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LONG-HOSP Score: A Novel Predictive Score for Length of Hospital Stay in Acute Lower Gastrointestinal Bleeding – A Multicenter Nationwide Study

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Keywords

Acute lower gastrointestinal bleeding · Cost of hospitalization · Length of hospitalization · Predictive model · Early colonoscopy

Abstract

Introduction: Length of stay (LOS) in hospital affects cost, patient quality of life, and hospital management; however, existing gastrointestinal bleeding models applicable at hospital admission have not focused on LOS. We aimed to construct a predictive model for LOS in acute lower gastrointestinal bleeding (ALGIB). ***Methods:*** We retrospectively analyzed the records of 8,547 patients emergently hospitalized for ALGIB at 49 hospitals (the CODE BLUE-J Study). A predictive model for prolonged hospital stay was developed using the baseline characteristics of 7,107 patients and externally validated in 1,440 patients. Furthermore, a multivariate analysis assessed the impact of additional variables during hospitalization on LOS. ***Results:*** Focusing on baseline characteristics, a predictive model for prolonged hospital stay was developed, the LONG-HOSP score, which consisted of low body mass index, laboratory data, old age, nondrinker status, nonsteroidal anti-inflammatory drug use, facility with ≥800 beds, heart rate, oral antithrombotic agent use, symptoms, systolic blood pressure, performance status, and past medical history. The score showed relatively high performance in predicting prolonged hospital stay and high hospitalization costs (area under the curve: 0.70 and 0.73 for derivation, respectively, and 0.66 and 0.71 for external validation, respectively). Next, we focused on in-hospital management. Diagnosis of colitis or colorectal cancer, rebleeding, and the need for blood transfusion, interventional radiology, and surgery prolonged LOS, regardless of

the LONG-HOSP score. By contrast, early colonoscopy and endoscopic treatment shortened LOS. ***Conclusions:*** At hospital admission for ALGIB, our novel predictive model stratified patients by their risk of prolonged hospital stay. During hospitalization, early colonoscopy and endoscopic treatment shortened LOS.

Introduction

Acute lower gastrointestinal bleeding (ALGIB) often requires in-hospital care, and it has various clinical outcomes such as severe bleeding, need for blood transfusion or therapeutic intervention, length of stay (LOS), cost of hospitalization, and mortality [1–30]. Prolonged hospital stay causes deterioration in patients' quality of life, as well as difficulties with cost-effective use of medical resources, and places a financial burden on society. The LOS and cost of ALGIB require attention because ALGIB has been reported to require a longer hospital stay and have a higher cost than peptic ulcer bleeding [8, 31]. If the LOS can be predicted using baseline patient profiles at an early stage of hospitalization, sharing information with patients, their families, and medical staff may improve early discharge planning and hospital bed management. However, no such clinical model has been reported for ALGIB.

Although some GIB risk models exist for predicting severity or mortality [1–6, 32, 33], these scores may be inferior to a novel score that specializes in predicting LOS because different predictors depend on each outcome. Therefore, an original prediction model focusing on prolonged hospital stay would be useful.

Several studies on ALGIB have examined the risks of prolonged hospital stays and the related high costs [7–19]; however, each report had specific limitations. One limitation was incorporating patient characteristics at the hospital visit and interventions during hospitalization into the multivariate analysis. Another problem was limiting patients to those with colonic diverticular bleeding. A different limitation was using too few predictors to develop a prediction model because of the small sample size. Lastly, single-center studies will be biased because of specific hospital characteristics, patient background, or management strategies.

To address these issues, we developed a novel prediction model for prolonged hospital stay using the baseline characteristics of a nationwide ALGIB cohort [20, 21]. Furthermore, we examined whether the novel model also predicted high hospitalization costs. Finally, we investigated whether in-hospital management was associated with LOS regardless of the predictions of the novel model.

Materials and Methods

Study Design, Setting, and Participants

We conducted a multicenter study of patients with outpatient-onset acute hematochezia who were emergently admitted to 49 hospitals throughout Japan between January 2010 and December 2019. The details of these patients have been reported previously (CODE BLUE-J Study: COlonic DivErticular Bleeding Leaders Update Evidence from multicenter Japanese Study) [20, 21]. This was a retrospective observational study carried out using the opt-out method and was approved by the ethics committees of all 49 participating institutions (online suppl. Table 1; for all online suppl. material, see https://doi.org/10.1159/000531646). Patients and/or the public were not involved in the design, conduct, reporting, or dissemination plans of this research.

As shown in Figure 1, among consecutive patients with acute hematochezia in the original cohort (n = 10,342), we excluded participants with the following: upper gastrointestinal bleeding (n = 153), in-hospital death (n = 89), received barium impaction therapy (n = 66), or insufficient clinical information (n = 1,487). We excluded participants who died during hospitalization in accordance with previous studies with an outcome of LOS [33, 34] because in-hospital death terminated hospitalization even though patients did not recover. Patients who underwent barium impaction therapy were also excluded because the therapy has not been established as standard management in ALGIB and its effect on LOS is unclear.

The remaining patients (basic cohort, n = 8,547) were geographically divided into two groups for the first study: (1) a derivation cohort (7,107 patients at 37 hospitals outside the Kyushu region) to develop a novel predictive score and (2) an external validation cohort (1,440 patients at 12 hospitals in the Kyushu region) to evaluate the validity of the score. The Kyushu region is located in the western end of Japan. Patients were geographically divided into two groups because we intended to confirm the generalizability of the novel predictive score obtained from the derivation cohort by applying it in external institutions. The second study analyzed the whole basic cohort of patients with ALGIB (n = 8,547).

Variables and Outcomes

All variables were collected from the medical records and electronic endoscopy database at each participating institution by gastroenterologists or dedicated researchers. Fifty-one baseline characteristics were analyzed as variables in the first study. Baseline characteristics included age, sex, body mass index (BMI), current drinking and smoking habits, performance status, facility with ≥800 beds, hospitalization at institutions with ≥5,000 ambulance visits/year, past medical history and comorbidities, presenting symptoms at hospitalization, initial vital signs, medication intake within 30 days of hospitalization, and initial laboratory data. In the second study, we focused on in-hospital management including lower gastrointestinal bleeding

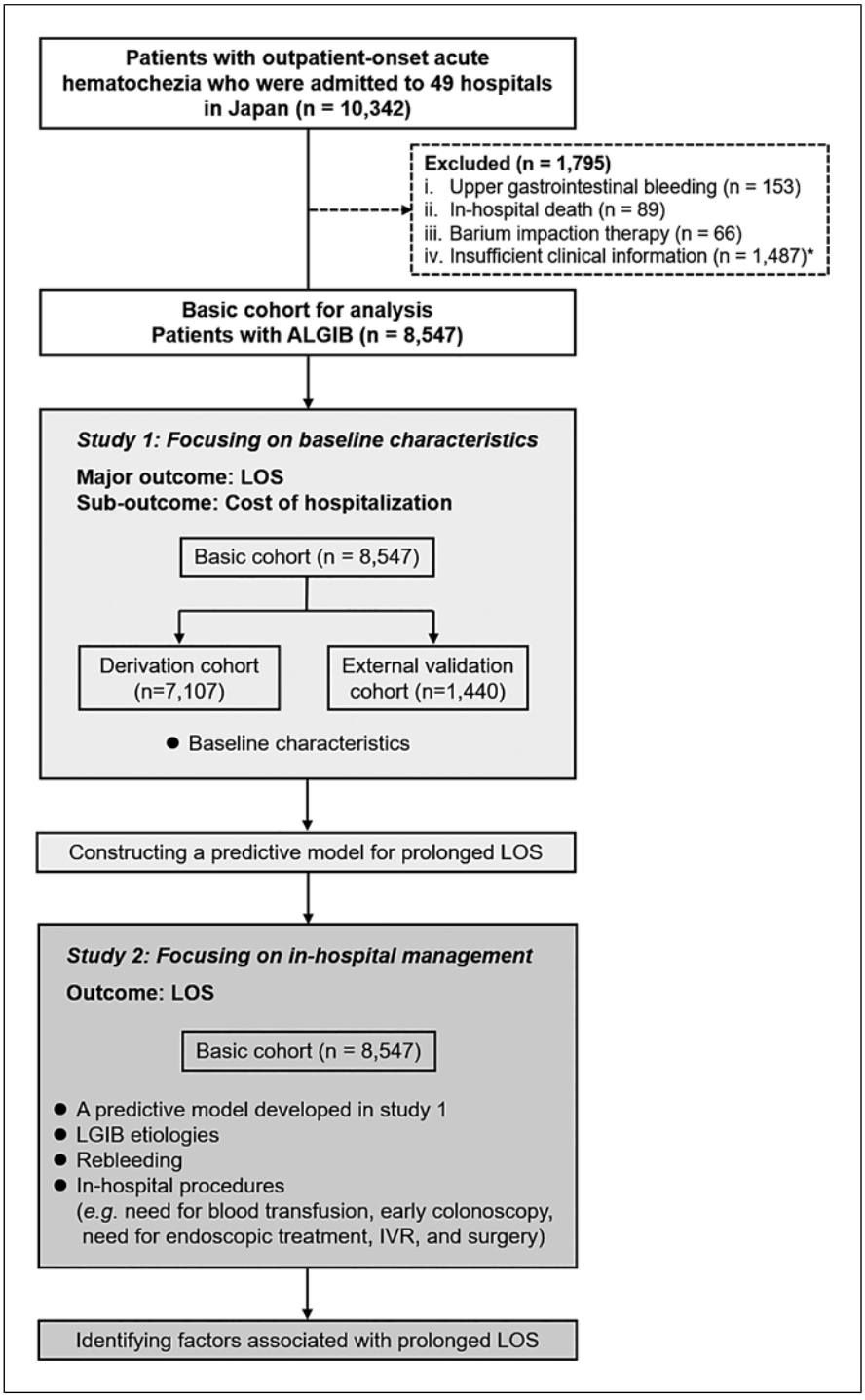

Fig. 1. Study flowchart. *Patients with missing data for study 1 (duplicated): BMI (n = 599), performance status (n = 120), malignancy (n = 7), IBD (n = 1), abdominal pain (n = 17), diarrhea (n = 33), concomitant tarry stool (n = 21), systolic blood pressure ≤100 mm Hg (n = 174), heart rate ≥100 beats/min (n = 193), hemoglobin (n = 7), albumin (n = 481), BUN (n = 67), CRP (n = 271), and PT-INR (n = 355). ALGIB, acute lower gastrointestinal bleeding; BMI, body mass index; BUN, blood urea nitrogen; CRP, C-reactive protein; IBD, inflammatory bowel disease; IVR, interventional radiology; LOS, length of stay; PT-INR, prothrombin time-international normalized ratio.

(LGIB) etiology, rebleeding, and in-hospital procedures. LGIB etiologies included diverticular bleeding, colitis, ulcerative lesion, hemorrhoid, colorectal cancer, angioectasia, radiation proctitis, miscellaneous, and unknown origin. In-hospital procedures included the need for transfusion, early colonoscopy within 24 h from the patient's visit to the hospital, need for endoscopic treatment, interventional radiology, and surgery. Endoscopic treatment included clipping, coagulation, band ligation, snare ligation, and hypertonic saline-epinephrine and was selected at the discretion of the endoscopist and in accordance with each hospital's policy.

The major outcome was prolonged hospital stay (>7 days), determined based on the median LOS (7 days) of our cohort and

Table 1. Patient characteristics

Characteristics	Total cohort, *n* = 8,547	Derivation cohort, *n* = 7,107	External validation cohort, *n* = 1,440	*p* value
Age, mean±SD, years	70.8±14.5	70.5±14.6	72.2±13.6	0.376
Sex (male), *n* (%)	5,211 (61.0)	4,355 (61.3)	856 (59.4)	0.196
BMI, %, mean±SD	22.7±3.9	22.7±3.9	23.0±4.0	**0.010**
Current drinker, *n* (%)	3,491 (40.8)	2,954 (41.6)	537 (37.3)	**0.002**
Current smoker, *n* (%)	1,372 (16.1)	1,183 (16.6)	189 (13.1)	<**0.001**
Performance status	1.2±0.6	1.2±0.5	1.2±0.6	**0.008**
Number of hospital beds ≥800, *n* (%)	2,677 (31.3)	2,400 (33.8)	277 (19.2)	<**0.001**
Hospitalization at institution with ≥5,000 ambulance visits/year, *n* (%)	4,772 (55.8)	4,654 (65.5)	118 (8.2)	<**0.001**
Past medical history and comorbidities, *n* (%)				
History of colorectal surgery	623 (7.3)	500 (7.0)	123 (8.5)	0.058
History of chemotherapy	284 (3.3)	247 (3.5)	37 (2.6)	0.057
History of radiation therapy	202 (2.4)	179 (2.5)	23 (1.6)	**0.016**
History of colorectal angioectasia	60 (0.7)	43 (0.6)	17 (1.2)	0.055
History of diverticular bleeding	2,223 (26.0)	1,823 (25.7)	400 (27.8)	0.092
History of ischemic colitis	198 (2.3)	173 (2.4)	25 (1.7)	0.073
Malignancy	1,239 (14.5)	1,056 (14.9)	183 (12.7)	**0.027**
IBD	208 (2.4)	164 (2.3)	44 (3.1)	0.125
Diabetes mellitus	1,620 (19.0)	1,351 (19.0)	269 (18.7)	0.771
Hemiplegia	223 (2.6)	183 (2.6)	40 (2.8)	0.669
Cerebrovascular diseases	1,208 (14.1)	994 (14.0)	214 (14.9)	0.394
Chronic pulmonary diseases	268 (3.1)	220 (3.1)	48 (3.3)	0.645
Dementia	446 (5.2)	384 (5.4)	62 (4.3)	0.068
Connective tissue diseases	356 (4.2)	277 (3.9)	79 (5.5)	**0.014**
Ischemic heart diseases	1,393 (16.3)	1,118 (15.7)	275 (19.1)	**0.003**
Heart failure	708 (8.3)	560 (7.9)	148 (10.3)	0.005
Peptic ulcer	556 (6.5)	465 (6.5)	91 (6.3)	0.751
Chronic kidney disease	1,263 (14.8)	1,034 (14.5)	229 (15.9)	0.198
Peripheral vascular disease and aneurysm	350 (4.1)	305 (4.3)	45 (3.1)	**0.024**
Chronic hepatitis (Child A)	179 (2.1)	142 (2.0)	37 (2.6)	0.203
Liver cirrhosis (Child B or C)	158 (1.8)	122 (1.7)	36 (2.5)	0.075
Hypertension	4,910 (57.4)	4,015 (56.5)	895 (62.2)	<**0.001**
Dyslipidemia	2,421 (28.3)	1,923 (27.1)	498 (34.6)	<**0.001**
Presenting symptoms, *n* (%)				
Syncope	538 (6.3)	398 (5.6)	140 (9.7)	<**0.001**
Abdominal pain	1,419 (16.6)	1,201 (16.9)	218 (15.1)	0.092
Body temperature ≥37.0°C	529 (6.2)	443 (6.2)	86 (6.0)	0.705
Diarrhea	871 (10.2)	741 (10.4)	130 (9.0)	0.095
Concomitant tarry stool	438 (5.1)	382 (5.4)	56 (3.9)	**0.010**
Vital signs				
Mean heart rate, min (±SD)	85.0±17.1	85.3±17.1	83.2±17.4	<**0.001**
Mean systolic blood pressure, mm Hg (±SD)	128.8±25.3	129.0±25.4	127.9±24.4	0.120
Medication, *n* (%)				
NSAIDs including LDA	2,520 (29.5)	2,078 (29.2)	442 (30.7)	0.274
Non-LDA antiplatelets*	1,218 (14.3)	1,032 (14.5)	186 (12.9)	0.101
Warfarin	579 (6.8)	471 (6.6)	108 (7.5)	0.247
Direct oral anticoagulant	514 (6.0)	430 (6.1)	84 (5.8)	0.749
Acetaminophen	233 (2.7)	176 (2.5)	57 (4.0)	**0.007**
Corticosteroid	490 (5.7)	378 (5.3)	112 (7.8)	**0.001**
Initial laboratory data, mean±SD				
Hemoglobin, g/dL	11.2±2.6	11.2±2.6	11.0±2.6	**0.002**
White blood cell count,/μL	7,843±3,826	7,851±3,454	7,801±5,295	0.729
Platelet count, × 10^4/μL	21.7±8.1	21.9±8.1	21.2±7.8	**0.002**
Albumin, g/dL	3.7±0.6	3.7±0.6	3.7±0.6	0.075
BUN, mg/dL	21.6±12.5	21.6±12.6	22.0±12.1	0.176
CRP, mg/dL	0.9±2.6	1.0±2.8	0.7±1.9	<**0.001**
PT-INR	1.16±0.62	1.16±0.61	1.19±0.67	0.128

Table 1 (continued)

Characteristics	Total cohort, *n* = 8,547	Derivation cohort, *n* = 7,107	External validation cohort, *n* = 1,440	*p* value
Diagnosis, *n* (%)				
Diverticular bleeding	5,567 (65.1)	4,491 (63.2)	1,076 (74.7)	<**0.001**
Definitive diverticular bleeding	2,056 (36.9)	1,667 (23.5)	389 (26.8)	**0.004**
Presumptive diverticular bleeding	3,511 (73.1)	2,824 (39.7)	687 (47.7)	<**0.001**
Colitis	1,166 (13.6)	1,032 (14.5)	134 (9.3)	<**0.001**
Ulcerative lesion	262 (3.1)	218 (3.1)	44 (3.1)	0.981
Hemorrhoid	147 (1.7)	136 (1.9)	11 (0.8)	<**0.001**
Colorectal cancer	142 (1.7)	136 (1.9)	6 (0.4)	<**0.001**
Angioectasia	116 (1.4)	88 (1.2)	28 (1.9)	0.068
Radiation proctitis	51 (0.6)	44 (0.6)	7 (0.5)	0.518
Miscellaneous	658 (7.7)	550 (7.7)	108 (7.5)	0.754
Unknown	438 (5.1)	412 (5.8)	26 (1.8)	<**0.001**
Existing clinical risk scores, mean±SD				
Sengupta score	2.1±6.1	2.0±6.1	2.4±5.9	**0.040**
Oakland score	16.7±6.1	16.6±6.1	17.1±6.0	**0.005**
Blatchford score	5.1±3.9	5.0±3.9	5.3±3.8	**0.002**
ABC score	2.3±1.9	2.3±1.9	2.5±1.9	<**0.001**
AIMS65 score	0.9±0.8	0.9±0.8	0.9±0.8	0.676
NOBLADS score	2.6±1.1	2.6±1.2	2.7±1.1	**0.009**
Strate score	1.9±1.0	1.9±1.0	1.9±1.0	0.068
Length of hospital stay, days, median (IQR)	7.0 (5.0–11.0)	7.0 (5.0–11.0)	7.0 (5.0–11.0)	0.376

Bold values indicate $p < 0.05$. BMI, body mass index; BUN, blood urea nitrogen; CRP, C-reactive protein; IBD, inflammatory bowel disease; IQR, interquartile range; LDA, low-dose aspirin; NSAIDs, nonsteroidal anti-inflammatory drugs; PT-INR, prothrombin time-international normalized ratio; SD, standard deviation. *Non-LDA antiplatelets included thienopyridine, cilostazol, and other antiplatelet drugs.

the previous definition of this outcome [9, 11]. The sub-outcome was high cost of hospitalization (>4,500 US dollars). The cost in our cohort was estimated based on a Japanese ALGIB dataset in a past report (online suppl. methods) [7]. The cutoff for high cost (4,500 US dollars) was determined based on the same report.

Statistical Analysis

The Pearson χ^2 test or a nonparametric trend test was used to compare proportions. A p value <0.05 was considered statistically significant.

In the first study, we developed a novel model for predicting prolonged hospital stay using the derivation cohort. To simplify the clinical application of the model, all continuous data were categorized at either standard clinical cutoff point or statistical break points. Predictive factors were evaluated using univariate analysis. Individual odds ratios and 95% confidence intervals (CIs) were computed for each variable using logistic regression analysis. A multivariate predictive score for prolonged hospital stay was constructed using backward stepwise logistic regression. Variables with univariate significance ($p < 0.10$) were entered into the multivariate analysis. Based on the coefficients in the multivariate analysis, a score for predicting prolonged hospital stay was generated. The discriminatory power of the score was assessed using area under the receiver operating characteristic curve (ROC-AUC) analysis. We assessed the validity of the predictive score using the external validation cohort. In addition, we evaluated whether the novel score also had the capability to predict the high cost.

In the second study, we explored the factors related to in-hospital management that were associated with LOS regardless of the predictions of the novel model developed in the first study. Adjusted odds ratios and 95% CIs were computed using multivariate logistic regression analysis. Furthermore, the interactions between our novel predictive score and in-hospital procedures were assessed to evaluate whether the effect of in-hospital procedures on reducing LOS differed depending on the score. All statistical computations were performed using IBM SPSS Statistics (version 27.0; IBM Corp., Armonk, NY, USA) and Stata software (version 14.0; Stata Corp., College Station, TX, USA).

Results

First Study for Developing a Predictive Model for Prolonged Hospital Stay Based on Baseline Characteristics

Development and External Validation of the Predictive Model

Patients' demographic data are presented in Table 1. We analyzed the data of 8,547 patients with ALGIB (males 61.0%; mean age 70.8 years; range 20–101 years). The median LOS was 7 days (interquartile range: 5–11 days). The most common bleeding type was colonic diverticular bleeding (65%) and the second most common bleeding type was colitis-related (14%).

Table 2. Association between baseline characteristics and prolonged hospital stay (≥8 days) (derivation cohort, n = 7,107)

Variables	Crude OR (95% CI)	p value	Adjusted OR (95% CI)	p value
Age ≥75 years	1.68 (1.54–1.84)	<**0.001**	1.32 (1.18–1.47)	<**0.001**
Male	0.82 (0.75–0.90)	<0.001		
BMI <18.5 kg/m^2	1.91 (1.67–2.19)	<**0.001**	1.23 (1.06–1.44)	**0.008**
Nondrinker	1.56 (1.43–1.70)	<**0.001**	1.21 (1.09–1.35)	<**0.001**
Current smoker	0.84 (0.74–0.94)	0.003		
Performance status ≥2	2.24 (1.95–2.58)	<**0.001**	1.31 (1.10–1.56)	**0.002**
Number of hospital bed ≥800	1.76 (1.60–1.93)	<**0.001**	1.69 (1.51–1.88)	<**0.001**
Hospitalization at institutions with ≥5,000 ambulances/year	0.98 (0.89–1.07)	0.623		
Past medical history and comorbidities				
History of colorectal surgery	1.32 (1.12–1.57)	**0.001**		
History of chemotherapy	1.89 (1.47–2.43)	<**0.001**		
History of radiation therapy	1.28 (0.97–1.70)	0.084		
History of colorectal angioectasia	1.66 (0.95–2.92)	0.077		
History of diverticular bleeding	0.85 (0.76–0.94)	**0.001**		
History of ischemic colitis	0.84 (0.63–1.12)	0.241		
Malignancy	1.63 (1.44–1.85)	<**0.001**	1.21 (1.55–1.39)	**0.010**
IBD	3.89 (2.77–5.48)	<**0.001**	3.31 (2.23–4.92)	<**0.001**
Diabetes mellitus	1.21 (1.08–1.35)	**0.001**		
Hemiplegia	1.92 (1.46–2.54)	<**0.001**		
Cerebrovascular diseases	1.29 (1.14–1.46)	<**0.001**		
Chronic pulmonary diseases	1.35 (1.05–1.74)	**0.019**		
Dementia	1.67 (1.38–2.02)	<**0.001**		
Connective tissue diseases	1.40 (1.12–1.75)	**0.003**		
Ischemic heart diseases	1.21 (1.08–1.37)	**0.001**		
Heart failure	1.85 (1.57–2.18)	<**0.001**		
Peptic ulcer	1.10 (0.92–1.31)	0.281		
Chronic kidney disease	1.74 (1.54–1.97)	<**0.001**		
Peripheral vascular disease and aneurysm	1.42 (1.14–1.76)	**0.002**		
Chronic hepatitis (Child A)	1.36 (1.00–1.86)	0.050		
Liver cirrhosis (Child B or C)	1.74 (1.22–2.49)	**0.002**		
Hypertension	1.06 (0.97–1.16)	0.192		
Dyslipidemia	0.99 (0.89–1.09)	0.782		
Presenting symptoms				
Syncope	1.09 (0.91–1.32)	0.343		
Abdominal pain	1.23 (1.09–1.38)	**0.001**	1.30 (1.12–1.52)	**0.001**
Body temperature ≥37.0°C	1.80 (1.50–2.17)	<**0.001**		
Diarrhea	1.29 (1.12–1.49)	<**0.001**	1.23 (1.02–1.48)	**0.027**
Concomitant tarry stool	2.02 (1.66–2.45)	<**0.001**	1.48 (1.18–1.86)	**0.001**
Vital signs				
Heart rate ≥100/min	1.20 (1.08–1.34)	**0.001**	1.24 (1.09–1.41)	**0.001**
Systolic blood pressure ≤100 mm Hg	1.63 (1.43–1.86)	<**0.001**	1.24 (1.06–1.45)	**0.006**
Medication				
NSAIDS including LDA	1.33 (1.21–1.46)	<**0.001**	1.16 (1.04–1.30)	**0.008**
Non-LDA antiplatelets*	1.40 (1.24–1.59)	<**0.001**	1.26 (1.09–1.46)	**0.001**
Direct oral anticoagulant	1.13 (0.94–1.35)	0.198		
Acetaminophen	1.41 (1.06–1.86)	**0.018**		
Corticosteroid	1.69 (1.39–2.06)	<**0.001**		
Initial laboratory data				
Hemoglobin				
≥13.0 g/dL	Ref		Ref	
11.0–12.9 g/dL	1.43 (1.27–1.61)	<**0.001**	1.22 (1.06–1.40)	**0.004**
9.0–10.9 g/dL	2.21 (1.95–2.50)	<**0.001**	1.50 (1.29–1.76)	<**0.001**
7.0–8.9 g/dL	2.87 (2.47–3.32)	<**0.001**	1.63 (1.35–1.97)	<**0.001**
<7.0 g/dL	3.83 (3.15–4.64)	<**0.001**	1.82 (1.43–2.34)	<**0.001**
White blood cell count >10,000/μL	1.30 (1.16–1.45)	<**0.001**		
Platelet count >15 × 10^4/μL	1.37 (1.21–1.55)	<**0.001**		

Table 2 (continued)

Variables	Crude OR (95% CI)	*p* value	Adjusted OR (95% CI)	*p* value
Albumin				
≥3.5 g/dL	Ref		Ref	
3.0–3.4 g/dL	2.17 (1.94–2.43)	<**0.001**	1.39 (1.21–1.59)	<**0.001**
2.5–2.9 g/dL	3.57 (2.96–4.31)	<**0.001**	1.76 (1.40–2.22)	<**0.001**
<2.5 g/dL	6.49 (4.70–8.97)	<**0.001**	2.79 (1.90–4.10)	<**0.001**
BUN				
<20.0 mg/dL	Ref		Ref	
20.0–44.9 mg/dL	1.49 (1.36–1.63)	<**0.001**	1.11 (1.00–1.24)	0.060
≥45.0 mg/dL	3.04 (2.43–3.81)	<**0.001**	1.38 (1.06–1.80)	**0.016**
CRP				
<0.5 mg/dL	Ref		Ref	
0.5–3.9 mg/dL	1.53 (1.37–1.71)	<**0.001**	1.13 (0.99–1.28)	0.078
≥4.0 mg/dL	3.56 (2.93–4.33)	<**0.001**	2.11 (1.66–2.69)	<**0.001**
Warfarin (–)	Ref		Ref	
Warfarin (+) PT-INR <2.5	1.57 (1.27–1.93)	<**0.001**	1.33 (1.05–1.69)	**0.019**
Warfarin (+) PT-INR ≥2.5	3.36 (2.40–4.71)	<**0.001**	2.27 (1.55–3.33)	<**0.001**

Bold values indicate $p < 0.05$. BMI, body mass index; BUN, blood urea nitrogen; CRP, C-reactive protein; IBD, inflammatory bowel disease; LDA, low-dose aspirin; NSAIDs, nonsteroidal anti-inflammatory drugs; OR, odds ratio; PT-INR, prothrombin time-international normalized ratio; Ref, reference. *Non-LDA antiplatelets included thienopyridine, cilostazol, and other antiplatelet drugs.

Forty different factors related to patients and hospital characteristics were found to be significant predictors of prolonged hospital stay in the univariate analysis of the derivation cohort (n = 7,107; Table 2). Multivariate logistic regression analysis identified the following independent predictive factors: age ≥75 years; BMI <18.5 kg/m^2; non-drinker; performance status ≥2; facility with ≥800 beds; comorbid inflammatory bowel disease (IBD) or malignancy; presenting symptoms of abdominal pain, diarrhea, or concomitant tarry stool; systolic blood pressure ≤100 mm Hg; heart rate ≥100 beats/min; treatment with nonsteroidal anti-inflammatory drugs (NSAIDs) or non-low-dose aspirin antiplatelet drugs; hemoglobin <13 g/dL; blood urea nitrogen (BUN) ≥20 mg/dL; C-reactive protein ≥0.5 mg/dL; and warfarin use stratified by prothrombin time-international normalized ratio (<2.5 and ≥2.5) (Table 2).

We developed a novel weighted score for predicting prolonged hospital stay (maximum 49 points) based on the coefficients in the multivariate analysis (Table 3). We named it the LONG-HOSP score: L, low BMI and laboratory data; O, old; N, nondrinker and NSAID use; G, giant hospital; H, heart rate; O, oral antithrombotic agent use; S, symptoms and systolic blood pressure; P, performance status and past medical history and comorbidities (IBD and malignancy). The AUC of the LONG-HOSP score for predicting prolonged hospital stay (>7 days) was 0.70 (95% CI, 0.69–0.71) in the derivation cohort and 0.66 (95% CI, 0.63–0.69) in the external validation cohort. We classified the LONG-HOSP score into seven categories: ≤5, 6–10, 11–15, 16–20, 21–25, 26–30, and ≥31. Based on these categories, the median LOS were 5, 6, 7, 8, 10, 14, and 20 days, respectively, in the derivation cohort (Fig. 2a) and 6, 6, 7, 9, 10, 12, and 13.5 days, respectively, in the external validation cohort (Fig. 2b) (p < 0.001 for trend in both cohorts).

Association between LONG-HOSP Score and Hospitalization Cost

The AUC of the LONG-HOSP score for predicting high cost (>4,500 US dollars) was 0.73 (95% CI, 0.71–0.74) in the derivation cohort and 0.71 (95% CI, 0.68–0.74) in the external validation cohort. Based on the seven categories of the LONG-HOSP score, the ratios of high cost were 27%, 45%, 59%, 71%, 81%, 88%, and 95% in the derivation cohort (Fig. 2c) and 31%, 42%, 57%, 71%, 84%, 86%, and 92% in the external validation cohort (Fig. 2d) (p < 0.001 for trend in both cohorts).

Second Study Focusing on In-Hospital Management

The rates of rebleeding, blood transfusion, early colonoscopy, endoscopic treatment, interventional radiology, and surgery during hospitalization in the basic cohort (n = 8,547) were 15%, 30%, 68%, 27%, 2%, and 1%, respectively. In relation to in-hospital management, diagnosis of colitis and colorectal cancer, rebleeding, the need for blood transfusion, interventional radiology, and surgery were significantly associated with prolonged hospital stay, regardless of the LONG-HOSP score category developed in the first study (Fig. 3). A diagnosis

Table 3. Predictors of prolonged hospital stay in multivariate logistic regression models; LONG-HOSP score (derivation cohort, n = 7,107)

LONG-HOSP score	Coefficient (95% CI)	Weighted points for score
L, low BMI and laboratory data		
BMI <18.5 kg/m^2	0.21 (0.05–0.37)	2
Hemoglobin		
11.0–12.9 g/dL	0.20 (0.06–0.34)	2
9.0–10.9 g/dL	0.41 (0.25–0.56)	4
7.0–8.9 g/dL	0.49 (0.30–0.68)	5
<7.0 g/dL	0.60 (0.35–0.85)	6
Albumin		
3.0–3.4 g/dL	0.33 (0.19–0.46)	3
2.5–2.9 g/dL	0.57 (0.33–0.80)	5
<2.5 g/dL	1.03 (0.64–1.41)	10
BUN		
20.0–44.9 mg/dL	0.11 (0.00–0.22)	1
≥45.0 mg/dL	0.32 (0.06–0.59)	3
CRP		
0.5–3.9 mg/dL	0.12 (−0.01–0.25)	1
≥4.0 mg/dL	0.75 (0.51–0.99)	7
O, old		
Age ≥75 years	0.28 (0.16–0.39)	3
N, nondrinker and NSAID use		
Nondrinker	0.19 (0.09–0.30)	2
NSAIDS including LDA	0.15 (0.04–0.26)	1
G, giant hospital		
Number of hospital bed ≥800	0.52 (0.41–0.63)	5
H, heart rate		
Heart rate ≥100/min	0.22 (0.09–0.34)	2
O, oral antithrombotic agent use		
Non-LDA antiplatelets*	0.23 (0.09–0.38)	2
S, symptoms and systolic blood pressure		
Abdominal pain	0.26 (0.11–0.42)	3
Diarrhea	0.21 (0.02–0.39)	2
Concomitant tarry stool	0.39 (0.17–0.62)	4
Systolic blood pressure ≤100 mm Hg	0.22 (0.06–0.37)	2
P, performance status and past medical history and comorbidities		
Performance status ≥2	0.27 (0.10–0.45)	3
Malignancy	0.19 (0.05–0.33)	2
IBD	1.20 (0.80–1.59)	11

BUN 20.0–44.9 mg/dL had the lowest coefficient (0.11), and the item was weighted as 1 point. The weighted point was calculated for other factors based on how many times of coefficients they had, compared with the lowest coefficient (0.11). BMI, body mass index; BUN, blood urea nitrogen; CI, confidence interval; CRP, C-reactive protein; IBD, inflammatory bowel disease; LDA, low-dose aspirin; NSAIDs, non-steroidal anti-inflammatory drugs.

of hemorrhoids, early colonoscopy, and endoscopic treatment were significantly associated with short hospital stay. Quantitative interactions for LOS were observed between these two procedures and the high/low LONG-HOSP score (low, category <4; high, category ≥4) (Fig. 4a). Thus, mean LOS was different depending on the factors of the LONG-HOSP score category, early colonoscopy, and endoscopic treatment (Fig. 4b).

Discussion

In this large, multicenter study with detailed data of ALGIB, a novel prediction model for prolonged hospital stay was developed based on baseline characteristics. We named the novel predictive score the LONG-HOSP score, and it included patient profiles, presenting symptoms, vital signs, medications, initial laboratory data,

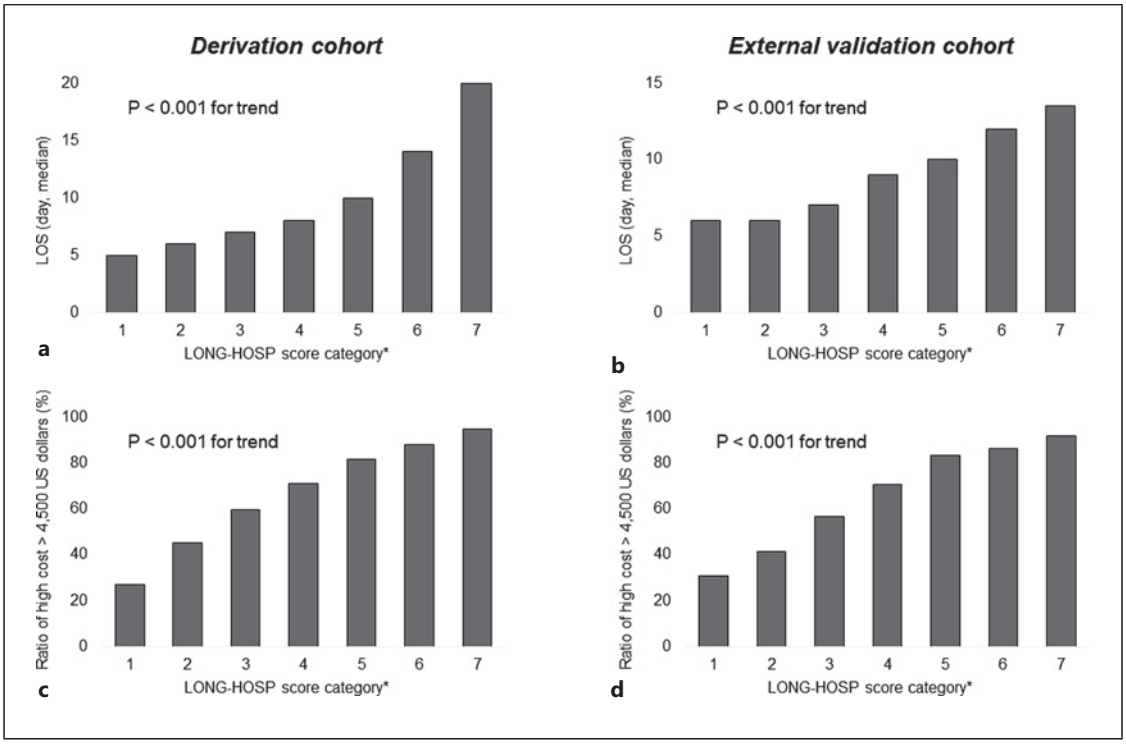

Fig. 2. LOS and cost of hospitalization based on LONG-HOSP score categories. **a** LOS in the derivation cohort. **b** LOS in the validation cohort. **c** High cost in the derivation cohort. **d** High cost in the validation cohort. *The LONG-HOSP score was classified into seven categories: ≤5, 6–10, 11–15, 16–20, 21–25, 26–30, and ≥31. LOS, length of stay.

past medical history, and comorbidities. The LONG-HOSP score also predicted the high cost of hospitalization. Next, we focused on in-hospital management. Diagnosis of colitis or colorectal cancer, rebleeding, and the need for blood transfusion, interventional radiology, and surgery prolonged LOS, regardless of the LONG-HOSP score. By contrast, early colonoscopy and endoscopic treatment shortened LOS, particularly in high LONG-HOSP score categories (LONG-HOSP score ≥16 points). Our study highlights the importance of comprehensive assessment of baseline characteristics upon patient arrival at hospital for predicting LOS.

Many predictive factors for prolonged hospital stay were identified in this study owing to the large dataset. The following factors in the LONG-HOSP score have been identified as predictive in previous ALGIB reports: age, systolic blood pressure, heart rate, hemoglobin, albumin, prothrombin time-international normalized ratio, NSAID use, non-low-dose aspirin antiplatelet drug use, and IBD [3, 8–11, 22]. Only a few studies on ALGIB have examined the risk of high hospitalization cost as the primary outcome, and these studies identified age and hemoglobin levels to be risks, consistent with this study [7, 8].

The unique factors in our analysis were high BUN levels and concomitant tarry stool. These factors suggest small-bowel bleeding in addition to colonic bleeding [35], which may lead to prolonged hospital stay because further diagnostic work-up is required. Indeed, in our study, the presence of tarry stools increased LOS in patients with a final diagnosis of presumptive colonic diverticular bleeding (source of bleeding was not identified on colonoscopy). This patient group had a significantly prolonged LOS compared with patients without tarry stools (mean LOS: 14 days vs. 11 days). Furthermore, patients with BUN ≥25 mg/dL also had significantly prolonged LOS compared with patients with BUN <25 mg/dL (mean LOS: 13 days vs. 11 days). In the current study, when additional workup led to a diagnosis of small-bowel bleeding (2.2% in this study cohort), management of this bleeding was time-consuming. Thus, compared with patients without small-bowel bleeding, those with this type of bleeding had significantly higher rates of interventional radiology (6.8% vs. 1.3%) and surgical intervention (4.2% vs. 1.0%).

Interestingly, the presence of diarrhea and abdominal pain were significant predictors of prolonged hospital stay, which conflicts with previously identified predictors of

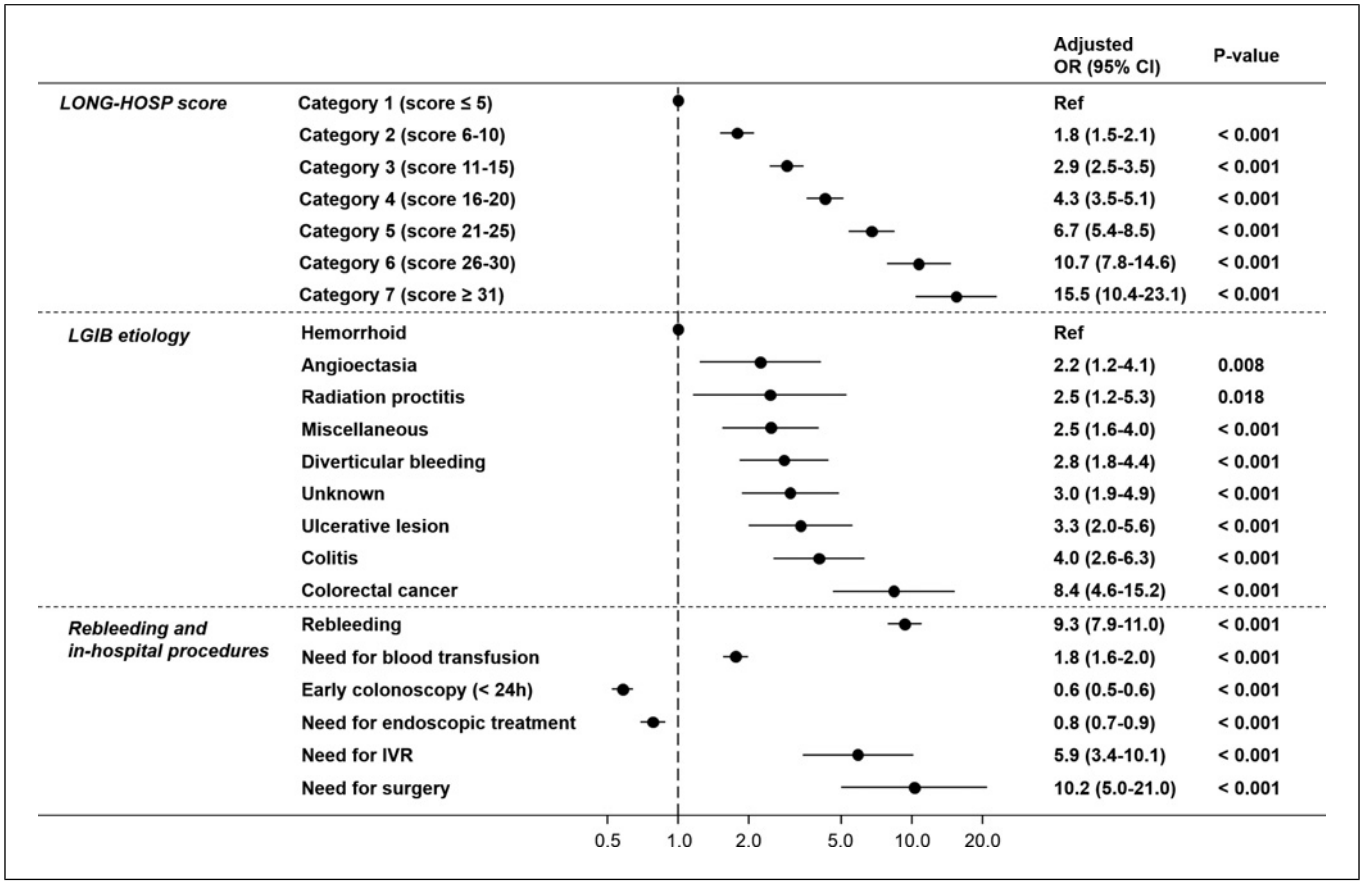

Fig. 3. Factors associated with LOS based on LONG-HOSP score categories and in-hospital management in the basic cohort (n = 8,547). CI, confidence interval; IVR, interventional radiology; LGIB, lower gastrointestinal bleeding; LOS, length of stay; OR, odds ratio; Ref, reference.

severe bleeding (namely, the absence of diarrhea and abdominal pain) [3, 4]. The presence of diarrhea, abdominal pain, and high C-reactive protein levels suggests severe colitis (ischemia, infection, or IBD). Severe colitis requiring hospitalization would demand an extended time period for conservative treatment or surgery. Indeed, in our study, the LOS in cases of colitis was significantly longer than that in other cases (median LOS: 12 days vs. 7 days, $p < 0.001$).

It is unclear why ≥800 inpatient beds were a predictive factor in the LONG-HOSP score. Our data indicated that large hospitals tended to treat patients whose bleeding management was difficult. For example, patients admitted to large hospitals (≥800 beds) had significantly higher rates of rebleeding (18.1% vs. 14.0%), transfusion needs (34.3% vs. 27.4%), and surgical intervention needs (1.5% vs. 0.9%) than patients admitted to smaller hospitals (<800 beds). These factors were significantly associated with LOS, independent of clinical factors at hospital visit (LONG-HOSP score) (Fig. 3). Although we did not investigate the referral of members of our patient population from small institutions to large institutions because of difficulties in bleeding management, this may have occurred. A previous report in patients with lumbar intervertebral disc disorder supports our results, as hospitalization in institutions with many inpatient beds was associated with prolonged hospital stays [36]. The same paper also suggested that not only the number of beds but also the number of doctors and registered nurses were associated with LOS. Information on hospital staff was not included in our database. Therefore, further investigation is warranted regarding hospital-level variables.

The LONG-HOSP score requires more factors to be calculated than for other GIB scores [1–6, 32, 33]. However, we emphasize the usefulness of our score because seven existing GIB scores failed to predict LOS (when compared with this score) because of factor variances (online suppl. Fig. 1). The LONG-HOSP score includes unique factors not included in other scores. However, we confirm that most factors in the LONG-HOSP score

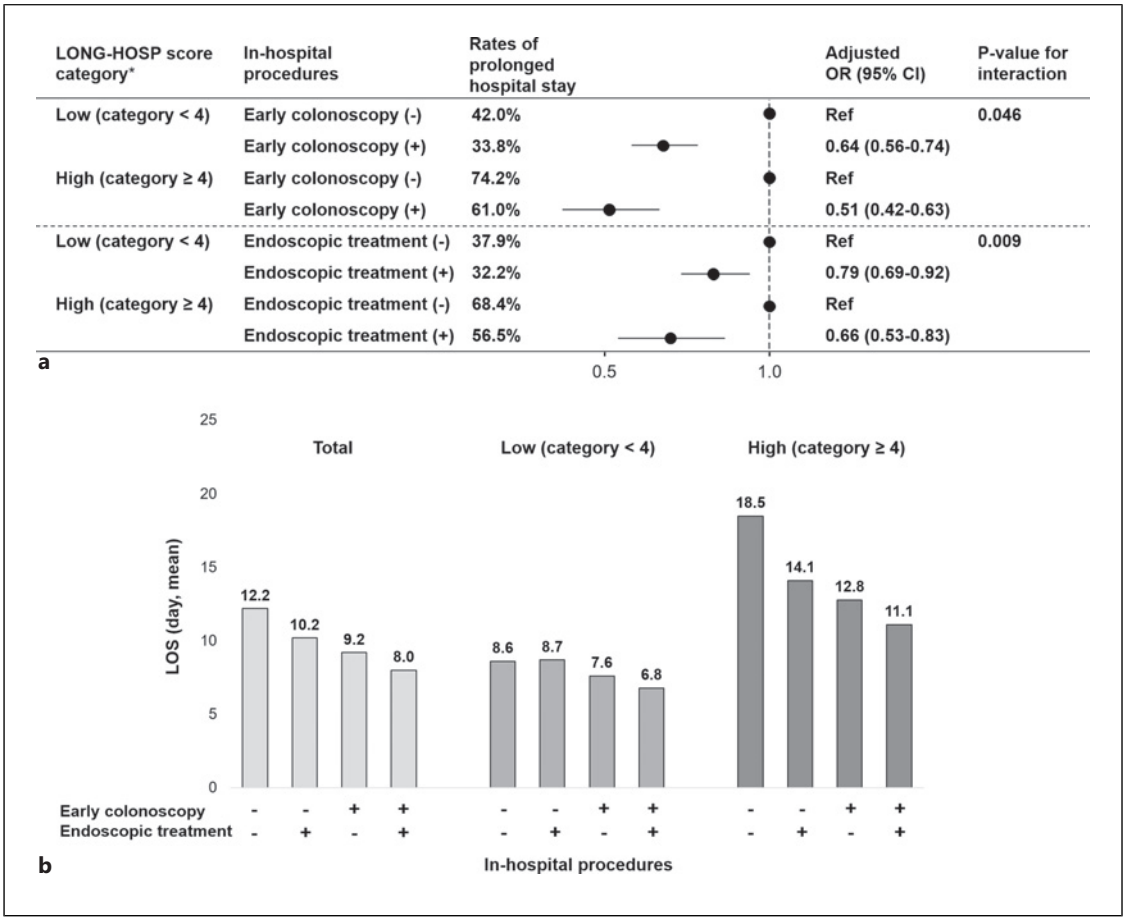

Fig. 4. Effects of in-hospital procedures on LOS based on the LONG-HOSP score category in the basic cohort (n = 8,547). **a** Interaction analysis between the LONG-HOSP score category and in-hospital procedures. **b** LOS in subgroups based on the LONG-HOSP score category, early colonoscopy, and endoscopic treatment. *The LONG-HOSP score was classified into seven categories: ≤5, 6–10, 11–15, 16–20, 21–25, 26–30, and ≥31. CI, confidence interval; LOS, length of stay; OR, odds ratio; Ref, reference.

overlap with factors in existing ALGIB scores. Therefore, the LONG-HOSP score simultaneously predicts not only LOS but also major clinical outcomes such as death and severity at the time of the hospital visit.

Multivariate analysis, including the LONG-HOSP score and in-hospital management, revealed several things. First, LONG-HOSP score category was associated with LOS, regardless of some crucial in-hospital factors such as rebleeding and need for interventional radiology/surgery. Second, LOS depended on LGIB etiology, and thus diagnosis of etiology could predict LOS. A diagnosis of hemorrhoids was associated with short LOS, probably because the rebleeding rate (5%) was lower than that of other etiologies (15%). Patients with colorectal cancer required the longest hospital stay. Possibly, endoscopic hemostasis could not be achieved and surgery was needed for hemostasis and/or cancer treatment (surgery rate: 18% for colorectal cancer vs. 1% for other etiologies). Finally, the performance of important procedures during hospitalization certainly reduced LOS, regardless of the LONG-HOSP score and LGIB etiology. Our analysis showed that early colonoscopy and endoscopic treatment contributed to reducing LOS, which is consistent with previous reports [11–16]. Why early colonoscopy reduces LOS is unclear. It could be that, compared with elective colonoscopy, early colonoscopy enables the early detection of patients who are at low risk of rebleeding or needing interventions, which can reduce the need for further diagnostic workup. In addition, endoscopic treatment can reduce the rebleeding risk. Therefore, early colonoscopy and endoscopic treatment may prompt an early start on a solid diet and thus result in earlier discharge. Importantly, these procedures seemed effective for reducing LOS, particularly

in patients with a high LONG-HOSP score. These findings suggest that the assessment of patients' baseline characteristics when they arrive at hospital could support the indications for these procedures.

The inclusion of a large number of facilities and patients with various LGIB etiologies is a strength of our study. Furthermore, we obtained detailed patient information that was comprehensively assessed, such as performance status, presenting symptoms, vital signs, and laboratory data. Nevertheless, our study was limited by its retrospective design. Further prospective and validation studies are warranted to overcome this limitation and confirm our results.

Conclusion

With the LONG-HOSP score, hospital admission data can be used to stratify patients with ALGIB who are at high risk of prolonged hospital stay. During hospitalization, early colonoscopy and endoscopic treatment can reduce LOS, particularly in patients with high LONG-HOSP scores.

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Statement of Ethics

The ethics committees and institutional review boards of all 49 participating hospitals approved conducting this study with the opt-out method.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

N.N. was the principal investigator of this study. M.F., T.A. (The University of Tokyo), and N.N. designed and conducted the study. M.F. and T.A. (The University of Tokyo) performed statistical analysis; M.F., T.A. (The University of Tokyo), N.M., Y.I., K.K. (Tokyo Metropolitan Bokutoh Hospital), A.Y. (Kitano Hospital), A.Y. (The University of Tokyo), J.O., T.I., T.A. (Hiroshima City Asa Citizens Hospital), N.T., Y.S. (St. Marianna University School of Medicine), T.K. (Nara City Hospital), N.I., T.S., M.M., A.T., K.M. (Oita University), K.K. (Fukuoka University Chikushi Hospital), S.F. (Chiba Hokusoh Hospital, Nippon Medical School), T.U., H.S., S.S., T.N., J.H., T.F., Y.K. (Naha City Hospital), A.M., S.K., T.M. (Hirosaki University Hospital), R.G., H.F., Y.F., N.G., Y.T., K.N. (National Defense Medical College), K.N. (Suita Municipal Hospital), T.K. (University of the Ryukyus Hospital), Y.S. (National Hospital Organization Kyushu Medical Center), S.F. (Fukuoka University Hospital), K.K. (Kitasato University), T.M. (Akita University Graduate School of Medicine), Y.K. (Kagoshima University Graduate School of Medical and Dental Sciences), K.M. (Tokyo Medical University), K.W., M.A., T.M. (Kawasaki Medical School), M.S., A.S., J.H., K.H. M.K., and N.N. collected and interpreted the data. M.F. drafted the article. T.A. (The University of Tokyo) and N.N. critically revised the article. All authors read and approved the submitted version of the manuscript.

Data Availability Statement

The datasets generated during and/or analyzed during the current study are not available. All data generated or analyzed during this study are included in this article and its online supplementary material files. Further inquiries can be directed to the corresponding author.

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