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ORIGINAL ARTICLE

Acute Hemorrhagic Rectal Ulcer: An Important Cause of Lower Gastrointestinal Bleeding in the Critically Ill Patients

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Abstract
Background and Aim The occurrence of acute hemorrhagic rectal ulcer (AHRU) in patients in the intensive care unit (ICU) has not been well investigated. The aims of this study were to evaluate the clinical manifestations and outcomes in these patients.
Method The patients developing significant acute lower gastrointestinal (LGI) bleeding after ICU admission from July 2002 to December 2007 were retrospectively reviewed. Bedside colonoscopy was performed within 24 h of bleeding, and those patients with bleeding from AHRU were studied. Ulcers with stigmata of recent bleeding were treated with endoscopic hemostasis, and the outcome of these patients was analyzed.
Results AHRU occurred in 36 of 114 patients (31.6%) and was the most common cause of acute LGI bleeding after ICU admission. Most patients had comorbidities, such as respiratory failure, renal failure, diabetes mellitus, or atherosclerosis. Fourteen patients (38.9%) developed hypovolemic shock after the onset of bleeding. Endoscopic therapy was performed in 29 patients with 97.2% success rate for hemostasis. Fourteen patients (48.3%) developed rebleeding within 4 weeks. This was controlled by repeated endoscopic intervention. Anticoagulant use was the risk factor for rebleeding after treatment. The survival rate at 4 weeks after bleeding was 52.8%. Logistic regression analysis revealed thrombocytopenia (platelet count $<150{,}000/mm^3$) and more than one comorbidity were independent predictors for mortality.
Conclusions AHRU is an important etiology of acute LGI bleeding in the patients with critical illness. Bedside colonoscopy is helpful for early diagnosis and treatment. The underlying comorbidities of the patients influence the outcome after bleeding.

Keywords Lower gastrointestinal bleeding · Acute hemorrhagic rectal ulcer · Colonoscopy · Intensive care unit

Abbreviations

AHRU	Acute hemorrhagic rectal ulcer
ICU	Intensive care unit
LGI bleeding	Lower gastrointestinal bleeding
APACHE-II	Acute Physiology and Chronic Health Evaluation II

Introduction

The incidence of significant lower gastrointestinal (LGI) bleeding after intensive care unit (ICU) admission has been reported from 0.15 to 0.94% [1, 2]. Among the causes, acute hemorrhagic rectal ulcer (AHRU) is commonly encountered in elderly patients with severe comorbidities. It is characterized by the sudden onset, painless, massive hematochezia from solitary or multiple rectal ulcer(s)

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[3, 4]. The bleeding is potentially life-threatening, and requires urgent identification, resuscitation, and management.

Although AHRU is increasingly recognized, reported cases in critically ill patients are still limited. The characteristics and outcomes of these patients are also not well-described. Therefore, we made a thorough review of the patients with AHRU in the ICUs of our institution. The manifestations, efficacy of endoscopic hemostasis, risks of rebleeding and outcomes of these patients were investigated.

Materials

We retrospectively reviewed the endoscopic report database to search for the patients who received colonoscopies during hospitalization in the ICUs of Far Eastern Memorial Hospital from July 2002 to December 2007. This hospital is a 1,053 beds tertiary care medical center with 20 beds in the medical ICU, 20 beds in the surgical ICU, and 25 beds in the coronary care unit.

Inclusion and Exclusion Criteria

The adult patients (≥18 years of age) who developed significant acute LGI bleeding after admission to one of the ICUs and who also received colonoscopic examination were enrolled. Clinically significant LGI bleeding was defined as hematochezia and either (a) decrease in hemoglobin ≥2 g/dl in 24 h, (b) need of transfusion of at least two units of packed red blood cells or whole blood, (c) decrease of systolic blood pressure ≥20 mmHg, or (d) increase of heart rate ≥20 beats per minute [1, 2]. The patients with hematochezia from an upper gastrointestinal source as determined by clinical presentations with hematemesis, bloody, or coffee ground materials in the nasogastric tube drainage were excluded.

Colonoscopy and Hemostasis Procedure

Bedside colonoscopy was performed after adequate resuscitation and stabilization of the patient. After obtaining informed consent, the colonoscopy was performed after colon preparation (either oral sodium phosphate laxative, or castor oil solution, and enema) within 24 h after the onset of bleeding. Colonoscopy was performed by one of three endoscopists (C.-K. Lin, C.-C. Liang, and T.-H. Lee), who were experienced in performing colonoscopy and therapeutic endoscopy. During examination, the colonoscope was inserted to the cecum if possible. For exclusion of the upper gastrointestinal bleeding, esophagogastroduodenoscopy was performed in cases whose source of bleeding was not identified on colonoscopy. The AHRU was defined as acute hematochezia with endoscopic documentation of rectal ulcer(s). The endoscopic features of AHRU were classified as round, geographic shaped, circumferential, or Dieulafoy-like lesion (Fig. 1) [4, 5]. Patients with stigmata of recent bleeding (such as an active bleeding vessel, adherent clot, non-bleeding visible vessel, or diffuse oozing blood) were treated. Endoscopic hemostasis was performed by various means including injection of a saline-epinephrine solution, heat probe, argon plasma coagulation, and hemoclipping, or a combination of these methods.

Outcome Parameters and Assessment

Demographic data, APACHE-II score, hemogram, and coagulation profile at the onset of bleeding were recorded. Thrombocytopenia was defined as platelet count <150,000/mm^3 and coagulopathy was defined as international normalized ratio (INR) >1.5. Clinical data including the reason for ICU admission, need of mechanical ventilation, the presence of sepsis, renal failure receiving hemodialysis, diabetes mellitus, coronary artery disease, congestive heart failure, arrhythmia, stroke, liver cirrhosis, use of anticoagulants or antiplatelet agents, and post-cardiopulmonary resuscitation were collected. We also collected data regarding the time from ICU admission to onset of bleeding, the presence of hemorrhagic shock (systolic blood pressure ≤90 mmHg and pulse rate ≥110 beat per min), amount of hematochezia before colonoscopy, decrease of hemoglobin, and total volume of blood transfused.

The immediate hemostasis was defined as verified cessation of bleeding after therapy during colonoscopy. Recurrent bleeding was defined as the occurrence of hematochezia with decrease of hemoglobin in excess of 2 g/dl, or hemodynamic instability after successful hemostasis [1]. The outcome variables included the duration of ICU stay, recurrent bleeding within 4 weeks, and survival at the fourth week.

Statistical Analysis

The quantitative data were compared with the *t* test and the categorical variables were compared with the chi-square test. Logistic regression analysis was used for determining the predicting factor of mortality. The cumulative rate of patients free from rebleeding after endoscopic hemostasis as a function of time was analyzed by the Kaplan–Meier method, and compared by the log-rank test. The P value < 0.05 was considered as statistically significant. All data analyses were performed with SPSS version 13 (SPSS Inc., Chicago, IL, USA).

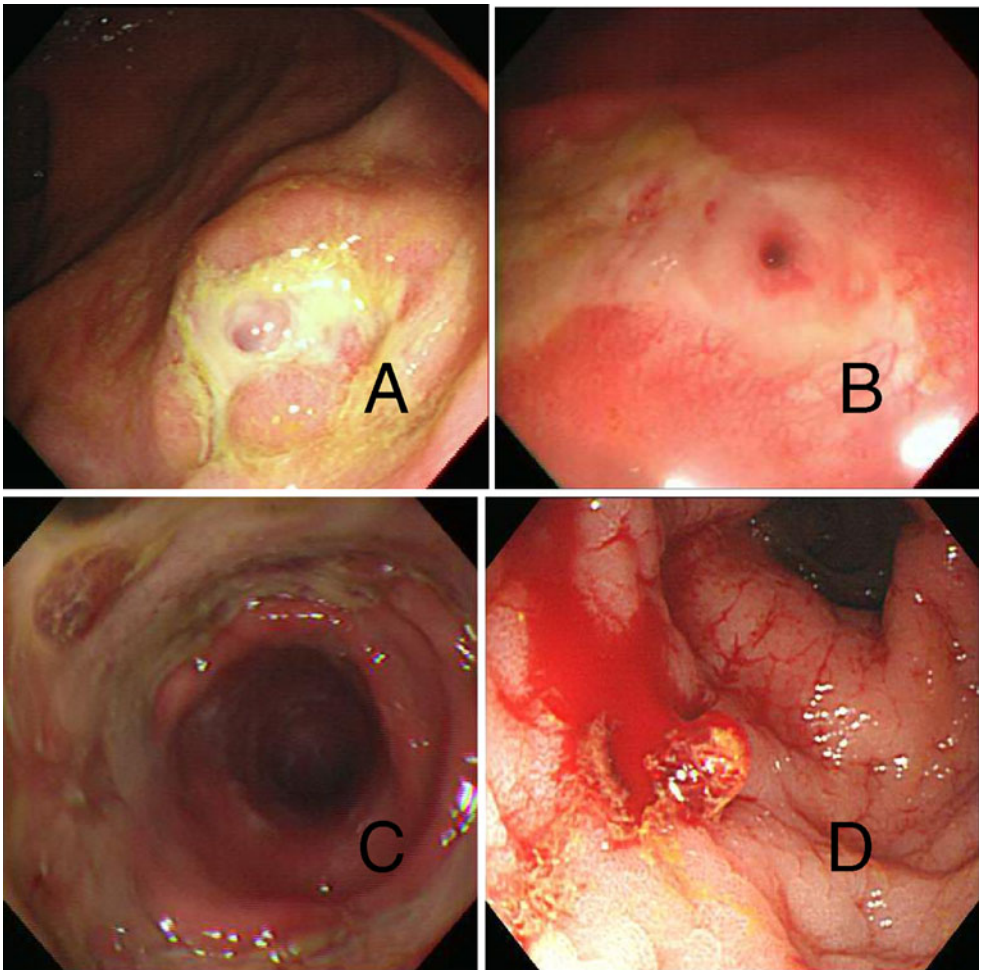

Fig. 1 The endoscopic appearance of rectal ulcers was classified as round (**a**), geographic (**b**), circumferential (**c**), or Dieulafoy-like lesion (**d**)

Results

Patient Demographic Characteristics

From July 2002 to December 2007, a total of 119 patients received colonoscopies for acute hematochezia in the ICUs. Two patients were excluded because they were admitted or transferred to the ICU due to LGI bleeding. In 103 of the 117 patients (88%), complete examination to the cecum was achieved. The remaining 14 patients had incomplete examinations due to interference by non-bloody formed stool. However, the bleeder was identified in the distal colon.

Thirty-six patients had bleeding from rectal ulcers. Fifty-seven patients had other identified colonic bleeders including ischemic colitis (31 patients), hemorrhoids (13 patients), angiodysplasia (4 patients), diverticulum (4 patients), colorectal cancer (3 patients), radiation colitis (1 patient), and polyp (1 patient). In the other 24 patients, no visible colonic bleeder could be identified. However, some blood was found in the cecum. Thus bleeding above the colon was considered. These 24 patients received esophagogastroduodenoscopy and three patients were found to have upper gastrointestinal bleeding from gastric or duodenal ulcers. After exclusion of these 3 patients, 114 patients developing LGI bleeding after ICU admission were included in the analysis. The algorithm of selection of the studied patients is shown in Fig. 2.

In total, 36 of 114 patients (31.6%) had AHRU. It was the most common cause of acute LGI bleeding in our ICU patients. The clinical characteristics of these patients are presented in Table 1. There were 20 men and 16 women with mean age of 69 ± 13 years (range, 43–93 years). The median APACHE-II score on the first day of ICU admission was 26 (range, 10–45). The median onset time of bleeding was 11 days after ICU admission (range, 3–39 days). All patients presented with the sudden onset of fresh blood, or blood clot passage from the anus. Fourteen of 36 patients (38.9%) developed hypovolemic shock at the time bleeding presented. The median amount of hematochezia before colonoscopy was 2,260 g (range, 120–11,200 g). The mean of initial decrease of hemoglobin before

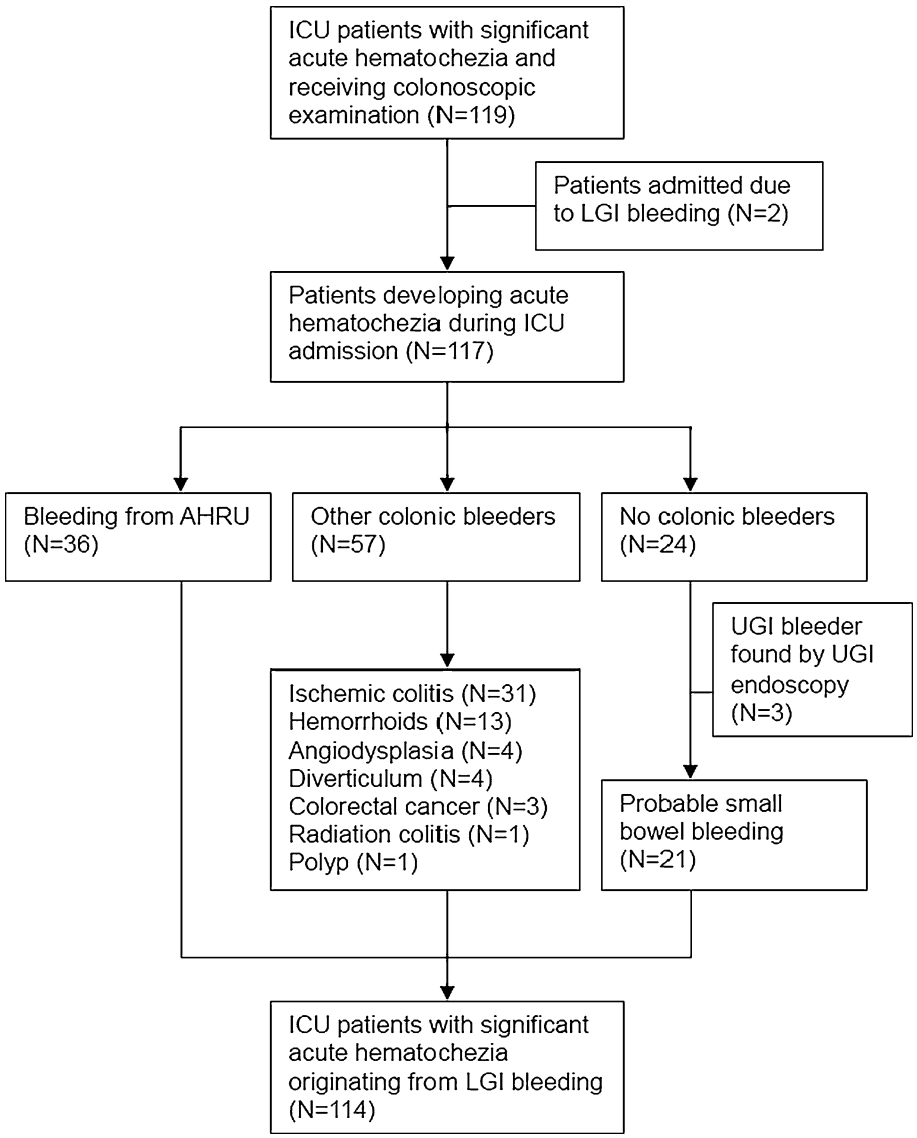

Fig. 2 Selection algorithm of the patients studied

colonoscopy was 1.89 ± 1.13 g/dl (range, 0.2–4.9 g/dl). The mean amount of blood transfused was 9.19 ± 5.5 units (range, 2–20 units).

Six patients with persistent massive bleeding received emergent angiography before preparation for colonoscopy. Only two of these six patients (33.3%) had identifiable bleeders on angiography. One patient with bleeding from the rectal artery received trans-arterial embolization and the other received intra-arterial vasopressin infusion. The hemostasis was achieved in both cases.

Endoscopic Hemostasis and Ulcer Morphology

Endoscopic hemostasis was performed in 29 patients (80.6% of all AHRU) with stigmata of recent bleeding. Fifteen patients (51.7%) had active bleeding vessels and ten patients (34.5%) had non-bleeding visible vessels. Three patients had diffuse ulcer base bleeding and one patient had an adherent blood clot. We used single modalities including injection with saline-epinephrine solution (13.8%), heat probe (34.5%), argon plasma coagulation (10.3%), and hemoclipping (6.9%), or combined methods with injection and heat probe/argon plasma coagulation (34.5%) for control of bleeding. The success rate of immediate hemostasis was 97.2%. Only one patient (2.8%) needed surgery for uncontrolled bleeding and hemostasis was achieved after per-anal suture. Fourteen of 29 patients (48.3%) who were treated developed rebleeding within 4 weeks. The time interval from initial endoscopic treatment to first rebleeding was 9 ± 6 days (range, 1–22 days). A further 1.56 ± 1.2 (range, 1–5) occurrences of endoscopic hemostasis were required to treat the rebleeding episodes.

Table 1 Clinical characteristics of patients with acute hemorrhagic rectal ulcer in the ICUs ($N = 36$)

Reason for ICU admission	Number (%)
Respiratory failure	28 (77.8)
Sepsis	22 (61.1)
Coronary artery disease	12 (33.3)
Acute stroke	8 (22.2)
Major surgery	5 (13.9)
Trauma	5 (13.9)
Post-cardiopulmonary resuscitation	2 (5.6)
Comorbid illnesses	
Renal failure	20 (55.6)
Diabetes mellitus	15 (41.7)
Congestive heart failure	12 (33.3)
Cerebrovascular accident	12 (33.3)
Cardiac arrhythmia	9 (25)
Cancer	6 (16.7)
Chronic obstructive pulmonary disease	5 (13.9)
Liver cirrhosis	4 (11.1)
Therapy and medications	
Mechanical ventilation	36 (100)
Hemodialysis	16 (44.4)
Inotropic agents	14 (38.9)
Antiplatelet agents (aspirin or clopidogrel)	9 (25)
Anticoagulant therapy (heparin or warfarin)	5 (13.9)
Steroid or non-steroid anti-inflammatory agents	3 (8.3)

In colonoscopy, the ulcer morphology included circumferential (44.4%), round (36.1%), Dieulafoy-like lesions (16.7%), and geographic shaped ulcers (2.8%). Multiple ulcers were observed in 23 patients (63.9%). After endoscopic hemostasis, there was no statistically significant difference in the number of rebleeding episodes between ulcer characteristics, or the hemostatic modalities used. Patients receiving anticoagulants were more likely to develop rebleeding after endoscopic treatment (log-rank test, $P = 0.005$) (Fig. 3). Patients with hypovolemic shock before colonoscopy had the tendency for rebleeding as compared to those without hypovolemic shock (57.1% vs. 26.7%, respectively, $P = 0.082$). Patients with hypovolemic shock had more liver cirrhosis (28.6% vs. 0%; $P = 0.008$) and Dieulafoy-like lesions (35.7% vs. 4.5%; $P = 0.014$) as compared to patients without shock.

Outcome of AHRU

The median duration of ICU stay after initial bleeding was 23 days (range, 6–125 days). The overall survival rate at the fourth week after bleeding was 52.8%. The causes of mortality were sepsis with multiple organ failure (70.6%), heart failure (5.9%), intracranial hemorrhage (5.9%), bradycardia (5.9%), and hepatic failure (5.9%). Only one patient (5.9%) died of uncontrolled recurrent LGI hemorrhage because the family did not consent to surgery.

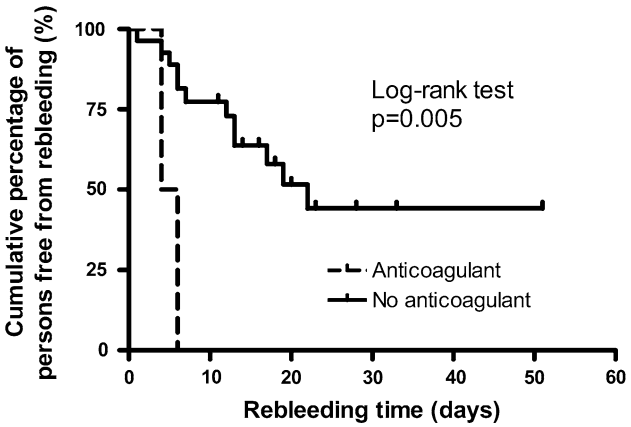

Fig. 3 Kaplan–Meier estimate of the cumulative percentage of patients free from recurrent bleeding after endoscopic hemostasis

Univariate logistic regression analysis revealed that thrombocytopenia on the initial presentation of bleeding (odds ratio [OR] = 5.19, $P = 0.036$) and having more than one comorbidity (OR = 4.47, $P = 0.042$) were risk factors for mortality at the fourth week after bleeding. Multivariate logistic regression analysis indicated that only thrombocytopenia (OR = 8.94, $P = 0.044$) was predictive of mortality at the fourth week after bleeding (Table 2). Fifteen of 23 patients (65.2%) with thrombocytopenia had sepsis. Among these 23 patients, six patients had evidence of disseminated intravascular coagulation with low fibrinogen, and high fibrin degraded products and D-dimer level. There were only three patients (13%) with liver cirrhosis.

Discussion

Because of the increasing use of colonoscopy in patients with critical illnesses, the etiology of acute LGI bleeding can be identified in two-thirds of the cases. Ischemic colitis and rectal ulcers are the two primary causes of LGI hemorrhage in medical ICU patients and hospital inpatients, which is different from that of outpatients [1, 2, 6]. As in a previous report, AHRU is the most common cause of acute LGI bleeding in patients after hospitalization for other morbidities in our series [7].

Soeno et al. [3] first used the term "acute hemorrhagic rectal ulcer" to describe such cases in Japan. Fujimaki et al. [9] subsequently recognized it as a syndrome. AHRU is most commonly encountered in elderly, bed-ridden patients with serious comorbidities [4, 5, 8]. All of our patients were bed-ridden, and in need of mechanical ventilator support. Many of them had renal failure requiring hemodialysis, hemodynamic instability receiving inotropic

Table 2 Predictors of mortality at the fourth week after bleeding in AHRU patients

Factor	Mortality number (%)	Univariate analysis		Multivariate analysis	
		OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Sex					
Female	6 (37.5)	1		–	–
Male	11 (55)	2.04 (0.53–7.79)	0.299	–	–
Age (years)					
<65	4 (36.4)	1		–	–
≥65	13 (52)	1.9 (0.44–8.14)	0.39	–	–
APACHE-II score					
<25	7 (41.2)	1		–	–
≥25	10 (52.9)	1.59 (0.42–5.95)	0.493	–	–
Thrombocytopenia					
No	3 (23.1)	1		1	
Yes	14 (60.9)	5.19 (1.11–24.14)	0.036*	8.94 (1.05–77.12)	0.044*
Coagulopathy					
No	12 (42.6)	1		–	–
Yes	5 (50)	1.17 (0.27–5.02)	0.836	–	–
≥2 comorbidities					
No	4 (26.7)	1		1	
Yes	13 (62.9)	4.47 (1.05–18.94)	0.042*	4.43 (0.66–30.02)	0.127
Hypovolemic shock					
No	11 (50)	1		–	–
Yes	6 (42.9)	0.75 (0.2–2.89)	0.676	–	–
Inotropic agent use					
No	8 (38.1)	1		–	–
Yes	9 (60)	0.41 (0.11–1.6)	0.198	–	–
Endoscopic therapy					
No	3 (42.9)	1		–	–
Yes	14 (48.3)	0.8 (0.15–4.25)	0.797	–	–
Blood transfusion					
<10 units	9 (47.4)	1		–	–
≥10 units	8 (47.1)	0.99 (0.27–3.66)	0.985	–	–

AHRU acute hemorrhagic rectal ulcer, *OR* odds ratio, *CI* confidence interval

Thrombocytopenia: platelet count <150,000/mm^3 at the onset of bleeding. Coagulopathy: international normalized ratio (INR) >1.5 at the onset of bleeding

* Statistically significant different, $P < 0.05$

agents, bleeding tendency, and atherosclerotic diseases. Reduced rectal mucosal blood flow in the supine position has been proposed as the pathogenesis of AHRU [10]. Atherosclerosis and diabetes mellitus have also been reported to have important associations with AHRU [5]. Thus, bed-ridden patients with multiple comorbidities in ICUs are particularly susceptible to this illness.

A clinically similar condition, termed "solitary rectal ulcer", which can result in massive LGI bleeding has been reported, and it is commonly associated with rectal prolapse after straining or pelvic floor incoordination caused by chronic constipation [11]. In contrast, there were multiple, rather than solitary, ulcers in 63.9% of our AHRU patients. Our patients did not have fecal impaction or receive rectal manipulation before the presentation of bleeding. Therefore, AHRU is the appropriate term for these groups of patients with sudden onset of rectal bleeding.

In a previous report, only 2.8% of AHRU patients in a general hospital population had massive bleeding with hypovolemic shock [4]. The proportion was higher (38.9%) in our patients, and likely due to the severe illnesses requiring ICU admission. The mortality rate in our cohort was also higher than in a previous report (47.2% vs. 33%) [12]. Our analysis indicated that patients with thrombocytopenia or more than one comorbidity were more likely to

have poorer outcomes. Another study indicated that transfusions ≥12 units, diabetes mellitus, or other comorbid diseases, lower performance status, and decreased serum albumin concentration were associated with greater need of surgical treatment and longer hospital stays after bleeding episode [13]. In our study, patients with greater amount of transfusions did not have worse outcomes. This may be due to early resuscitation with aggressive component therapy, and endoscopic treatment while in the ICUs.

In our study, the success rate of endoscopic hemostasis using a variety of modalities was similar to previous reports [4, 5]. However, the rebleeding risk after endoscopic treatment was high (48.3%) in our patients, and was similar to that in a previous report (42%) [12]. If endoscopic hemostasis fails, other treatment modalities should be considered. Angiographic embolization is an alternative before surgery for the treatment of life-threatening hemorrhage [14]. Only one-third of our patients were found to have an identifiable bleeder during angiography, and were treated with trans-arterial embolization or intra-arterial vasopressin infusion. If medical therapy fails, surgical intervention using per-anal suturing provides an alternative choice for hemostasis. However, 42% of patients still had recurrent hemorrhage and 81.8% of these patients with recurrent bleeding responded to repeated therapy [15].

Even though current endoscopic hemostasis is effective, AHRU is still associated with high rebleeding rate. It is important to develop an appropriate adjuvant therapy after endoscopic treatment. Previous studies reported sucralfate retention enemas can promote healing of solitary rectal ulcers [16, 17]. Besides, we assume that second-look endoscopy with hemostasis as needed, similar to the policy for peptic ulcer bleeding [18], may have a role in the prevention of AHRU rebleeding. The limitations of previous and this study are retrospective design, heterogeneity of studied population, and no standardized use of hemostasis modalities. Further prospective studies regarding the optimal therapeutic modalities and prevention of rebleeding after endoscopic therapy are needed to improve the management of AHRU in the critically ill patients.

In conclusion, AHRU should be considered as an important etiology of acute LGI bleeding in critically ill patients. These patients often have underlying comorbidities, such as respiratory failure, renal failure, diabetes mellitus, or atherosclerosis. Bedside colonoscopy can be helpful in early diagnosis and treatment. The prognosis of these patients depends on both accurate diagnosis and management of their underlying diseases.

Conflict of interest There were no potential conflicts of interest to be disclosed.

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