Identification of diverticular bleeding needs early colonoscopy rather than preparation

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ABSTRACT

Background and study aims When patients present with acute colonic diverticulum bleeding (CDB), a colonoscopy is performed to identify stigmata of recent hemorrhage (SRH), but valuable time can be lost in bowel preparation. This study retrospectively examined groups of patients who either had a standard pre-colonoscopy regimen or no preparation.

Patients and methods This study compared data from 433 patients who either followed a lengthy regimen of bowel preparation (prepared group, 266 patients) or had no preparation (unprepared group, 60 patients). We compared the association between time (hours) between admission before starting a colonoscopy (TMS) and identification of SRH using a chi-square test.

Results In 48 of 60 cases (80.0 %) in the unprepared group, a total colonoscopy was performed and the time to identify SRH was decreased. The respective rates of SRH identification in the unprepared and prepared groups were 55.2 % (16/29) vs. 46.7 % (7/15) if the TMS was <3 hours; 47.1 % (8/7) vs. 36.8 % (35/95) in 3 to 12 hours; 0 % (0/3) vs. 22.0 % (13/59) in 12 to 18 hours; and 21.8 % (3/11) vs. 20.6 % (42/204) in >18 hours. There were no significant differences between the two groups. However, the SRH identification rates before and after 12 hours were 42.3 % (66/156) and 20.9 % (58/277) (P<0.001).

Conclusions Our data suggest that the bowel preparation method before colonoscopy is an independent variable predicting success in identifying SRH among patients with CDB. Decreasing the time before colonoscopy to no more than 12 hours after admission played an important role in identifying SRH.

Introduction

Colonic diverticulosis is characterized by “diverticula,” sac-like protrusions that occur when colonic mucosa and submucosa herniate through defects in the muscular layer of the colon wall [1]. If the diverticula become infected and inflamed, the condition becomes diverticulitis. In Western populations, diverticula occur in the sigmoid descending colon (pseudodiverticula) [1], while Asian populations experience diverticula in the right colon (true diverticula) [1]. Infected diverticula can rupture and cause hemorrhagic bleeding. Colonoscopy is a useful diagnostic or therapeutic tool for patients presenting with acute lower gastrointestinal bleeding (LGIB) such as acute colonic diverticular bleeding (CDB) [2, 3].

CDB is a challenge for gastroenterologists. Bleeding stops spontaneously in 75 % of patients [4], making it difficult to identify and treat the underlying diverticulum. One of the key clinical problems in treating a hemorrhagic diverticulum is the

difficulty in identifying the stigmata of recent hemorrhage (SRH). If a source of bleeding is found, it is treated by one of several methods.

The American Gastroenterology Association's clinical guidelines (Management of Patients with Acute Lower Gastrointestinal Bleeding) recommend bowel preparation before colonoscopy [3]. Once patients are hemodynamically stable, a colonoscopy is performed. It is a standard procedure to perform colonoscopy only after adequate colon cleansing [4], which is considered important for endoscopic visualization and diagnosis. A colonoscopy should be performed as soon as possible, however, to identify the SRH, but colon purging is inconvenient and time-consuming. This study retrospectively investigated bowel preparation methods before colonoscopy.

Patients and methods

Study design

This study protocol was approved by the ethics committee at the Saiseikai Central Hospital, Tokyo, Japan (study no. 307) and was performed under the Declaration of Helsinki.

Patients

We retrospectively enrolled 433 consecutive patients diagnosed with CDB between January 2000 and December 2019 at the Saiseikai Central Hospital. Patients were excluded if a colonoscopy was not performed within 48 hours of admission. Patients were diagnosed based on colonoscopy findings, CT reports, or discharge summaries. We reviewed the medical records, operative notes, and colonoscopy records.

Patient classification and the time from admission to starting colonoscopy (TMS)

Patients were divided into two groups based on their pre-colonoscopy treatment: prepared and unprepared. To remove clots, stool, and blood and sufficiently clean the colon, patients in the prepared group underwent a 2- to 4-hour oral sulfate purge with 2 to 4 L of PEG (Niflec, Ajinomoto, Tokyo, Japan). The unprepared group did not undergo this regimen before colonoscopy.

The time from admission to starting colonoscopy (TMS) was defined as the period (hours) from admission to starting colonoscopy. In the prepared cases, TMS included the period when preparing with oral sulfate purge with 2 to 4 L of PEG

Diagnosis of CDB and recurrence

Based on the criteria by Jensen et al., patients presenting with the chief complaint of hematochezia were diagnosed with CDB if: (a) the condition was shown during a colonoscopy; or (b) by process of elimination if the upper and/or lower endoscopy did not show a bleeding source [5]. According to Jensen et al., the diagnosis was made if endoscopy found blood clots in the colon, presence of diverticula, absence of blood in the terminal ileum, and no other demonstrable cause of bleeding [5]. A definitive diagnosis of diverticulosis as the source of bleeding required finding one of these conditions: SRH, an actively bleeding vessel, a nonbleeding visible vessel, or an adherent clot [5].

Colonoscopists were well trained and skilled at endoscopic hemostasis. The two colonoscopists had experience with over 500 cases, two colonoscopists had experience with over 1000 cases, and other two colonoscopists had experience with over 2000 cases.

Treatment procedure

Jensen's technique for endoscopic injection therapy outlined 1– or 2-mL aliquots of epinephrine (1:20,000) injected into the four quadrants of the bleeding diverticulum [5]. Endoscopic hemostasis was performed by clipping the exposed vessel or lesion (direct method) or the entire diverticular orifice (reefing method) [6]. For actively bleeding vessels, injection therapy was given first, followed by endoscopic clipping as needed. For visible blood vessels and blood clots without bleeding, endoscopic clipping was performed.

Outcome measurement

The primary endpoint (short-term outcome) was to identify SRH and stop bleeding. The secondary endpoint (long-term outcome) was to prevent rebleeding within 30 days, defined as significant fresh blood loss after the first colonoscopy with: (1) hemorrhagic shock; (2) need for blood transfusion; (3) effect of blood pooling on further colonoscopy identification; or (4) lower gastrointestinal SRH.

Statistical analysis

Student *t*-test and chi-square tests were used to assess the significance of differences between the two groups. Continuous data were expressed as the mean (SD). A follow-up study evaluated recurrence of CDB within 30 days of short-term hospitalization. The significance of the rates was determined by the chi-square test. All statistical analyses were performed using commercial software (SPSS 26, IBM-SPSS Japan, Inc., Tokyo, Japan).

Results

Patient characteristics

The study included 309 patients diagnosed with CDB who underwent colonoscopy within 48 hours of hospitalization between January 2000 and December 2016. The patients were divided into two groups: (1) the prepared group (373 patients) had a regimen of bowel preparation before colonoscopy and the unprepared group (60 patients) had no preparation before colonoscopy. ▶ **Table 1** summarizes patient characteristics. The non-prepared group had a significantly higher number of cases with active bleeding and transfusion volume than the prepared group. There were no significant differences in age, gender, or other patient characteristics.

SRH identification

In 48 of 60 patients (80.0 %) in the unprepared group, colonoscopy was completed without adverse events (AEs). SRH was identified in 27 of 60 patients (45.0 %) in the unprepared group (20 active bleeding, three nonbleeding visible vessels, and four adherent clots). SRH was identified in 97 of 373 patients (26.0 %) in the prepared group (44 active bleeding, seven nonbleed-

▶ **Table 1** Patient characteristics.

	Prepared group	Unprepared group	
	n = 373	n = 60	*P* value
Mean (SD) age (yr.)	68.8(13.3)	73.1(15.9)	< 0.05
Sex (M/F)	289/84	40/20	NS
History of CDB	146 (39.1 %)	22 (36.7 %)	NS
History of ACD	55(14.8 %)	6 (10.0 %)	NS
Smoking	64 (17.2 %)	11 (14.7 %)	NS
Dinking	148(39.7 %)	16(26.7 %)	NS
LDA	53(14.2 %)	10(16.7 %)	NS
Antiplatelet drugs	12(3.2 %)	3(5.0 %)	NS
Warfarin	13(3.5 %)	4(6.7 %)	NS
Comorbidities	296(79.4 %)	48(80.0 %)	NS
Hb (mg/dL)(mean and SD)	11.7(2.5)	10.7(2.5)	< 0.05
Active bleeding	44(45.4 %)	20(71.4 %)	< 0.05
Blood transfusion (unit)(mean and SD)	1.3(3.0)	3.9(3.1)	< 0.001
Location (right/left)	59/27	18/31	< 0.05

CBD, colonic diverticular bleeding; ACD, acute colonic diverticulitis; LDA, low-dose aspirin; NS, not significant; Location, culprit diverticula of CDB; Right, ascending, hepatic flexure; Left, descending, sigmoid colon.

▶ **Table 2** Primary and secondary outcomes.

	Prepared group	Unprepared group	
	n = 373	n = 60	*P* value
Outcome of Shor period			
▪ SRH identification (%)	97 (26.0 %)	27 (45.0 %)	0.003
▪ Endoscopic treatment	104 (27.9 %)	33(55.0 %)	< 0.001
▪ Need for interventional radiology	6	2	NS
▪ Need for surgery	1	0	NS
▪ Hospital stay (day) (mean SD)	7.7 (4.8)	10.6 (11.2)	< 0.05
▪ Mortality	0	0	NS
▪ Adverse events[1]	2	1	NS
Outcome of long period			
▪ Rebleeding (%)	19 (5.1 %)	6 (10.0 %)	NS

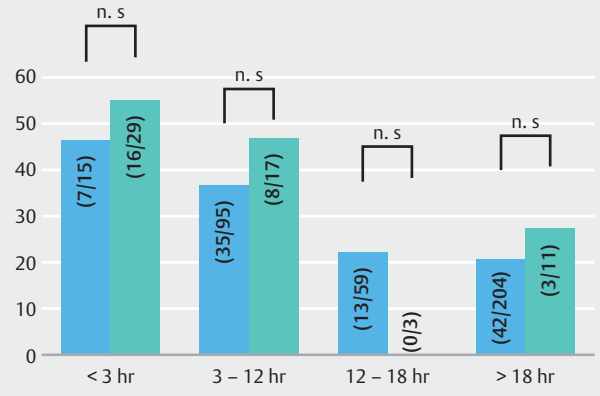
SRH, stigmata of recent hemorrhage
[1] Nausea during the preparation.

ing visible vessels and 46 adherent clots). The SRH detection rate was higher in the unprepared group than in the prepared group (▶ **Table 2**).

Time from admission to starting colonoscopy (TMS)

The mean (SD) of TMS was 7.5 hours (9.8) in the unprepared group and 18.7 hours (11.0) in the prepared group ($P < 0.001$). Where SRH was identified, the mean (SD) of TMS was 4.8 hours (8.8) in the unprepared group and 15.9 (11.1) in the prepared group ($P < 0.001$). In cases with active bleeding, the mean (SD) of TMS was 4.8 hours (8.8) in the unprepared group and 16.0 hours (11.1) in the prepared group ($P < 0.001$).

▶ **Fig. 1** compares the rate of SRH identification between the two groups by TMS. There is a significant difference ($P = 0.001$),



▶ **Fig. 1** The rate of stigmata of recent hemorrhage (SRH) identification from admission to start of colonoscopy comparing prepared and unprepared group. Blue bars show the prepared group. Orange bars show the unprepared group. Statistics were performed using a chi-squire test. n.s = not significant.

with the rate of identification, which decreases as TMS increases. There was also a significant difference ($P<0.001$) between cases identified within or after more than 3 hours. In the unprepared group, the SRH identification rate within 3 hours was 55.2% (16/29). In the prepared group, the SRH identification within 3 hours was 46.7% (7/15).

The SRH identification rate before or after more than 12 hours was also significantly different: the SRH identification rate before 12 hours was 42.3% (66/156), and after 12 hours, it was 20.9% (58/277) ($P<0.001$). By the period of TMS, there was no significant difference between unprepared and prepared groups.

Rebleeding and the duration of hospital admission

We applied endoscopic treatment for 104 patients in the prepared group and 33 patients in the unprepared group. Nineteen patients in the prepared group and six patients in the unprepared group had rebleeding. Six and two rebleeding cases, respectively, were not controlled by endoscopic treatment and interventional radiology was needed. One case in the prepared group needed surgery. The mean duration of hospital stay was 7.7 days (4.8) in the prepared group and 10.6 days (11.2) in the unprepared group ($P=0.050$), probably because the patients in the latter group had more acute comorbidities. There were two cases with nausea during preparation and there were no AEs in either group during preparation or colonoscopy.

Discussion

This study compared colonic purging regimens before colonoscopy for CDB diagnosis and identification of SRH. Our results suggest SRH can be better identified by shortening the time between patient admission and colonoscopy, with the procedure ideally taking place within 12 hours of admission.

Endoscopic management of diverticular bleeding can be challenging for multiple reasons, including the inconvenience of rapid bowel preparation, difficulty of carefully examining each diverticulum in the colon, identifying the true SRH, and achieving hemostasis of small lesions within the diverticula. Even after adequate bowel preparation, an urgent colonoscopy could cause an incomplete examination in up to 45% of cases. The method allows a positive diagnosis in approximately two-thirds of cases and hemostasis in one-third, resulting in shorter hospitalization [7–10]. However, no randomized controlled trial (RCT) has determined whether the 2– or 4-L preparation produces a better outcome [5].

Jensen et al. reported the necessity of colon preparation [5]. They performed an urgent colonoscopy within 6 to 12 hours after hospitalization. The colon preparation used a 5- to 6-L sulfate purge, and the authors reported that the diagnosis by colonoscopy was determined in 23.3% (17/73) and 20.8% of cases (10/48) in two series [5].

Our previous reports showed the usefulness of a purge before colonoscopy. In a retrospective study of 110 patients with CDB, colon preparation with a polyethylene glycol purge compared to no purge allowed for a higher rate of identifiable bleeding diverticula (28.2% vs. 12.0%, $P=0.11$), although the difference was not statistically significant [11]. In addition, 12.0% (3/25) of the group with no preparation demonstrated no stool in the colon except for the focal streaming of blood [11].

Over a 7-year period, Chaudry et al. performed urgent colonoscopy within 24 hours of presentation for LGIB without colonic preparation [8]. The source of bleeding was correctly identified in 82 of 85 patients (97%): diverticulosis (20%), ischemic colitis (18%), hemorrhoids (14%), and other sources of bleeding. They claimed that the information gained from the amount and distribution of blood in the colon aids diagnosis [8]. Rossini et al. reported correct localization of colonic bleeding in 311 of 409 patients (76%) who underwent unprepared colonoscopy for LGIB [12].

In a prospective study by Repaka et al., 13 procedures were performed in patients with severe LIGB using a hydroflush colonoscopy (a colonoscopy technique using a combination of the standard colonoscopy, a water-jet irrigation pump, and a mechanical endoscope suction device); complete colonoscopy to the cecum was performed in only nine of 13 patients (69.2%) [13]. However, in 13 cases, endoscopic visualization was adequate for identifying the source of bleeding without repeat colonoscopies due to inadequate preparation. A definite source of bleeding was identified in five of 13 procedures (38.5%) with diverticular bleeding being the presumed etiology in the remaining cases [13].

In our retrospective study of 110 patients with CDB [11], the detection rate was significantly higher when the colonoscopy was performed within 18 hours of the final hematochezia and lower when it was performed more than 18 hours later (40.5 vs. 10.5%; $P<0.01$).

Recent meta-analyses comparing early colonoscopy with elective colonoscopy have not proven a clinical benefit for early colonoscopy (< 3 hours) [14], but no definitive conclusions were drawn in these studies [15, 16]. One randomized trial showed that an early colonoscopy in LGIB identified the source of bleed-

ing more often than an elective or delayed colonoscopy; however, there was no benefit in clinical outcomes such as rebleeding rates, blood transfusions, or intensive care unit (ICU) or hospital stay durations [15].

In a retrospective cohort study of 326 patients by Laine and Shah, patients presenting with LGIB had an early colonoscopy (performed within the first 24 hours of hospital admission) or elective colonoscopy (performed after 24 hours of admission). The earlier intervention led to a shorter length of stay (10 vs. 13 days), an increase in detection of the source of active bleeding (26.4 vs. 9.2 %), and, therefore an increase in the rate of successful endoscopic treatment (25.8 vs. 8.6 %) [16].

Niikura et al. conducted a large (n = 170) and well-designed randomized trial to determine the efficacy of early (< 24 hours) vs. elective (24 to 96 hours) colonoscopy in detecting LGIB. Their objectives paralleled those of our study: identification of SRH and reduction of rebleeding within 30 days. They concluded that colonoscopies within 24 hours of hospital admission did not increase the identification of SRH or reduce rebleeding compared with colonoscopies at 24 to 96 hours [17]. Their SRH detection rate was low: 21.5 % in early colonoscopy or 21.3 % in elective colonoscopy [17].

CDB is the most common cause of severe LGIB in adults, accounting for 30 % to 50 % of cases of massive rectal bleeding [18–21]. In most cases, CDB bleeding stops spontaneously [18–21]. It is difficult, however, to prove effectiveness when the detection rate of SRH is as low as 20 %, as in Nikura's study [17]. We had a much higher rate of SRH identification: 50 % to 60 % within 3 hours of admission. After 3 hours, the SRH detection rate dropped to 20 % to 30 %, similar to Niikura's findingsky. In our study, the majority of patients in the unprepared group had a colonoscopy within 3 hours (29/45 [64.4 %]), resulting in SRH identification of 53 %.

The SRH identification was better before 12 hours than after 12 hours, 42.3 % and 20.9 %, respectively ($P < 0.01$). These data suggest that early colonoscopy should be performed within early periods without or with preparation and ideally should not be delayed beyond 12 hours. However, early colonoscopy without preparation may have some risks exposed to infectious disease such as COVID-19 and then we should select the patients in whom we should perform an early colonoscopy on a case-by-case. We previously reported that urgent dynamic CT with intravenous contrast may contribute to subsequent decisions about whether an urgent colonoscopy should be performed in patients with CDB [22]. Findings on an urgent dynamic CT could be a good marker for presence of active bleeding, and the bleeding points could be detected by urgent colonoscopic examinations and then be treated.

This study had several limitations. First, it was moderately sized and retrospective. Most cases of active bleeding and SRH identification occurred in patients who underwent colonoscopy within 3 hours. Characteristics of patients who underwent earlier (< 3 hours) showed more active bleeding and more urgent cases. Actually, the results of high detection rate of SRH may be due to selection bias. However, our results show that earlier endoscopy should be performed, with or without pretreatment in cases with active bleeding, and then SRH will be detected more frequently. Second, this study was performed on Japanese patients, the majority of whom had right-sided diverticula. We believe, however, this regional diverticular difference does not create a bias because a right-side colonoscopy is more difficult to perform.

Conclusions

Earlier colonoscopy could be useful in making a diagnosis and treating CDB more safely. Further large-scale RCTs should be performed to confirm the effectiveness of earlier colonoscopy, regardless of preparation, for outcomes of SRH, need for blood transfusion, length of stay, and rebleeding within 30 days.

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Competing interests

The authors declare that they have no conflict of interest.

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