Open

Identifying Bleeding Etiologies by Endoscopy Affected Outcomes in 10,342 Cases With Hematochezia: CODE BLUE-J Study

Naoyoshi Nagata, MD, PhD[1,2], Katsumasa Kobayashi, MD[3], Atsushi Yamauchi, MD[4], Atsuo Yamada, MD, PhD[5], Jun Omori, MD[6], Takashi Ikeya, MD[7], Taiki Aoyama, MD, PhD[8], Naoyuki Tominaga, MD, PhD[9], Yoshinori Sato, MD, PhD[10], Takaaki Kishino, MD[11], Naoki Ishii, MD, PhD[12], Tsunaki Sawada, MD, PhD[13], Masaki Murata, MD[14], Akinari Takao, MD, PhD[15], Kazuhiro Mizukami, MD, PhD[16], Ken Kinjo, MD, PhD[17], Shunji Fujimori, MD, PhD[18], Takahiro Uotani, MD, PhD[19], Minoru Fujita, MD, PhD[20], Hiroki Sato, MD, PhD[21], Sho Suzuki, MD[22], Toshiaki Narasaka, MD, PhD[23,24], Junnosuke Hayasaka, MD[25], Tomohiro Funabiki, MD, PhD[26,27], Yuzuru Kinjo, MD, PhD[28], Akira Mizuki, MD, PhD[29], Shu Kiyotoki, MD, PhD[30], Tatsuya Mikami, MD, PhD[31], Ryosuke Gushima, MD, PhD[32], Hiroyuki Fujii, MD, PhD[33], Yuta Fuyuno, MD, PhD[34], Naohiko Gunji, MD, PhD[35], Yosuke Toya, MD, PhD[36], Kazuyuki Narimatsu, MD, PhD[37], Noriaki Manabe, MD, PhD[38], Koji Nagaike, MD[39], Tetsu Kinjo, MD, PhD[40], Yorinobu Sumida, MD, PhD[41], Sadahiro Funakoshi, MD[42], Kana Kawagishi, MD[43], Tamotsu Matsuhashi, MD, PhD[44], Yuga Komaki, MD, PhD[45], Kuniko Miki, MS[1], Kazuhiro Watanabe, MD, PhD[2], Masakatsu Fukuzawa, MD, PhD[46], Takao Itoi, MD, PhD[46], Naomi Uemura, MD, PhD[1,47], Takashi Kawai, MD, PhD[1] and Mitsuru Kaise, MD, PhD[6]

INTRODUCTION: **The bleeding source of hematochezia is unknown without performing colonoscopy. We sought to identify whether colonoscopy is a risk-stratifying tool to identify etiology and predict outcomes and whether presenting symptoms can differentiate the etiologies in patients with hematochezia.**

METHODS: **This multicenter retrospective cohort study conducted at 49 hospitals across Japan analyzed 10,342 patients admitted for outpatient-onset acute hematochezia.**

[1]Department of Gastroenterological Endoscopy, Tokyo Medical University, Tokyo, Japan; [2]Department of Gastroenterology and Hepatology, National Center for Global Health and Medicine, Tokyo, Japan; [3]Department of Gastroenterology, Tokyo Metropolitan Bokutoh Hospital, Tokyo, Japan; [4]Department of Gastroenterology and Hepatology, Kitano Hospital, Tazuke Kofukai Medical Research Institute, Osaka, Japan; [5]Department of Gastroenterology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan; [6]Department of Gastroenterology, Nippon Medical School, Graduate School of Medicine, Tokyo, Japan; [7]Department of Gastroenterology, St. Luke's International University, Tokyo, Japan; [8]Department of Gastroenterology, Hiroshima City Asa Citizens Hospital, Hiroshima, Japan; [9]Department of Gastroenterology, Saga Medical Center Koseikan, Saga, Japan; [10]Division of Gastroenterology and Hepatology, Department of Internal Medicine, St. Marianna University School of Medicine, Kanagawa, Japan; [11]Department of Gastroenterology and Hepatology, Center for Digestive and Liver Diseases, Nara City Hospital, Nara, Japan; [12]Department of Gastroenterology, Tokyo Shinagawa Hospital, Tokyo, Japan; [13]Department of Endoscopy, Nagoya University Hospital, Aichi, Japan; [14]Department of Gastroenterology, National Hospital Organization Kyoto Medical Center, Kyoto, Japan; [15]Department of Gastroenterology, Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital, Tokyo, Japan; [16]Department of Gastroenterology, Oita University, Oita, Japan; [17]Department of Gastroenterology, Fukuoka University Chikushi Hospital, Fukuoka, Japan; [18]Department of Gastroenterology, Chiba Hokusoh Hospital, Nippon Medical School, Chiba, Japan; [19]Department of Gastroenterology, Japanese Red Cross Shizuoka Hospital, Shizuoka, Japan; [20]Division of Endoscopy and Ultrasonography, Department of Clinical Pathology and Laboratory Medicine, Kawasaki Medical School General Medical Center, Okayama, Japan; [21]Division of Gastroenterology, Graduate School of Medical and Dental Sciences, Niigata University, Niigata, Japan; [22]Department of Gastroenterology and Hepatology, Center for Digestive Disease and Division of Endoscopy, University of Miyazaki Hospital, Miyazaki, Japan; [23]Department of Gastroenterology, University of Tsukuba, Ibaraki, Japan; [24]Division of Endoscopic Center, University of Tsukuba Hospital, Ibaraki Japan; [25]Department of Gastroenterology, Toranomon Hospital, Tokyo, Japan; [26]Department of Emergency Medicine, Fujita Health University Hospital, Aichi, Japan; [27]Emergency and Critical Care Center, Saiseikai Yokohamashi Tobu Hospital, Kanagawa, Japan; [28]Department of Gastroenterology, Naha City Hospital, Okinawa, Japan; [29]Department of Internal Medicine, Tokyo Saiseikai Central Hospital, Tokyo, Japan; [30]Department of Gastroenterology, Shuto General Hospital, Yamaguchi, Japan; [31]Division of Endoscopy, Hirosaki University Hospital, Aomori, Japan; [32]Department of Gastroenterology and Hepatology, Graduate School of Medical Sciences, Kumamoto University, Kumamoto, Japan; [33]Department of Gastroenterology and Hepatology, National Hospital Organization Fukuokahigashi Medical Center, Fukuoka, Japan; [34]Department of Medicine and Clinical Science, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan; [35]Department of Gastroenterology, Fukushima Medical University, Fukushima, Japan; [36]Division of Gastroenterology, Department of Internal Medicine, Iwate Medical University, Iwate, Japan; [37]Department of Internal Medicine, National Defense Medical College, Saitama, Japan; [38]Division of Endoscopy and UltrasonograPhy, Department of Clinical Pathology and Laboratory Medicine, Kawasaki Medical School, Okayama, Japan; [39]Department of Gastroenterology and Hepatology, Suita Municipal Hospital, Osaka, Japan; [40]Department of Endoscopy, University of the Ryukyu Hospital, Okinawa, Japan; [41]Department of Gastroenterology, National Hospital Organization Kyushu Medical Center, Fukuoka, Japan; [42]Department of Gastroenterological Endoscopy, Fukuoka University Hospital, Fukuoka, Japan; [43]Department of Gastroenterology, Kitasato University, School of Medicine, Kanagawa, Japan; [44]Department of Gastroenterology and Neurology, Akita University Graduate School of Medicine, Akita, Japan; [45]Digestive and Lifestyle Diseases, Kagoshima University Graduate School of Medical and Dental Sciences, Kagoshima, Japan; [46]Department of Gastroenterology and Hepatology, Tokyo Medical University, Tokyo, Japan; [47]Department of Gastroenterology and Hepatology, National Center for Global Health and Medicine, Kohnodai Hospital, Chiba, Japan.

Collaborators: The names and affiliations of the CODE BLUE-J study group members are listed in Supplementary Table 1 (see Supplementary Digital Content 4, http://links.lww.com/AJG/C147).**Correspondence:** Naoyoshi Nagata, MD, PhD. E-mail: nnagata_ncgm@yahoo.co.jp.

Received April 9, 2021; accepted June 24, 2021; published online August 13, 2021

RESULTS: **Patients were mostly elderly population, and 29.5% had hemodynamic instability. Computed tomography was performed in 69.1% and colonoscopy in 87.7%. Diagnostic yield of colonoscopy reached 94.9%, most frequently diverticular bleeding. Thirty-day rebleeding rates were significantly higher with diverticulosis and small bowel bleeding than with other etiologies. In-hospital mortality was significantly higher with angioectasia, malignancy, rectal ulcer, and upper gastrointestinal bleeding. Colonoscopic treatment rates were significantly higher with diverticulosis, radiation colitis, angioectasia, rectal ulcer, and postendoscopy bleeding. More interventional radiology procedures were needed for diverticulosis and small bowel bleeding. Etiologies with favorable outcomes and low procedure rates were ischemic colitis and infectious colitis. Higher rates of painless hematochezia at presentation were significantly associated with multiple diseases, such as rectal ulcer, hemorrhoids, angioectasia, radiation colitis, and diverticulosis. The same was true in cases of hematochezia with diarrhea, fever, and hemodynamic instability.**

DISCUSSION: **This nationwide data set of acute hematochezia highlights the importance of colonoscopy in accurately detecting bleeding etiologies that stratify patients at high or low risk of adverse outcomes and those who will likely require more procedures. Predicting different bleeding etiologies based on initial presentation would be challenging.**

SUPPLEMENTARY MATERIAL accompanies this paper at http://links.lww.com/AJG/C144, http://links.lww.com/AJG/C145, http://links.lww.com/AJG/C146, http://links.lww.com/AJG/C147

Am J Gastroenterol 2021;116:2222–2234. https://doi.org/10.14309/ajg.0000000000001413

INTRODUCTION

Acute lower gastrointestinal bleeding (ALGIB) manifests as relatively mild hematochezia but can progress to massive hemorrhage with shock (1–3). Approximately 30%–50% of adults with ALGIB will progress to severe bleeding (4–7), and bleeding episodes can frequently recur, requiring reexaminations, rehospitalizations, and repeated transfusions (1–7). ALGIB episodes have also been shown to increase the risk of subsequent thromboembolism and death, regardless of antithrombotic use (8). ALGIB, therefore, presents a significant economic burden (9). Unlike upper GIB (UGIB), which can be treated with antiacid therapy, there are no effective therapies for preventing ALGIB or its recurrence (1). As such, there is likely to be considerable variation in the management of ALGIB.

In contrast to UGIB, there have been few large studies with more than 1,000 cases with ALGIB, especially using real-world clinical data. Although 1 large UK study demonstrated clinical courses of ALGIB in detail, it could not accurately identify the bleeding etiology because of infrequently performed endoscopy (10). The source of bleeding in patients with hematochezia varies and mainly includes not only colorectal diseases (e.g., diverticular bleeding, ischemic colitis, and hemorrhoids) but also small bowel bleeding and UGIB. Many physicians empirically suspect etiology based on the presenting symptoms. For example, hematochezia without pain or fever could be highly suspicious of diverticular bleeding, but subsequent colonoscopy may reveal a precise diagnosis of small bowel bleeding, rectal ulcer, or colorectal angioectasia, not diverticular bleeding. The same may be true in cases of hematochezia with abdominal pain. Therefore, the accurate bleeding source of hematochezia will not be known unless colonoscopy is performed.

Patients with hematochezia are at risk of various adverse outcomes, which may be significantly affected by different bleeding etiologies identified on colonoscopy. Moreover, if the precise etiology is not known and suspected incorrectly, errors in treatment and triage may occur. For example, without endoscopy, severe UGIB can be missed and antiacid therapy will not be administered, which could result in repeated rebleeding. Without colonoscopy, inflammatory bowel disease or infectious colitis may be mistakenly suspected, leading to incorrect treatment (11). Such situations may have potentially serious consequences.

Although guidelines recommend colonoscopy as the first-line procedure for patients presenting with hematochezia, its value remains unclear (1,3) because of the small number of endoscopy-based large cohort studies conducted to date. Therefore, we have collected data on more than 10,000 cases of acute hematochezia and comprehensively examined the bleeding etiologies identified by endoscopy. The aim of this study was to identify patients at risk for adverse outcomes based on bleeding etiology and to determine whether presenting symptoms and hemodynamic instability can predict the various bleeding etiologies.

METHODS

Study design, setting, and participants

We conducted this multicenter retrospective cohort study in 49 hospitals across Japan. To collect real-world clinical data, we sought the participation of gastroenterology physicians who were directly involved in the treatment of hematochezia. In total, 49 hospitals located in 25 prefectures, from Okinawa in the south to Aomori in the north, agreed to participate. Representative physicians at each hospital agreed to participate in this detailed investigation of clinical data for patients with acute hematochezia. The study was named the CODE BLUE-J Study (COlonic DivErticular Bleeding Leaders Update Evidence from multicenter Japanese Study). The ethics committees and institutional review boards approved conducting this study using the opt-out method in all participating hospitals (see Supplementary Table 1, Supplementary Digital Content 4, http://links.lww.com/AJG/C147). Patients and/or the members of the public were not involved in the design, conduct, reporting, or dissemination plan of this research. The case enrollment period at each institution ended at roughly 2019, with a target period of at least 1 year and at least 100

cases per institution, which was decided at several meetings based on the consensus of the participating institutions. The median enrollment period for the 49 participating institutions was 63 months (interquartile range [IQR], 40–78), and the median number of patients enrolled was 131 (IQR, 88–205) per institution (see Supplementary Table 1, Supplementary Digital Content 4, http://links.lww.com/AJG/C147). The median number of patients with acute hematochezia who were urgently hospitalized per month was estimated as 2.4 cases (IQR, 1.9–4.0). There was variability between facilities in this number of registrations because of the number of hospital beds, and the setting of the emergency medical care system included both university hospitals and emergency hospitals (see Supplementary Table 1, Supplementary Digital Content 4, http://links.lww.com/AJG/C147).

We selected patients who presented with hematochezia within 24 hours and were urgently hospitalized for bleeding treatment management between January 2010 and December 2019 and included patients aged ≥20 years at the onset of hematochezia regardless of the presence of tarry stools, diarrhea, abdominal pain, or fever. Symptom-based subjects in our study included patients with hematochezia with small bowel bleeding and UGIB and ALGIB defined as colorectal bleeding. The research office reviewed the data of each patient in detail, including the date of onset of symptoms, date of hospitalization, and date of examination, and confirmed the data several times with the representatives of each facility. As a result, the following patients were excluded because they were not considered to be acute, not for bleeding control purposes, or not of outpatient origin: patients with bleeding that had stopped for more than 24 hours, patients admitted for anemia investigation, and patients with in-hospital onset of hematochezia. Data for a total of 11,035 patients were collected and rigorously reevaluated by the secretariat's institution (Tokyo Medical University). After 693 patients were excluded, this left with 10,342 patients emergently admitted with outpatient-onset of acute, continuous, or frequent hematochezia for evaluation.

Data collection

Before data collection started, we held 3 research meetings with representatives from the 49 participating hospitals to discuss the content and definition of the survey items. At these meetings, it was agreed to aim for registration of at least 100 cases from each institution. The survey items were prepared using Excel sheets formatted to define each clinical factor, and data entry rules were sent to the participating institutions. To prevent data omissions or entry errors and to reduce the number of missing values, we used the data validation rules in Excel to input the values and unknowns for categorical variables (e.g., diabetes mellitus: 0, 1, and unknown) with free input for continuous variables (see Supplementary Table 2, Supplementary Digital Content 4, http://links.lww.com/AJG/C147). At each hospital, data were collected from electronic endoscopic records and medical records and entered into an Excel sheet. This sheet was then forwarded to secretariat's institution for evaluation of omissions and errors (e.g., admission or endoscopy date and data errors) in the input values for the data sent from each hospital (see Supplementary Table 2, Supplementary Digital Content 4, http://links.lww.com/AJG/C147). Data requiring correction were communicated to the physicians responsible for data input at each institution with detailed comments. Such communications were made more than 3 times per hospital, using Excel sheets sent by e-mail.

Variables and outcomes

In total, 219 survey items on clinical data during hospitalization and after discharge were assessed (see Supplementary Table 2, Supplementary Digital Content 4, http://links.lww.com/AJG/C147). Baseline characteristics consisted of 75 items, including presenting symptoms, vital signs, blood sample data, history, comorbidities, and medication use within 30 days of admission (see Supplementary Table 2, Supplementary Digital Content 4, http://links.lww.com/AJG/C147). Nineteen comorbidities were evaluated using the Charlson Comorbidity Index (CCI) (12), which is widely used and has been validated for use in GIB research (6,8,10). Data on the comorbidities of hypertension and dyslipidemia, which are not included in the CCI, were also collected. Information that was recorded during hospitalization was collected for computed tomography (CT) and endoscopic diagnosis consisting of 80 items (e.g., stigmata of recent hemorrhage [SRH] on endoscopy and etiology of bleeding). We also evaluated 41 items concerning procedures, such as type of endoscopic treatment, interventional radiology (IVR), and surgery (see Supplementary Table 2, Supplementary Digital Content 4, http://links.lww.com/AJG/C147). Because patients may have undergone 2 different or identical procedures during hospitalization because of events occurring between examination and treatment, we evaluated the procedure items twice.

Final diagnosis was made mainly based on findings from the initial and second endoscopies and after excluding other diseases by combining colonoscopy with other imaging tests, such as CT, small bowel endoscopy (capsule or balloon endoscopy), or upper gastrointestinal (GI) endoscopy (see Supplementary Figure 1, Supplementary Digital Content 1, http://links.lww.com/AJG/C144). Small bowel endoscopy and upper GI endoscopy were performed based on symptoms and test results in line with the policies of each participating institution. Definitive diverticular bleeding was based on colonoscopic visualization of diverticulum with SRH (3,13). Presumptive diverticular bleeding was based on the following: very little possibility of bleeding source other than colonic diverticulum by colonoscopy with other tests showing negative results, including upper GI endoscopy and small bowel endoscopy; and the CT visualization of contrast medium extravasation localized to the diverticulum (3,13). Clinical outcomes were evaluated and consisted of 23 items, including rebleeding, thromboembolism, and mortality (see Supplementary Table 2, Supplementary Digital Content 4, http://links.lww.com/AJG/C147). Dates of occurrence of outcomes were evaluated during hospitalization and after discharge. After discharge, we followed up patients from the index date to the occurrence of any clinical outcomes, and data were censored at the time of the last visit, end of follow-up, or death. In the survival analysis, the end point was death, and data were censored as of the time of the last visit or the end of follow-up. Rebleeding and second rebleeding episodes were evaluated and defined as significant amounts of fresh bloody or wine-colored stool after admission (6,8,10). Diagnosis of thromboembolism was based on typical symptoms and confirmed by imaging such as CT, magnetic resonance imaging, coronary angiography, ventilation-perfusion scans, ultrasonography, or electrocardiography (8). Date and cause of death were ascertained from death certificates and review of the medical record (8). Cause of death was also determined based on findings from laboratory tests, multiple imaging modalities, or autopsy (8). Secondary outcomes were need for blood transfusion during hospitalization and length of hospital stay.

Statistical methods

Descriptive statistics, reported as number and percentage or as median and IQR, were used to describe patient characteristics, procedures, and clinical outcomes. To compare clinical data between 2 groups, we used the χ^2 test or Fisher exact test for categorical variables, as appropriate. *P* values less than 0.05 were considered significant. All statistical analysis was performed using STATA version 14 software (StataCorp, College Station, TX).

RESULTS

Baseline characteristics

The median number of ambulances available at the 49 participating hospitals was 5,859, and 24/7 colonoscopy was available in all institutions (Table 1). Median patient age was 74 years, and 61.1% were male. Approximately half of the patients were current drinkers (46.3%) or current or ever smokers (48.8%). Almost one-third had hemodynamic instability (29.5%). All patients presented with hematochezia, and some had additional symptoms of abdominal pain (16.1%), fever (6.4%), and diarrhea (9.9%). Thirty percentage of patients had a history of ALGIB. More than half of patients had a CCI ≥1 (60.1%), and the most common comorbidities were hypertension (56.5%), dyslipidemia (27.3%), and diabetes (18.7%). Median laboratory values for white blood cells, hemoglobin, and albumin were 7,150/μL, 11.4 g/dL, and 3.7 g/dL, respectively. At presentation, 11.4% of patients were on nonsteroidal antiinflammatory drugs, 20.0% on low-dose aspirin, 9.8% on thienopyridine, 6.8% on warfarin, 6.0% on direct oral anticoagulants, 2.7% on acetaminophen, and 5.6% on corticosteroids. In addition, 6.1% was on dual antiplatelet therapy.

Identification of SRH and bleeding etiology by CT and endoscopy

Abdominal or pelvic CT was performed in 69.1% of all cases (Table 2). The ascending colon (10.4%) was most commonly identified by extravasation on CT, more than twice as often as the sigmoid colon (4.3%). Initial colonoscopy was performed in 87.7% of all cases. SRH was identified on endoscopy in 30.9% of cases, followed by active bleeding in 16.4%, adherent clots in 9.2%, and visible vessels in 5.9%. Similar to CT extravasation, the ascending colon (12.9%) was the most frequent site where SRH was identified, again almost twice as often as the sigmoid colon (7.0%). Overall, 59.2% of patients (6,117/10,342) underwent both endoscopy and CT for further investigation of the source of bleeding, and only 2.4% (244/10,342) did not undergo any imaging tests such as colonoscopy and CT (see Supplementary Figure 1, Supplementary Digital Content 1, http://links.lww.com/AJG/C144).

The diagnostic yield of the initial and second colonoscopies reached 94.9%, and 22 bleeding source categories, covering 48 diseases, were identified (Table 2). The most common final diagnosis was colonic diverticular bleeding (63.6%), followed by ischemic colitis (9.1%), postendoscopic bleeding (4.5%), and rectal ulcer (2.5%). Bleeding sources other than the colon, rectum, and anus were also evident, including small bowel bleeding (2.4%) and UGIB (1.5%). When the rates of the different etiologies were compared between final diagnosis and initial endoscopic diagnosis, slight differences were evident (see Supplementary Table 3, Supplementary Digital Content 4, http://links.lww.com/AJG/C147); in particular, there was a lower rate of unknown cases and a higher rate of definitive diverticular bleeding.

Regarding annual trends of imaging tests, rates of CT and contrast-enhanced CT angiography increased over time, whereas colonoscopic rates slightly declined over time (see Supplementary Figure 2, Supplementary Digital Content 2, http://links.lww.com/AJG/C145). Thus, we analyzed whether these imaging trends affect the SRH or final diagnostic rates. However, between the 2 time phases (2010–14 and 2015–19), there was no significant difference in the rate of SRH identification, unknown cases, or final diagnoses except for angioectasia, postendoscopy bleeding, and small bowel bleeding (see Supplementary Figure 3, Supplementary Digital Content 3, http://links.lww.com/AJG/C146).

Endoscopic treatment and other procedures

Multiple procedures or devices were often used to identify the source of bleeding in periendoscopic management, including bowel preparation with polyethylene glycol in 66.4% of patients, enema in 19.1%, endoscopic cap in 72.1%, and water-jet scope in 77.0% (Table 3). Endoscopic treatment was performed in 30.7% of patients undergoing endoscopy, mostly clipping (63.8%), followed by band ligation (24.2%), coagulation (8.2%), snare ligation (3.9%), and hypertonic saline-epinephrine injection (1.8%). The success rate of endoscopic therapy was 95.7%, and failure of hemostasis occurred in the remaining 4.4% of cases. When initial endoscopic treatment failed, clipping (63.6%) was the most commonly used follow-up technique. Identified postcolonoscopy complications were 0.1% perforation and 0.04% diverticulitis (Table 3).

An IVR procedure was performed in 1.4% of cases and surgery in 1.0%. Secondary endoscopic therapy was performed in 39.5% of patients undergoing repeat colonoscopy (see Supplementary Table 4, Supplementary Digital Content 4, http://links.lww.com/AJG/C147). The treatment rate for rebleeding was conservative therapy in 53.1% of cases, endoscopic therapy in 40.6%, IVR in 3.6%, and surgery in 1.7% (see Supplementary Table 4, Supplementary Digital Content 4, http://links.lww.com/AJG/C147). The IVR and surgical procedure rates were significantly higher for second rebleeding episodes than for first rebleeding episodes ($P < 0.01$). Overall, the procedure rates during hospitalization were 32.7% for endoscopic treatment, 2.1% for IVR, and 1.4% for surgery (Table 3).

Clinical outcomes

In-hospital rebleeding was identified in 15.2% of patients: 10.8% had 1 episode and 4.4% had 2 episodes (Table 4). After discharge, rebleeding occurred in 25.6% of patients: 22.9% had 1–4 episodes, 1.7% had 5–9 episodes, and 1.0% had ≥10 episodes. Thromboembolic events occurred in 0.6% of patients, including acute coronary syndrome in 0.2%, cerebrovascular disease in 0.3%, and pulmonary embolism/deep vein thrombosis in 0.2%. In-hospital mortality was 0.9%, mainly due to worsening comorbidities and nonbleeding-related causes. Only 13% of deaths were directly related to GI bleeding. Out-of-hospital mortality was 6.8% during a median follow-up of 239 days after discharge. Blood transfusion was needed in 29.8% of patients, with a median number of 4 units transfused. The median length of stay was 7 days.

Association of bleeding etiologies with adverse outcomes and need for a procedure

The proportions of adverse outcomes and need for a procedure differed according to bleeding etiology (Table 5). Etiologies that were more likely to have adverse outcomes included diverticular bleeding, malignancy, angioectasia, rectal ulcer, small bowel bleeding, and UGIB. By contrast, etiologies with relatively

Table 1. Characteristics of patients admitted for outpatient-onset acute hematochezia

Variable	Value	Data available for analysis	Missing values
Outpatient onset	10,342 (100)	10,342	0
Ambulances at facility	5,859 (3,854–9,246)	49	0
24/7 colonoscopy access	49 (100)	49	0
Age (yr)	74 (63–82)	10,342	0
Age ≥60 yr	8,327 (80.5)	10,342	0
Male sex	6,317 (61.1)	10,342	0
Blood type, O	3,312 (33.7)	9,841	501 (4.8)
Blood type, A	3,644 (37.0)	9,841	501 (4.8)
Blood type, B	2,021 (20.5)	9,841	501 (4.8)
Blood type, AB	864 (8.8)	9,841	501 (4.8)
Height (cm)	160 (152–167)	9,789	553 (5.3)
Body weight (kg)	57.3 (48.9–66.4)	9,921	421 (4.1)
Body mass index	22.5 (20.1–24.9)	9,715	627 (6.1)
Body mass index >25	2,381 (24.5)	9,715	627 (6.1)
Alcohol, current drinker	4,130 (46.3)	8,918	1,424 (13.8)
Smoking, never	4,702 (51.2)	9,179	1,163 (11.2)
Smoking, current	1,661 (18.1)	9,179	1,163 (11.2)
Smoking, ever	2,816 (30.7)	9,179	1,163 (11.2)
Performance status 1	8,976 (87.8)	10,220	122 (1.2)
Performance status 2	694 (6.8)	10,220	122 (1.2)
Performance status 3	304 (3.0)	10,220	122 (1.2)
Performance status 4	244 (2.4)	10,220	122 (1.2)
Blood pressure (mm Hg)	127 (111–145)	10,161	181 (1.8)
Heart rate (/min)	83 (73–96)	10,140	202 (2)
Syncope/loss of consciousness	668 (6.5)	10,324	18 (0.2)
Hemodynamic instability[a]	3,046 (29.5)	10,342	0
Abdominal pain	1,664 (16.1)	10,323	19 (0.2)
Fever	660 (6.4)	10,320	22 (0.2)
Diarrhea	1,016 (9.9)	10,307	35 (0.3)
Hematochezia	10,342 (100)	10,342	0
Tarry stools	593 (5.8)	10,321	21 (0.2)
Hemoglobin (g/dL)	11.4 (9.3–13.1)	10,334	8 (0.1)
Hemoglobin ≤7.0 g/dL	798 (7.7)	10,342	0
White blood cells (/μL)	7,150 (5,600–9,300)	10,335	7 (0.1)
Platelet count (/μL)	20.8 (16.8–25.3)	10,331	11 (0.1)
Albumin (g/dL)	3.7 (3.3–4.1)	9,857	485 (4.7)
PT-INR	1.0 (1.0–1.0)	9,012	1,330 (12.9)
Hematocrit (%)	34.2 (28.4–39)	10,322	20 (0.2)
Blood urea nitrogen (mg/dL)	19.0 (14.7–25.0)	10,273	69 (0.7)
Creatinine (mg/dL)	0.8 (0.7–1.1)	10,269	73 (0.7)
C-reactive protein (mg/dL)	0.2 (0.1–0.5)	10,067	275 (2.7)
History of bowel resection	752 (7.3)	10,340	2 (0.01)
History of chemotherapy	338 (3.3)	10,319	23 (0.2)
History of radiation therapy	241 (2.3)	10,325	17 (0.2)
History of LGIB	3,090 (30.0)	10,342	0
History of angioectasia	72 (0.7)	10,341	1 (0.01)
History of IBD	233 (2.3)	10,341	1 (0.01)
History of diverticular bleeding	2,603 (25.2)	10,334	8 (0.1)
History of ischemic colitis	223 (2.2)	10,341	1 (0.01)
CCI, 0	4,124 (39.9)	10,342	0
CCI, 1	2,431 (23.5)	10,342	0
CCI, ≥2	3,787 (36.6)	10,342	0
Diabetes mellitus, uncomplicated	1,933 (18.7)	10,342	0
Diabetes mellitus, end-organ damage	350 (3.4)	10,342	0
Hemiplegia	278 (2.7)	10,334	8 (0.1)
Cerebrovascular accident or TIA	1,475 (14.3)	10,340	2 (0.02)
COPD	315 (3.1)	10,342	0
Dementia	565 (5.5)	10,334	8 (0.1)
Connective tissue disease	418 (4.0)	10,342	0
Myocardial infarction	1,660 (16.1)	10,342	0
Chronic heart failure	854 (8.3)	10,340	2 (0.02)
Peptic ulcer disease	726 (7.0)	10,342	0
Moderate chronic kidney disease	1,479 (14.3)	10,340	2 (0.02)
Severe chronic kidney disease	326 (3.2)	10,342	0

Table 1. (*continued*)

Variable	Value	Data available for analysis	Missing values
Peripheral vascular disease	421 (4.1)	10,342	0
Leukemia/myeloma	68 (0.7)	10,342	0
AIDS	19 (0.2)	10,333	9 (0.1)
Solid tumor, localized	1,332 (12.9)	10,335	7 (0.1)
Solid tumor, metastatic	254 (2.5)	10,342	0
Liver disease, mild	217 (2.1)	10,341	1 (0.01)
Liver disease, moderate to severe	207 (2.0)	10,341	1 (0.01)
Malignant lymphoma	83 (0.8)	10,342	0
Hypertension	5,842 (56.5)	10,342	0
Dyslipidemia	2,822 (27.3)	10,341	1 (0.01)
NSAIDs	1,177 (11.4)	10,342	0
NSAIDs (noncoxib)	929 (9.0)	10,342	0
COX-2 selective inhibitors	272 (2.6)	10,342	0
Low-dose aspirin	2,056 (20.0)	10,342	0
Thienopyridine	1,014 (9.8)	10,342	0
Cilostazol	243 (2.4)	10,342	0
Other antiplatelet drugs	303 (2.9)	10,342	0
Antiplatelet drugs, 0	7,420 (71.8)	10,342	0
Antiplatelet drugs, 1	2,262 (21.9)	10,342	0
Antiplatelet drugs, 2	626 (6.1)	10,342	0
Antiplatelet drugs, 3	34 (0.3)	10,342	0
Warfarin	705 (6.8)	10,342	0
DOACs	615 (6.0)	10,342	0
Acetaminophen	277 (2.7)	10,342	0
Corticosteroids	579 (5.6)	10,342	0

Data are presented as n (%).
AIDS, acquired immune deficiency syndrome; CCI, Charlson Comorbidity Index; COPD, chronic obstructive pulmonary disease; COX, cyclooxygenase; DOAC, direct oral anticoagulant; IBD, inflammatory bowel disease; IQR, interquartile range; LGIB, lower gastrointestinal bleeding; NSAID, nonsteroidal antiinflammatory drug; PT-INR, international normalized ratio of prothrombin time; TIA, transient ischemic attack.
[a]Hemodynamic instability was defined as initial systolic blood pressure <90 mm Hg, initial heart rate ≥100/min, or presence of syncope.

favorable outcomes were ischemic colitis, infectious colitis, inflammatory bowel disease, and postendoscopy bleeding. Regarding adverse outcomes, 30-day rebleeding rates were significantly higher in patients with diverticular bleeding and small bowel bleeding and lower in those with ischemic colitis, malignancy, infectious colitis, inflammatory bowel disease, hemorrhoids, postendoscopy bleeding, and unknown cases compared with other etiologies. Thromboembolism rates were higher with malignancy and UGIB than with other etiologies. In-hospital mortality rates were significantly higher with angioectasia, malignancy, rectal ulcer, UGIB, and unknown cases and lower in with diverticulosis and ischemic colitis compared with other etiologies.

Among the procedures required, need for transfusion was significantly higher with diverticular bleeding, malignancy, angioectasia, rectal ulcer, small bowel bleeding, UGIB, and unknown cases but lower in with the various types of colitis and postendoscopy bleeding compared with other etiologies. Need for endoscopic treatment was significantly higher with diverticular bleeding, radiation colitis, angioectasia, rectal ulcer, and postendoscopy bleeding but lower with malignancy, other types of colitis, hemorrhoids, and small bowel bleeding compared with other etiologies. The rate of need for surgery was significantly higher with malignancy, hemorrhoids, and small bowel bleeding but lower with diverticular bleeding compared with other etiologies. Need for IVR procedure was significantly greater with diverticular bleeding and small bowel bleeding but lower with ischemic colitis and postendoscopy bleeding compared with other etiologies.

Results of association between rebleeding and mortality risk and each etiology in a logistic regression model remain unchanged after survival curve analysis with the Cox proportional hazard regression model (see Supplementary Table 5, Supplementary Digital Content 4, http://links.lww.com/AJG/C147).

Association of bleeding etiologies with symptoms and hemodynamic instability

Differences in the proportions of elderly patients and male patients were noted between the etiologies (Table 6). At presentation, higher rates of painless hematochezia were significantly associated with multiple diseases, such as diverticular bleeding, rectal ulcer, hemorrhoids, angioectasia, and radiation colitis. The same was true in cases of hematochezia with diarrhea and fever. Diverticular bleeding and UGIB were associated with a significantly higher rate of hemodynamic instability compared with other etiologies, whereas ischemic colitis was associated with a lower rate.

DISCUSSION

We have accumulated an unprecedentedly large data set for 10,342 patients emergently admitted for outpatient-onset of acute hematochezia, which contains information on baseline characteristics (Table 1), etiologies (Table 2), interventions (Table 3), and clinical outcomes (Table 4). With endoscopy, we could reach a high diagnostic yield of 94.9%, enabling one-third of all cases to be treated endoscopically (Table 3), which is a much higher rate than that reported in previous studies (6,10,14). Notably, confirmation of the bleeding etiology allowed patients at risk for adverse outcomes to be identified (Table 5). Some of the bleeding etiologies had the same presenting symptoms and hemodynamic instability (Table 6), indicating that prediction of etiology based on initial presentation would be challenging. These findings highlight the importance of performing endoscopy in patients with acute hematochezia (1,3).

Only 5% of etiologies remained unknown in this study (Table 2), which is lower than the respective rates of 9%, 23%, and 18% reported in the United States (6), the United Kingdom (10), and Spain (15). Making an accurate diagnosis in patients with hematochezia is of importance because unknown cases are at high risk of death and transfusion use (Table 5). One of the

Table 2. Examinations and bleeding etiologies

Factor	Value	Data available for analysis	Missing values
Abdominal or pelvic CT	7,149 (69.1)	10,342	0
Contrast-enhanced CT	5,240 (73.3)	7,149	0
Urgent CT	6,968 (97.5)	7,149	0
Time to CT scan (hr)	1 (1–2)	7,149	0
Extravasation on CT	1,151 (22.0)	5,240	0
Extravasation at jejunum	7 (0.1)	5,240	0
Extravasation at ileum	57 (1.1)	5,240	0
Extravasation at cecum	53 (1.0)	5,240	0
Extravasation at ascending colon	547 (10.4)	5,240	0
Extravasation at transverse colon	83 (1.6)	5,240	0
Extravasation at descending colon	138 (2.6)	5,240	0
Extravasation at sigmoid colon	224 (4.3)	5,240	0
Extravasation at rectum	49 (0.9)	5,240	0
Extravasation in upper GI tract	1 (0.02)	5,240	0
Colonic diverticular bleeding on CT	1,846 (25.8)	7,149	0
Enterocolitis on CT	953 (13.3)	7,149	0
Tumor lesion on CT	90 (1.3)	7,149	0
Other diagnosis on CT	190 (2.7)	7,149	0
Initial colonoscopic examination	9,066 (87.7)	10,342	0
Time to first colonoscopy (hr)	16 (4–32)	9,066	0
SRH on initial endoscopy	2,801 (30.9)	9,066	0
SRH, active bleeding	1,489 (16.4)	9,066	0
SRH, visible vessel	535 (5.9)	9,066	0
SRH, adherent clot	829 (9.1)	9,066	0
Location of SRH, cecum	163 (1.8)	9,066	0
Location of SRH, ascending colon	1,166 (12.9)	9,066	0
Location of SRH, transverse colon	262 (2.9)	9,066	0
Location of SRH, descending colon	182 (2.0)	9,066	0
Location of SRH, sigmoid colon	630 (7.0)	9,066	0
Location of SRH, rectum	349 (3.9)	9,066	0
Location of SRH, jejunum	5 (0.06)	9,066	0
Location of SRH, ileum	94 (1.0)	9,066	0
Location of SRH, upper GI tract	1 (0.01)	9,066	0
Second colonoscopic examination	1,992 (19.2)	10,342	0
Time to second colonoscopy (hr)	53 (29–96)	1,992	0
Final diagnosis			
Colonic diverticular bleeding	6,575 (63.6)	10,342	0
Definitive diverticular bleeding	2,386 (23.1)	10,342	0
Presumptive diverticular bleeding	4,189 (40.5)	10,342	0
Ischemic colitis	941 (9.1)	10,342	0
Postprocedure bleeding	463 (4.5)	10,342	0
Post-ESD	140 (1.4)	10,342	0
Postpolypectomy	73 (0.7)	10,342	0
Post-EMR	223 (2.2)	10,342	0
Postbiopsy	16 (0.2)	10,342	0
Other procedures	12 (0.1)	10,342	0
Rectal ulcer	257 (2.5)	10,342	0
IBD	210 (2.0)	10,342	0
Hemorrhoids	184 (1.8)	10,342	0
Colorectal angioectasia	133 (1.3)	10,342	0
Colorectal malignancy	193 (1.9)	10,342	0
Colorectal cancer	168 (1.6)	10,342	0
Metastatic tumor	16 (0.2)	10,342	0
Other colorectal tumor[a]	9 (0.1)	10,342	0
Colorectal polyp	37 (0.4)	10,342	0
Infectious colitis	134 (1.3)	10,342	0
Radiation colitis	66 (0.6)	10,342	0
Nonspecific colitis	47 (0.5)	10,342	0
Drug-induced ulcer	14 (0.1)	10,342	0
Nonspecific ulcer	56 (0.5)	10,342	0
Colorectal varix	25 (0.2)	10,342	0
Dieulafoy ulcer	12 (0.1)	10,342	0
Postoperative anastomotic bleeding	14 (0.1)	10,342	0
Anal bleeding other than hemorrhoids[b]	12 (0.1)	10,342	0
Diverticulitis	7 (0.1)	10,342	0
Small bowel bleeding	246 (2.4)	10,342	0
Definitive	114 (1.1)	10,342	0
Presumptive	121 (1.2)	10,342	0
Bleeding from Meckel diverticulum	11 (0.1)	10,342	0
UGIB	153 (1.5)	10,342	0
Other diagnosis[c]	37 (0.4)	10,342	0

Table 2. (*continued*)

Factor	Value	Data available for analysis	Missing values
Unknown etiology	526 (5.1)	10,342	0
Missing data	0	10,342	0

Data are presented as n (%).
CT, computed tomography; EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection; GI, gastrointestinal; IBD, inflammatory bowel disease; IQR, interquartile range; SRH, stigmata of recent hemorrhage; UGIB, upper gastrointestinal bleeding.
[a]Other tumors included malignant lymphoma (n = 2), gastrointestinal stromal tumor (n = 1), pseudomyxoma of the appendix (n = 1), and submucosal tumor of unknown origin (n = 5).
[b]Anal bleeding other than hemorrhoids included anal laceration or fissure (n = 10), bleeding postanal surgery (n = 1), and anal condyloma (n = 1).
[c]Other diagnosis included mucosal bleeding (n = 8), mucosal prolapse syndrome (n = 6), colorectal laceration (n = 4), fistula or penetration into the colorectum (n = 3), colorectal perforation (n = 2), mucosal lymphoid hyperplasia (n = 2), Kaposi sarcoma (n = 1), stoma-related bleeding (n = 2), pseudoaneurysm (n = 2), intussusception (n = 1), postoperative stenosis (n = 1), graft-vs-host disease (n = 1), hematoma (n = 2), Henoch-Schönlein purpura (n = 1), and Cronkhite-Canada syndrome (n = 1). Urgent CT was defined as CT performed within 24 hours of the hospital visit.

reasons for the high rate of final diagnosis is the fact that imaging test-based diagnosis is well-established in Japanese hospitals (see Supplementary Figure 1, Supplementary Digital Content 1, http://links.lww.com/AJG/C144), which is also stated in the guidelines (3). Endoscopy is often conducted in Japanese hospitals; 87.7% and 19.2% of all cases underwent initial and repeated colonoscopy, respectively. Moreover, 59.2% of patients underwent both endoscopy and CT in our study, and 66% (5,981/9,064) of patients had CT performed before the colonoscopy (see Supplementary Figure 1, Supplementary Digital Content 1, http://links.lww.com/AJG/C144), which may be unique to the Japanese strategy (3). Other reasons are high use of bowel preparation before endoscopy and more frequent use of additional endoscopic devices (e.g., endoscopic cap in 73% of cases and water-jet in 77%; Table 3), all of which increase detection rates of bleeding sources (16). Furthermore, repeat colonoscopies or CTs at recurrence may reveal a definitive source of bleeding in patients who were diagnosed as unknown or presumptive diagnosis at the initial colonoscopy. It is true that colonoscopy detects coincidental cases such as diverticulosis with small bowel bleeding or hemorrhoids, but this situation seems rare because final diagnosis was based on a combination of colonoscopy with CT, small bowel endoscopy, and upper GI endoscopy to exclude other diseases (see Supplementary Figure 1, Supplementary Digital Content 1, http://links.lww.com/AJG/C144).

The most common etiology was diverticular bleeding, at 64%, which is consistent with previous reports on ALGIB (10,15), although the rates are different: 30% (75/252) in the United States (6), 26% (668/2,528) in the United Kingdom (10), and 39% (163/415) in Spain (15). The next most common diagnoses after diverticulosis in our Japanese population were ischemic colitis, postendoscopy bleeding, and rectal ulcer, which are similar to hemorrhoids, ischemic colitis, and postendoscopic bleeding reported in the United States (6) but not to hemorrhoids, undetermined colitis, and malignancy reported in the United Kingdom (10). The differences in order and proportions of the etiologies between countries probably reflect differences in colonoscopy rates and in hospital departments where patients are managed (e.g., surgery departments in the United Kingdom vs gastroenterology departments in Japan) (10).

Among the various bleeding sites identified, the ascending colon was most common in cases of SRH both on colonoscopy and with extravasation on CT (Table 2), underscoring the importance of total colonoscopy. If only sigmoidoscopy had been performed, 89% of SRH and endoscopically treatable lesions would have been missed. Compared with previously reported SRH rates of 8%–26% (17–19), we found a high rate of 31% (Table 3), probably because our cohort underwent a high rate of early colonoscopy (64.6%) with a high use of endoscopic attachment (73%) and water-jet (77%).

Among the endoscopic treatments currently used, clipping is the most common endoscopy procedure worldwide, including in Japan (Table 3). By contrast, injection of hypertonic saline-epinephrine and coagulation, which are commonly used in the United States (20), are used in ≤10% of cases in Japan. Endoscopic treatment in Japan includes novel therapies such as band ligation and snare ligation, on which there have been few reports from the United States and United Kingdom (20,21). In recent years, mounting evidence suggests that band ligation is more effective than clipping in preventing rebleeding (20,21), so it may become the mainstream treatment for ALGIB. We found that the rates of IVR and surgery were less than 5% (Table 3), which is similar to the rates reported for the United Kingdom (10). Both treatments were performed more frequently for second rebleeding episodes than for first rebleeding episodes, suggesting that physicians are more likely to perform endoscopy first, even if there is extravasation on CT, and to opt for IVR or surgery when there is uncontrolled bleeding, which is consistent with Japanese and US guidelines (1,3) but not with UK guidelines (2).

The Japanese and US guidelines state that the value of colonoscopy for ALGIB lies in its ability to identify the bleeding etiology and enable hemostasis if indicated (1,3). We hypothesized that colonoscopy can also affect important clinical outcomes. Regrettably, previous ALGIB studies did not evaluate the association between bleeding etiology and outcomes (4–7,22). Notably, we found that the etiologies associated with a high risk of adverse outcomes in patients with hematochezia were diverticular bleeding, malignancy, rectal ulcer, small bowel bleeding, UGIB, and unknown cases (Table 5). By contrast, the etiologies with low risk were ischemic colitis, infectious colitis, and postendoscopy bleeding. This indicates that precise identification of the bleeding etiology can stratify patients at risk for adverse outcomes, which would help physicians determine whether intensive care is needed or whether the patient can be discharged promptly after endoscopy.

In our cohort, 12.3% of the patients did not undergo colonoscopy during their hospitalization. Detailed reasons for not performing colonoscopy are unknown, but this was possibly because diagnosis was primarily based on CT with typical clinical manifestations or on past information. Supplementary Table 6 (see Supplementary Digital Content 4, http://links.lww.com/AJG/C147) summarizes that 81% of patients who did not undergo colonoscopy had CT (58% for CT angiography). Moreover, the diagnosis of patients who did not undergo colonoscopy included 10.7% unknown cases, 10.3% UGIB, and 33.6% ischemic colitis. It is likely that UGIB was suspected clinically, and upper endoscopy

Table 3. Endoscopic and nonendoscopic procedures

Procedure	Value	Data available for analysis	Missing values
Bowel preparation, PEG or enema	7,595 (83.8)	9,066	0
Bowel preparation, PEG	6,022 (66.4)	9,066	0
Bowel preparation, enema	1,731 (19.1)	9,066	0
Endoscopic cap	6,537 (72.1)	9,066	0
Endoscopic cap, long	1,822 (20.1)	9,066	0
Endoscopic cap use, short	4,638 (51.2)	9,066	0
Endoscopic cap, ST hood	69 (0.8)	9,066	0
Endoscopic cap, other	8 (0.1)	9,066	0
Water-jet scope	6,971 (77.0)	9,066	0
PEG in water-jet scope	390 (4.3)	9,066	0
Conservative therapy after endoscopy	6,092 (67.2)	9,066	0
Endoscopic therapy	2,784 (30.7)	9,066	0
Clipping	1,759 (63.8)	2,784	0
Indirect	1,212 (43.5)	2,784	0
Direct	547 (19.7)	2,784	0
Band ligation	674 (24.2)	2,784	0
Snare ligation	109 (3.9)	2,784	0
HSE	50 (1.8)	2,784	0
OTSC	0	2,784	0
Coagulation	228 (8.2)	2,784	0
Other endoscopic therapy[a]	20 (0.7)	2,784	0
Successful endoscopic therapy	2,663 (95.7)	2,784	0
Failed endoscopic therapy	121 (4.4)	2,784	0
Treatment for failure, clipping	77 (63.6)	121	0
Treatment for failure, band ligation	8 (6.6)	121	0
Treatment for failure, HSE	14 (11.6)	121	0
Treatment for failure, OTSC	1 (0.8)	121	0
Treatment for failure, coagulation	8 (6.6)	121	0
Treatment for failure, other therapy	11 (9.1)	121	0
Postendoscopy perforation	11 (0.1)	9,066	0
Postendoscopy diverticulitis	4 (0.04)	9,066	0
IVR	143 (1.4)	10,342	0
Surgery	101 (1.0)	10,342	0
Barium impaction therapy	66 (0.6)	10,342	0
Endoscopic therapy during hospitalization	3,379 (32.7)	10,342	0
Need for IVR during hospitalization	217 (2.1)	10,342	0
Need for surgery during hospitalization	142 (1.4)	10,342	0

Data are presented as n (%).
Preendoscopic and endoscopic procedures were evaluated in patients who underwent endoscopy (n = 9,066).
HSE, hypertonic saline-epinephrine; IQR, interquartile range; IVR, interventional radiology; OTSC, over the scope clip; PEG, polyethylene glycol.
[a]Other endoscopic therapy included hot biopsy, polypectomy, and endoscopic mucosal resection.

was performed instead of colonoscopy, and that ischemic colitis was strongly suspected based on CT with clinical symptoms, so the physician decided colonoscopy was unnecessary. Finally, it is possible that during previous hospitalization for hematochezia management, the patient had undergone detailed imaging tests such as endoscopy and CT, and colonoscopy was deemed unnecessary for this new hospitalization. Of interest, we also found that aforementioned associations between etiology and outcome

Table 4. Clinical outcomes

Outcome	Value	Data available for analysis	Missing values
In-hospital rebleeding	1,573 (15.2)	10,342	0
Second rebleeding during hospitalization	458 (4.4)	10,342	0
Out-of-hospital rebleeding	2,650 (25.6)	10,342	0
Out-of-hospital rebleeding episodes, 1–4	2,372 (22.9)	10,342	0
Out-of-hospital rebleeding episodes, 5–9	178 (1.7)	10,342	0
Out-of-hospital rebleeding episodes, ≥10	100 (1.0)	10,342	0
Occurrence of thromboembolism	65 (0.6)	10,342	0
Occurrence of acute coronary syndrome	19 (0.2)	10,342	0
Occurrence of cerebrovascular accident	28 (0.3)	10,342	0
Occurrence of PE/DVT	18 (0.2)	10,342	0
In-hospital death	97 (0.9)	10,342	0
GI bleeding-related death	13 (13.4)	97	0
Out-of-hospital death	694 (6.8)	10,245	0
Follow-up after discharge (d), median (IQR)	239 (21–809)	10,245	0
Blood transfusion	3,080 (29.8)	10,342	0
Blood transfusions (n), median (IQR)	4 (2–8)	3,080	0
Blood transfusion ≥4 units	2,291 (22.2)	10,342	0
Length of stay, median (IQR, range)	7 (5–11)	10,342	0
Length of stay ≥8 d	4,744 (45.9)	10,342	0

Data are presented as n (%).
DVT, deep vein thrombosis; GI, gastrointestinal; IQR, interquartile range; PE, pulmonary embolism.

in the whole cohort remain unchanged regardless of unperformed colonoscopy (see Supplementary Table 7, Supplementary Digital Content 4, http://links.lww.com/AJG/C147). If diverticular bleeding, small bowel bleeding, or UGIB is suspected based on clinical diagnosis or nonendoscopic imaging, intensive care may be required, and patients should be followed up carefully after admission.

In clinical practice, diverticular bleeding may be suspected in a patient with acute hematochezia who presents without abdominal pain and diarrhea, but our colonoscopy data revealed that lower rates of painless hematochezia at presentation were significantly associated with multiple diseases, such as rectal ulcer, hemorrhoids, angioectasia, radiation colitis, and diverticulosis (Table 6). The same was true in cases of hematochezia with diarrhea, fever, and hemodynamic instability, suggesting that predicting different bleeding etiologies based on initial presentation would be challenging. Although there was no high-quality evidence to show that hemodynamic instability is indicative of an UGIB source and warrants an upper endoscopy (1,2), our data strongly support this.

This study has some limitations. First, there are 2 large ALGIB databases with >1,000 cases: 1,198 cases in Italy (14) and 2,528 cases in the United Kingdom (10); the median age was 78, 73, and 74 years in Italy, the United Kingdom, and Japan, in that order, although comorbidity scores (CCI) of zero are 29.3%, 43.6%, and 39.9%, CCI ≥2 was 47.4%, 33.4%, and 36.6%, respectively, which was similar among the 3 countries. However, generalizability might be limited by low BMI, with a median of 22.5 in Japan. Although no information is available in the Italy and UK databases, a study in the United States (23), reported that approximately 20% of participants had a BMI ≥30, compared with only 9.6% (988/10,342) in our study. Second, it had a retrospective design, which resulted in some missing values for baseline characteristics, which is potentially a source of bias. However, there were no missing values for diagnosis, procedures, or outcomes in our Japanese data set, and items with missing values and their rates were lower than in the prospective study done in the United Kingdom (10). Third, the degree of cleanliness of bowel preparation may affect SRH identification, diagnostic yield, and outcomes, but we could not collect these data.

In conclusion, we have provided clinical findings useful for ALGIB management obtained from a large-scale analysis of 10,342 patients with acute hematochezia. Our high colonoscopy rate identified bleeding etiologies accurately and allowed us to stratify patients at high or low risk of adverse outcomes and those who will likely require more procedures. Our results highlighted the value of colonoscopy in diagnosis and subsequent management in patients with acute hematochezia.

ACKNOWLEDGMENT

We thank Kazuyo Jo, Shiho Kamimura, Sanae Habu, Akiko Takamatsu, Minako Kajihara, and Kenko Yoshida for their help with the data collection and analysis.

CONFLICTS OF INTEREST

Guarantor of the article: Naoyoshi Nagata, MD, PhD.
Specific author contributions: N.N.: was the principal investigator of this study. N.N.: designed and conducted the study, interpreted the

Table 5. Association of bleeding etiologies with adverse clinical outcomes and procedures needed in patients with hematochezia

	30-d rebleeding			Thromboembolism			In-hospital mortality			Need for endoscopic therapy		
	Absent	Present	*P*	Absent	Present	*P*	Absent	Present	*P*	Absent	Present	*P*
Diverticular bleeding	325 (8.6)	1,501 (22.8)	<0.001	27 (0.7)	38 (0.6)	0.390	81 (2.2)	16 (0.2)	<0.001	935 (24.8)	2,444 (37.2)	<0.001
Ischemic colitis	1,796 (19.1)	30 (3.2)	<0.001	61 (0.7)	4 (0.4)	0.52	94 (1.0)	3 (0.3)	0.033	3,374 (35.9)	5 (0.5)	<0.001
Malignancy	1,812 (17.9)	14 (7.3)	<0.001	61 (0.6)	4 (2.1)	0.033	82 (0.8)	15 (7.8)	<0.001	3,358 (33.1)	21 (10.9)	<0.001
Infectious colitis	1,823 (17.9)	3 (2.2)	<0.001	64 (0.6)	1 (0.8)	0.573	94 (0.9)	3 (2.2)	0.131	3,378 (33.1)	1 (0.8)	<0.001
IBD	1,809 (17.9)	17 (8.1)	<0.001	64 (0.6)	1 (0.5)	1.000	97 (1.0)	0	0.27	3,371 (33.3)	8 (3.8)	<0.001
Radiation colitis	1,814 (17.7)	12 (18.2)	0.911	65 (0.6)	0	1.000	97 (0.9)	0	1.000	3,327 (32.4)	52 (78.8)	<0.001
Other colitis	1,816 (17.8)	10 (8.6)	0.009	65 (0.6)	0	1.000	95 (0.9)	2 (1.7)	0.300	3,351 (32.8)	28 (23.9)	0.043
Colorectal angioectasia	1,803 (17.7)	23 (17.3)	0.912	64 (0.6)	1 (0.8)	0.570	95 (0.9)	2 (1.5)	0.355	3,282 (32.2)	97 (72.9)	<0.001
Rectal ulcer	1,773 (17.6)	48 (18.7)	0.664	63 (0.6)	2 (0.8)	0.677	84 (0.8)	13 (5.1)	<0.001	3,217 (31.9)	162 (63.0)	<0.001
Hemorrhoids	1,813 (17.9)	13 (7.1)	<0.001	63 (0.6)	2 (1.1)	0.322	97 (1.0)	0	0.422	3,369 (33.2)	10 (5.4)	<0.001
Postendoscopy bleeding	1,802 (18.2)	24 (5.2)	<0.001	65 (0.7)	0	0.120	97 (1.0)	0	0.023	2,963 (30.0)	416 (89.9)	<0.001
Small bowel bleeding	1,771 (17.5)	55 (22.4)	0.05	62 (0.6)	3 (1.2)	0.201	93 (0.9)	4 (1.6)	0.295	3,322 (32.9)	57 (23.2)	0.001
UGIB	1,821 (17.9)	5 (3.3)	<0.001	61 (0.6)	4 (2.6)	0.016	89 (0.9)	8 (5.2)	<0.001	3,378 (33.2)	1 (0.7)	<0.001
Unknown etiology	1,778 (18.1)	48 (9.1)	<0.001	61 (0.6)	4 (0.76)	0.573	71 (0.7)	26 (4.9)	<0.001	3,373 (34.4)	6 (1.1)	<0.001

	Need for surgery			Need for IVR			Need for transfusion			Need for transfusion ≥4 units		
	Absent	Present	*P*	Absent	Present	*P*	Absent	Present	*P*	Absent	Present	*P*
Diverticular bleeding	97 (2.6)	45 (0.7)	<0.001	41 (1.1)	176 (2.7)	<0.001	974 (25.9)	2,106 (32.0)	<0.001	750 (19.9)	1,541 (23.4)	<0.001
Ischemic colitis	135 (1.4)	7 (0.7)	0.082	216 (2.3)	1 (0.1)	<0.001	3,042 (32.4)	38 (4.0)	<0.001	2,267 (24.1)	24 (2.6)	<0.001
Malignancy	110 (1.1)	32 (16.6)	<0.001	215 (2.1)	2 (1.0)	0.445	3,005 (29.6)	75 (38.9)	0.005	2,233 (22.0)	58 (30.1)	0.008
Infectious colitis	140 (1.4)	2 (1.5)	0.707	217 (2.1)	0	0.120	3,067 (30.1)	13 (9.7)	<0.001	2,281 (22.4)	10 (7.5)	<0.001
IBD	136 (1.3)	6 (2.9)	0.062	215 (2.1)	2 (1.0)	0.331	3,048 (30.1)	32 (15.2)	<0.001	2,273 (22.4)	18 (8.6)	<0.001
Radiation colitis	142 (1.4)	0	1.000	217 (2.1)	0	0.650	3,061 (29.8)	19 (28.8)	0.859	2,281 (22.2)	10 (15.2)	0.169
Other colitis	141 (1.4)	1 (0.9)	1.000	217 (2.1)	0	0.182	3,041 (29.7)	39 (33.3)	0.398	2,261 (22.1)	30 (25.6)	0.361
Angioectasia	142 (1.4)	0	0.267	215 (2.1)	2 (1.5)	1.000	3,001 (29.4)	79 (59.4)	<0.001	2,224 (21.8)	67 (50.4)	<0.001
Rectal ulcer	137 (1.4)	5 (2.0)	0.406	215 (2.1)	2 (0.8)	0.182	2,952 (29.3)	128 (49.8)	<0.001	2,186 (21.7)	105 (40.9)	<0.001
Hemorrhoids	134 (1.3)	8 (4.4)	<0.001	217 (2.1)	0	0.035	3,036 (29.9)	44 (23.9)	0.079	2,257 (22.2)	34 (18.5)	0.226
Postendoscopy bleeding	140 (1.4)	2 (0.4)	0.097	216 (2.2)	1 (0.2)	0.001	3,041 (30.8)	39 (8.4)	<0.001	2,265 (22.9)	26 (5.6)	<0.001
Small bowel bleeding	119 (1.2)	23 (9.4)	<0.001	198 (2.0)	19 (7.7)	<0.001	2,943 (29.2)	137 (55.7)	<0.001	2,177 (21.6)	114 (46.3)	<0.001
UGIB	140 (1.4)	2 (1.3)	1.000	214 (2.1)	3 (2.0)	1.000	2,993 (29.4)	87 (56.9)	<0.001	2,219 (21.8)	72 (47.1)	<0.001
Unknown etiology	139 (1.4)	3 (0.6)	0.122	212 (2.2)	5 (1.0)	0.060	2,895 (29.5)	185 (35.2)	0.006	2,157 (22.0)	134 (25.5)	0.060

Bleeding etiologies with 50 or more cases were included in the analysis. "Other" diagnosis includes various bleeding etiologies (Table 2), which are difficult to interpret and were not included in the analysis. Data are presented as n (%).
IBD, inflammatory bowel disease; UGIB, upper gastrointestinal bleeding.

Table 6. Association of bleeding etiologies with presenting symptoms and hemodynamic instability in patients with hematochezia

	Elderly patients (age>65 yr)			Male sex			Abdominal pain			Fever		
	Absent	Present	*P*	Absent	Present	*P*	Absent	Present	*P*	Absent	Present	*P*
Diverticular bleeding	2,511 (66.7)	4,992 (75.9)	<0.001	1,931 (51.3)	4,386 (66.7)	<0.001	1,249 (33.2)	415 (6.3)	<0.001	478 (12.7)	182 (2.8)	<0.001
Ischemic colitis	6,838 (72.7)	665 (70.7)	0.175	6,074 (64.6)	243 (25.8)	<0.001	915 (9.8)	749 (79.8)	<0.001	515 (5.5)	145 (15.4)	<0.001
Malignancy	7,349 (72.4)	154 (79.8)	0.023	6,204 (61.1)	113 (58.6)	0.466	1,623 (16.0)	41 (21.2)	0.051	638 (6.3)	22 (11.4)	0.004
Infectious colitis	7,454 (73.0)	49 (36.6)	<0.001	6,248 (61.2)	69 (51.5)	0.022	1,573 (15.4)	91 (67.9)	<0.001	617 (6.1)	43 (32.1)	<0.001
IBD	7,455 (73.6)	48 (22.9)	<0.001	6,203 (61.2)	114 (54.3)	0.041	1,542 (15.3)	122 (58.1)	<0.001	585 (5.8)	75 (35.9)	<0.001
Radiation colitis	7,441 (72.4)	62 (93.9)	<0.001	6,271 (61.0)	46 (69.7)	0.15	1,661 (16.2)	3 (4.6)	0.007	658 (6.4)	2 (3.0)	0.443
Other colitis	7,428 (72.7)	75 (64.1)	0.04	6,265 (61.3)	52 (44.4)	<0.001	1,623 (15.9)	41 (35.0)	<0.001	647 (6.3)	13 (11.1)	0.036
Colorectal angioectasia	7,389 (72.4)	114 (85.7)	0.001	6,259 (61.3)	58 (43.6)	<0.001	1,654 (16.2)	10 (7.5)	0.007	653 (6.4)	7 (5.3)	0.606
Rectal ulcer	7,272 (72.1)	231 (89.9)	<0.001	6,205 (61.5)	112 (43.6)	<0.001	1,639 (16.3)	25 (9.7)	0.005	639 (6.4)	21 (8.2)	0.224
Hemorrhoids	7,379 (72.6)	124 (67.4)	0.114	6,209 (61.1)	108 (58.7)	0.503	1,653 (16.3)	11 (6.0)	<0.001	646 (6.4)	14 (7.6)	0.497
Postendoscopy bleeding	7,260 (73.5)	243 (52.5)	<0.001	5,970 (60.4)	347 (75.0)	<0.001	1,651 (16.7)	13 (2.8)	<0.001	647 (6.6)	13 (2.8)	0.001
Small bowel bleeding	7,341 (72.7)	162 (65.9)	0.017	6,158 (61.0)	159 (64.6)	0.247	1,633 (16.2)	31 (12.7)	0.135	637 (6.3)	23 (9.4)	0.055
UGIB	7,418 (72.8)	85 (55.6)	<0.001	6,198 (60.8)	119 (77.8)	<0.001	1,635 (16.1)	29 (19.0)	0.337	631 (6.2)	29 (19.1)	<0.001
Unknown etiology	7,103 (72.4)	400 (76.1)	0.065	6,020 (61.3)	297 (56.5)	0.026	1,599 (16.3)	65 (12.4)	0.016	606 (6.2)	54 (10.3)	<0.001

	Diarrhea			Low blood pressure (<90 mm Hg)			Tachycardia (>100 beats/min)			Syncope/loss of consciousness		
	Absent	Present	*P*	Absent	Present	*P*	Absent	Present	*P*	Absent	Present	*P*
Diverticular bleeding	734 (19.6)	282 (4.3)	<0.001	209 (5.6)	298 (4.5)	0.021	682 (18.5)	1,318 (20.4)	0.021	192 (5.1)	476 (7.3)	<0.001
Ischemic colitis	698 (7.5)	318 (33.9)	<0.001	483 (5.1)	24 (2.6)	<0.001	1,866 (20.3)	134 (14.4)	<0.001	637 (6.8)	31 (3.3)	<0.001
Malignancy	994 (9.8)	22 (11.5)	0.453	495 (4.9)	12 (6.2)	0.393	1,970 (19.8)	30 (16.0)	0.202	657 (6.5)	11 (5.7)	0.66
Infectious colitis	931 (9.2)	85 (63.9)	<0.001	500 (4.9)	7 (5.2)	0.862	1,966 (19.6)	34 (26.0)	0.071	664 (6.5)	4 (3.0)	0.111
IBD	891 (8.8)	125 (59.5)	<0.001	501 (4.9)	6 (2.9)	0.166	1,941 (19.5)	59 (28.6)	0.001	662 (6.6)	6 (2.9)	0.032
Radiation colitis	1,013 (9.9)	3 (4.6)	0.21	506 (4.9)	1 (1.5)	0.38	1,993 (19.8)	7 (10.6)	0.062	665 (6.5)	3 (4.6)	0.8
Other colitis	981 (9.6)	35 (30.2)	<0.001	502 (4.9)	5 (4.3)	1	1,977 (19.7)	23 (20.2)	0.903	659 (6.5)	9 (7.7)	0.589
Angioectasia	1,007 (9.9)	9 (6.8)	0.229	497 (4.9)	10 (7.5)	0.16	1,977 (19.8)	23 (17.8)	0.586	662 (6.5)	6 (4.6)	0.366
Rectal ulcer	1,004 (10.0)	12 (4.7)	0.005	478 (4.7)	29 (11.3)	<0.001	1,953 (19.8)	47 (18.5)	0.621	647 (6.4)	21 (8.2)	0.262
Hemorrhoids	1,011 (10.0)	5 (2.7)	<0.001	498 (4.9)	9 (4.9)	0.994	1,973 (19.8)	27 (15.3)	0.14	655 (6.5)	13 (7.1)	0.741
Post-endoscopy bleeding	1,006 (10.2)	10 (2.2)	<0.001	493 (5.0)	14 (3.0)	0.055	1,937 (20.0)	63 (14.3)	0.004	648 (6.6)	20 (4.3)	0.054
Small bowel bleeding	987 (9.8)	29 (11.8)	0.304	484 (4.8)	23 (9.4)	0.001	1,942 (19.6)	58 (24.5)	0.063	654 (6.5)	14 (5.7)	0.626
UGIB	1,000 (9.9)	16 (10.5)	0.802	481 (4.7)	26 (17.0)	<0.001	1,940 (19.4)	60 (39.7)	<0.001	645 (6.3)	23 (15.0)	<0.001
Unknown etiology	965 (9.9)	51 (9.7)	0.922	476 (4.9)	31 (5.9)	0.280	1,914 (19.9)	86 (16.5)	0.055	645 (6.6)	23 (4.4)	0.046

Bleeding etiologies with 50 or more cases were included in the analysis. Data are presented as n (%).
IBD, inflammatory bowel disease; UGIB, upper gastrointestinal bleeding.

data, and mainly wrote the article. K.K. (Bokuto hospital), A. Yamauchi, A. Yamada, J.O., T.I., T.A., N.T., Y. Sato, T. Kishino, N.I., T.S., M.M., A.T., K.M., K.K. (Fukuoka University Chikushi Hospital), S. Fujimori, T.U., M.F., H.S., S.S., T.N., J.H., T.F., Y. Kinjo, A.M., S.K., T.M., R.G., H.F., Y.F., N.G., Y.T., K. Narimatsu, N.M., K. Nagaike, T. Kinjo, Y.S., S. Funakoshi, K.K., T.M., Y. Komaki, K.M., K.W., and M.K.: designed the study, made decisions and definitions of survey items, and interpreted the data. N.N. and K.M.: performed the statistical analysis. M.F., T.I., N.U., T. Kinjo, and M.K.: provided corrections and advice on the preparation of the article.

Financial support: This work was partially supported by grants from the Ministry of Health, Labour and Welfare, Japan (grant number: 19HB1003), JSPS KAKENHI grant (JP17K09365 and 20K08366), Smoking Research Foundation, Takeda Science Foundation, Tokyo Medical University Cancer Research Foundation, Tokyo Medical University Research Foundation, Grants-in-Aid for Research from the National Center for Global Health and Medicine (29-2001, 29-2004, 19A1011, 19A1022, 19A-2015, 29-1025, and 30-1020). The funders played no role in the study design, analysis, and decision to publish the manuscript.

Potential competing interests: None to report.

Study Highlights

WHAT IS KNOWN

- ✓ Many physicians empirically suspect bleeding etiology based on the presenting symptoms.
- ✓ The precise bleeding source of hematochezia is not known unless colonoscopy is performed.
- ✓ How bleeding sources are identified may affect adverse outcomes, which may trigger changes in management.

WHAT IS NEW HERE

- ✓ Colonoscopy had a high diagnostic yield of 95% and identified 48 bleeding etiologies.
- ✓ Differences in outcomes based on bleeding etiology suggest that endoscopy can guide the management of hematochezia.
- ✓ Differentiating between bleeding etiologies based on presenting symptoms and hemodynamic instability alone would be challenging.

REFERENCES

1. Strate LL, Gralnek IM. ACG clinical guideline: Management of patients with acute lower gastrointestinal bleeding. Am J Gastroenterol 2016;111:459–74.
2. Oakland K, Chadwick G, East JE, et al. Diagnosis and management of acute lower gastrointestinal bleeding: Guidelines from the British Society of Gastroenterology. Gut 2019;68:776–89.
3. Nagata N, Ishii N, Manabe N, et al. Guidelines for colonic diverticular bleeding and colonic diverticulitis: Japan Gastroenterological Association. Digestion 2019;99(Suppl 1):1–26.
4. Oakland K, Jairath V, Uberoi R, et al. Derivation and validation of a novel risk score for safe discharge after acute lower gastrointestinal bleeding: A modelling study. Lancet Gastroenterol Hepatol 2017;2:635–43.
5. Aoki T, Nagata N, Shimbo T, et al. Development and validation of a risk scoring system for severe acute lower gastrointestinal bleeding. Clin Gastroenterol Hepatol 2016;14:1562–70.e2.
6. Strate LL, Orav EJ, Syngal S. Early predictors of severity in acute lower intestinal tract bleeding. Arch Intern Med 2003;163:838–43.
7. Velayos FS, Williamson A, Sousa KH, et al. Early predictors of severe lower gastrointestinal bleeding and adverse outcomes: A prospective study. Clin Gastroenterol Hepatol 2004;2:485–90.
8. Nagata N, Sakurai T, Shimbo T, et al. Acute severe gastrointestinal tract bleeding is associated with an increased risk of thromboembolism and death. Clin Gastroenterol Hepatol 2017;15:1882–9.e1.
9. Parker DR, Luo X, Jalbert JJ, et al. Impact of upper and lower gastrointestinal blood loss on healthcare utilization and costs: A systematic review. J Med Econ 2011;14:279–87.
10. Oakland K, Guy R, Uberoi R, et al. Acute lower GI bleeding in the UK: Patient characteristics, interventions and outcomes in the first nationwide audit. Gut 2018;67:654–62.
11. Nagata N, Shimbo T, Sekine K, et al. Combined endoscopy, aspiration, and biopsy analysis for identifying infectious colitis in patients with ileocecal ulcers. Clin Gastroenterol Hepatol 2013;11:673–80.e2.
12. Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. J Chronic Dis 1987;40:373–83.
13. Nagata N, Niikura R, Aoki T, et al. Colonic diverticular hemorrhage associated with the use of nonsteroidal anti-inflammatory drugs, low-dose aspirin, antiplatelet drugs, and dual therapy. J Gastroenterol Hepatol 2014;29:1786–93.
14. Radaelli F, Frazzoni L, Repici A, et al. Clinical management and patient outcomes of acute lower gastrointestinal bleeding. A multicenter, prospective, cohort study [internet]. Dig Liver Dis 2021. doi: 10.1016/j.dld.2021.01.002.
15. Lanas Á, Carrera-Lasfuentes P, Arguedas Y, et al. Risk of upper and lower gastrointestinal bleeding in patients taking nonsteroidal anti-inflammatory drugs, antiplatelet agents, or anticoagulants. Clin Gastroenterol Hepatol 2015;13:906–12.e2.
16. Niikura R, Nagata N, Aoki T, et al. Predictors for identification of stigmata of recent hemorrhage on colonic diverticula in lower gastrointestinal bleeding. J Clin Gastroenterol 2015;49:e24–30.
17. Strate LL, Syngal S. Timing of colonoscopy: Impact on length of hospital stay in patients with acute lower intestinal bleeding. Am J Gastroenterol 2003;98:317–22.
18. Niikura R, Nagata N, Yamada A, et al. Efficacy and safety of early vs elective colonoscopy for acute lower gastrointestinal bleeding. Gastroenterology 2020;158:168–75.e6.
19. Nagata N, Niikura R, Sakurai T, et al. Safety and effectiveness of early colonoscopy in management of acute lower gastrointestinal bleeding on the basis of propensity score matching analysis. Clin Gastroenterol Hepatol 2016;14:558–64.
20. Ishii N, Omata F, Nagata N, et al. Effectiveness of endoscopic treatments for colonic diverticular bleeding. Gastrointest Endosc 2018;87:58–66.
21. Nagata N, Niikura R, Ishii N, et al. Cumulative evidence for reducing recurrence of colonic diverticular bleeding using endoscopic clipping versus band ligation: Systematic review and meta-analysis [internet]. J Gastroenterol Hepatol 2020;36:1738–43.
22. 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;130:601.e1–8.
23. Strate LL, Liu YL, Aldoori WH, et al. Obesity increases the risks of diverticulitis and diverticular bleeding. Gastroenterology 2009;136:115–22.e1.