risk factors for adverse outcomes in acute lower GI bleeding. Gastrointest Endosc. 2019 May;89(5):1005–13.e2.

11. Kollef MH, O'Brien JD, Zuckerman GR, Shannon W. Bleed: A classification tool to predict outcomes in patients with acute upper and lower gastrointestinal hemorrhage. Crit Care Med. 1997.

12. Wira C, Sather J. Clinical risk stratification for gastrointestinal hemorrhage: still no consensus. Crit Care. 2008;12(3):154.

13. Kwak MS, Cha JM, Han YJ, Yoon JY, Jeon JW, Shin HP, et al. The Clinical Outcomes of Lower Gastrointestinal Bleeding Are Not Better than Those of Upper Gastrointestinal Bleeding. J Korean
14. Das A, Ben-Menachem T, Cooper GS, Chak A, Sivak MV, Gonet JA, et al. Prediction of outcome in acute lower-gastrointestinal haemorrhage based on an artificial neural network: internal and external validation of a predictive model. Lancet. 2003 Oct;362(9392):1261–6.

15. Strate LL, Saltzman JR, Ookubo R, Mutinga ML, Syngal S. Validation of a clinical prediction rule for severe acute lower intestinal bleeding. Am J Gastroenterol. 2005.

16. Oakland K. Risk stratification in upper and upper and lower GI bleeding: Which scores should we use? Best Pract Res Clin Gastroenterol. 2019 Oct;42–43:101613.

17. Sengupta N, Tapper EB. Derivation and Internal Validation of a Clinical Prediction Tool for 30-Day Mortality in Lower Gastrointestinal Bleeding. Am J Med. 2017 May;130(5):601.e1-601.e8.

18. Chong V, Hill AG, MacCormick AD. Accurate triage of lower gastrointestinal bleed (LGIB) - A cohort study. Int J Surg. 2016;25(2016):19–23.

19. Blatchford O, Murray WR, Blatchford M. A risk score to predict need for treatment for upper gastrointestinal haemorrhage. Lancet. 2000 Oct;356(9238):1318–21.

20. Vreeburg EM, Terwee CB, Snel P, Rauws EA, Bartelsman JFWM, Meulen JHP, vd, et al. Validation of the Rockall risk scoring system in upper gastrointestinal bleeding. Gut. 1999 Mar 1;44(3):331–5.

21. Strate LL. Lower GI, Bleeding. Epidemiology and Diagnosis. Gastroenterol Clin North Am. 2005 Dec;34(4):643–64.

22. Caldeira D, Barra M, Ferreira A, Rocha A, Augusto A, Pinto FJ, et al. Systematic review with meta-analysis: the risk of major gastrointestinal bleeding with non-vitamin K antagonist oral anticoagulants. Aliment Pharmacol Ther. 2015 Dec;42(11–12):1239–49.

23. Carlin N, Asslo F, Sison R, Shaaban H, Baddoura W, Manji F, et al. Dual Antiplatelet Therapy and the Severity Risk of Lower Intestinal Bleeding. J Emerg Trauma Shock. 10(3):98–102.

24. Oakland K, Chadwick G, East JE, Guy R, Humphries A, Jairath V, et al. Diagnosis and management of acute lower gastrointestinal bleeding: guidelines from the British Society of Gastroenterology. Gut. 2019 May;68(5):776–89.

25. Zuckerman GR, Prakash C. Acute lower intestinal bleeding Part II: Etiology, therapy, and outcomes. Gastrointest Endosc. 1999 Feb;49(2):228–38.

26. Charilaou P, Devani K, Enjamuri D, Radadiya D, Reddy CM, Young M. Epidemiology of Lower GI Bleed in the United States - An Update From the National Inpatient Survey 2005–2014. Am J Gastroenterol. 2018 Oct;113(Supplement):319.

27. Imaeda H, Hibi T. The Burden of Diverticular Disease and Its Complications: West versus East. Inflamm Intest Dis. 2018;3(2):61–8.

28. Bai Y, Peng J, Gao J, Zou D-W, Li Z-S. Epidemiology of lower gastrointestinal bleeding in China: Single-center series and systematic analysis of Chinese literature with 53 951 patients. J Gastroenterol Hepatol. 2011 Apr;26(4):678–82.
29. Gerson LB, Fidler JL, Cave DR, Leighton JA. ACG Clinical Guideline: Diagnosis and Management of Small Bowel Bleeding. Am J Gastroenterol. 2015 Sep;110(9):1265–87.

30. Diamantopoulou G, Konstantakis C, Kottorou A, Skroubis G, Theocharis G, Theopistos V, et al. Acute Lower Gastrointestinal Bleeding: Characteristics and Clinical Outcome of Patients Treated With an Intensive Protocol. Gastroenterol Res. 2017;10(6):352–8.

31. Ghassemi KA, Jensen DM. Lower Gl bleeding: Epidemiology and management topical collection on large intestine. Curr Gastroenterol Rep. 2013.

32. BROWDER W, CERISE EJ. LITWIN MS. Impact of Emergency Angiography in Massive Lower Gastrointestinal Bleeding. Ann Surg. 1986 Nov;204(5):530–6.

33. Aoki T, Hirata Y, Yamada A, Koike K. Initial management for acute lower gastrointestinal bleeding. World J Gastroenterol. 2019 Jan;7(1):69–84. 25(.

34. Rockey DC. Lower Gastrointestinal Bleeding. Gastroenterology. 2006 Jan;130(1):165–71.

Figures

Receiver Operating Characteristics (ROC) Curve for a 6-variable prognostic model predicting severe LGIB
Figure 2

Algorithm for initial triage and management of patients presenting with LGIB