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Efficacy and safety of conservative treatment for colonic diverticular bleeding: A prospective study.

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Trial registration: UMIN000028007, UMIN Japan (http://www.umin.ac.jp/english/)
, Prospective, Single-Center study

Abstract:
Background and study aims: This prospective study aimed to establish the efficacy and safety of conservative treatment for non-severe cases of colonic diverticular bleeding and to verify whether early colonoscopy is necessary only in limited cases.
Patients and methods: Patients who were urgently hospitalized due to hematochezia and were diagnosed with colonic diverticular bleeding were included. During hospitalization, early colonoscopy within 24 h after admission was performed only when both systolic blood pressure <90 mmHg and extravasation on contrast-enhanced computed tomography were observed. However, in patients who failed to recover from hemorrhagic shock, interventional radiology was performed. In other cases, patients received conservative treatment.
Results: Of the 172 patients, 15 (8.7%) met the criteria for undergoing early colonoscopy; 12 and 3 attained successful hemostasis via early colonoscopy and interventional radiology, respectively. Meanwhile, 157 patients received conservative treatment, resulting in spontaneous hemostasis in 148 patients (94.3%). The remaining nine patients required hemostatic intervention. No patient died from bleeding. Between the conservative treatment and the urgent hemostasis groups, early rebleeding rate within 30 days (14.6% vs. 33.3%, P=0.0733) and overall 1-year cumulative rebleeding rate after 30 days of hospitalization (9.2% vs. 23.1%, P=0.2271) were not significant. In multivariate analyses, only systolic blood pressure and extravasation were associated with the 24 patients who required hemostatic intervention. Moreover, multivariate analyses showed that patients with a history of diverticular bleeding, patients undergoing hemodialysis, and oral thienopyridine were significantly associated with late rebleeding.
Conclusions: Conservative treatment for non-severe colonic diverticular bleeding is appropriate and efficient.

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Introduction

Colonic diverticular bleeding is the most common cause of lower gastrointestinal bleeding, accounting for more than one-fourth of total cases [1,2], and has been increasing along with an elevated number of patients with colonic diverticula and those taking antithrombotic drugs [3]. Colonic diverticular bleeding generally stops spontaneously in 87–96% of patients [4-6]. Japanese guidelines for colonic diverticular bleeding advocate early colonoscopy within 24 h of a hospital visit to identify the stigma of recent hemorrhage (SRH) [7], which is considered an indicator of a bleeding point. However, recent studies on the effectiveness of early colonoscopy have not reported improved outcomes regarding rebleeding rate and length of hospital stay [8,9]. However, some severe cases require hemostatic intervention, and detecting such cases is important. Additionally, the effectiveness of hemostatic methods, such as endoscopic band ligation (EBL), over-the-scope clip (OTSC), and endoscopic detachable snare ligation [10-12], and new techniques, such as the underwater method, gel immersion endoscopy, and traction devices have been reported [13-15]; however, the SRH identification rate is initially low, ranging from 15–42% even when performing early colonoscopy [7,8,16-19]. Considering the high rate of spontaneous hemostasis of diverticular bleeding, SRH may spontaneously regress during conservative treatment, except in some cases. Based on these hypotheses, we developed a treatment strategy for diverticular bleeding. In cases with both low systolic blood pressure, which could be regarded as an indicator of hemodynamic instability, and extravasation on

contrast-enhanced computed tomography (CECT), which would indicate the site of active bleeding, early colonoscopy was performed. In the other cases, conservative treatment with fasting and fluid administration was administered. We have previously conducted a retrospective study using this treatment strategy, and spontaneous hemostasis was achieved in all patients in the conservative treatment group [20]. Based on these backgrounds, this prospective study aimed to establish the efficacy and safety of conservative treatment for non-severe cases of colonic diverticular bleeding and to verify that early colonoscopy is necessary only in limited cases.

Materials and methods

Patients

Consecutive outpatients with bloody stools between January 2017 and December 2023 were eligible for inclusion. The inclusion criteria were as follows: (i) urgent hospitalization due to hematochezia and (ii) colonic diverticulum observed on CECT or previous colonoscopy. The exclusion criteria were as follows: (i) colonoscopy was not performed within 7 days of hospitalization, (ii) total colonoscopy was not possible, (iii) CECT was not performed due to allergy to contrast media or severe renal dysfunction (estimated glomerular filtration rate <30 mL/min/1.73 m^2), and (iv) other bleeding sources were identified. Presumptive diverticular bleeding was diagnosed when spontaneous hemostasis was achieved without hemostatic

intervention and no source of bleeding other than diverticular bleeding was found on colonoscopy or other examinations [7,8]. This study was approved by the institutional ethics review board at our hospital. All patients provided informed consent regarding the risks and benefits of their treatment depending on their physical condition. The trial was registered at UMIN-CTR (UMIN000028007).

Flowchart of the treatment strategy

Treatment options are shown in Figure 1. In all cases, during hospital visits, procedures, such as infusion to stabilize the patient's general condition, were first performed. All patients underwent CECT to assess extravasation within the bowel lumen. Only when both low systolic pressure (<90 mmHg) and extravasation were observed, early colonoscopy was performed within 24 h. When SRH was identified, endoscopic hemostasis was performed using a clipping method or an OTSC. Conversely, if SRH was not observed because of spontaneous hemostasis, follow-up observation without colonoscopy was performed. In cases where patients could not recover from shock or when endoscopic hemostasis was challenging, interventional radiology (IVR) was performed to achieve hemostasis by arterial embolization. Otherwise, if the patient's vital signs were stable during the hospital visit or extravasation was not detected on CECT, conservative treatment with fasting and fluid resuscitation without early colonoscopy was administered. An elective colonoscopy was performed within 1 week after spontaneous

hemostasis. Additionally, even if conservative treatment was chosen, if vital signs became unstable again after admission or if bleeding persisted for >24 h, a colonoscopy was performed as soon as possible.

Food intake was resumed for >24 h after the disappearance of hematochezia, meals were gradually solidified each day, and the patients were discharged with a regular diet. Regarding the indications for blood transfusion, in principle, patients with a serum hemoglobin (Hb) level of <7 g/dL were considered for blood transfusion. However, in some patients with comorbidities or general conditions such as shock, blood transfusion was considered even if the Hb level was 9 g/dL. Antithrombotic drugs were generally continued when vital signs were stable but were discontinued in patients who were in shock and immediately resumed after hemostasis.

Rebleeding

Rebleeding was defined as the presence of fresh blood in the stool along with low blood pressure (systolic blood pressure drops >20 mmHg) or a decrease in the Hb level of ≥2.0 g/dL. Early and late rebleeding were defined as rebleeding within 30 days of hospitalization and after 30 days of hospitalization, resulting in a second hospitalization, respectively. The presence or absence of rebleeding was evaluated in all patients until April 2024 according to the following methods: (i) in the case of outpatients in our hospital, it was evaluated on the onset day or at a recent visit; and (ii) in cases of patients who were not followed up in our hospital, it was

evaluated by telephone call with a questionnaire survey, which provided a recent history of the presence or absence of hospitalization due to hematochezia.

Colonoscopy

Colonoscopy was performed after preparation with 2 L of polyethylene glycol in all patients, whether early or elective. Carbon dioxide insufflation was used to reduce abdominal discomfort, except in patients with chronic obstructive pulmonary disease. PCF-Q260AZI (Olympus, Tokyo, Japan), which has a water jet system, was used for early colonoscopy with a cap attachment, and PCF-Q260AZI, CF-XZ1200AZI, or CF-H260AZI (Olympus, Tokyo, Japan) was used for elective colonoscopy.

If SRH was identified, hemostasis was performed using only the clipping method or OTSC. With regard to OTSC (OTSC® 12/6t, 2200 mm; Ovesco Endoscopy, Tübingen, Germany), we have been using it in our hospital since August 2019 and actively used it in cases that met the following criteria: (i) cases that were not difficult to insert because reinsertion was necessary; (ii) cases where the bleeding point could be reliably identified because of its high cost. If possible, clips (HX-610-135; Olympus, Tokyo, Japan) were placed directly on the visible vessel or stigmata. When direct placement was difficult because of the diverticular dome location, massive hemorrhage, or small diverticular orifice, indirect placement was performed using multiple clips in a zipper fashion [21].

Interventional radiology

IVR was performed in the femoral artery using a 4-Fr Shepherd hook catheter, and a nonionic contrast medium was injected into the superior mesenteric artery (5 mL/s) and inferior mesenteric artery (3 mL/s) to identify the bleeding sites. Once the bleeding sites were identified, a microcatheter was carefully advanced to the bleeding site, and arterial embolization was performed using coils. Embolization was selectively performed whenever possible to minimize intestinal ischemia.

Statistical analysis

Mean±standard deviation, median, or percentage was used for all data. Categorical data were compared using the chi-square test or Fisher's exact test, whereas continuous data were compared using the Wilcoxon rank-sum test. The relationship between the necessity of hemostatic intervention and background was examined using multivariate logistic regression analyses. The Kaplan–Meier method and log-rank test were used in the time-to-event analysis of patients with cumulative late bleeding, and the Cox proportional hazard model was used to examine the factors affecting late bleeding. JMP (version 14; SAS Institute Inc., the USA) was used for the statistical analysis, and a *P*-value <0.05 was considered statistically significant.

Results

Patient characteristics

Out of 248 patients who met the inclusion criteria, 76 patients were excluded due to failure to perform colonoscopy within 7 days in 38, incapability of cecal intubation in one, other sources of bleeding in 20 (angiodysplasia in six, upper gastrointestinal bleeding in four, small intestinal bleeding in two, ischemic colitis in two, tumor bleeding in two, rectal ulcer in two, and rectal varices in two), and difficulty using iodinated contrast medium in 17. Consequently, 172 patients were enrolled in this prospective study. Patient characteristics are shown in Table 1. Of the participants, which consisted of 125 males and 47 females, with an average age of 70.0±12.6 years (range: 34–97). Diverticula were located on the right side in 51 patients, on the left side in 12 and bilaterally in 109. A total of 44 patients (25.6%) had a previous history of diverticular bleeding and antithrombotic drugs were administered to 59 patients (34.3%): single antiplatelet therapy in 39, anticoagulant therapy in 25 and dual antiplatelet therapy in 10. A total of 32 patients (18.6%) had a systolic blood pressure <90 mmHg on arrival and 42 patients (24.4%) showed extravasation on CECT.

Treatment outcome of hemostasis

Treatment outcomes are presented in Tables 2 and 3. Out of 172 patients, 157 (91.3%) received conservative treatment according to our strategy: 111 with neither of the two signs, 17 with only systolic blood pressure <90 mmHg, and 29 with only extravasation on CECT. Consequently, 148 patients (94.3%) experienced spontaneous hemostasis. The remaining nine patients

received hemostatic interventions due to intermitted bleeding, resulting in endoscopic hemostasis in eight patients. However, one patient underwent elective surgery due to difficulty identifying SRH in the ascending colon via colonoscopy, despite repeated life-threatening rebleeding. Meanwhile, 15 patients met the criteria for early colonoscopy and 12 patients underwent endoscopic intervention, achieving successful initial hemostasis in all cases with SRH identification. The remaining three patients underwent IVR due to difficulty recovering from hemorrhagic shock. The bleeding sites were located in the right-sided colon in 14 cases and the left-sided colon in only one case. Although two of six patients with direct replacement and both two patients with zipper fashion experienced early rebleeding after initial endoscopic hemostasis, none of the patients with OTSC suffered from rebleeding. All patients eventually achieved successful hemostasis and no patients died by hemorrhagic shock, although one patient who received conservative treatment, a 74-year-old woman on dialysis, died of sepsis from phlegmon of the lower extremities after achieving spontaneous hemostasis.

A total of 24 patients required hemostatic intervention, while 148 patients achieved spontaneous hemostasis. In the univariate analysis, as shown in Table 4, significant differences were observed between patients who required hemostatic intervention and those who achieved spontaneous hemostasis in terms of systolic blood pressure <90 mmHg (62.5% vs. 11.5%, P<0.0001), positive extravasation (58.3% vs. 18.9% P=0.0001), and patients on hemodialysis (16.7% vs. 4.7%, P=0.0494). Multivariable logistic analyses showed systolic blood pressure

<90mmHg (odds ratio 21.39, *P*<0.0001, 95% confidence interval [CI] 6.83–66.99) and positive extravasation (odds ratio 5.84, *P*=0.0024, 95% CI 1.87–18.21) as significant relative factors for hemostatic intervention. Moreover, the risk factors for patients in the conservative treatment group who required hemostatic intervention were examined, but no significant differences were found between patients with systolic blood pressure <90 mmHg (22.2% vs. 10.1%, *P*=0.2523) or positive extravasation (11.1% vs. 18.9%, *P*=0.4556), indicating that meeting either of these criteria would not be an indicator for early colonoscopy. No other significant associated factors were identified.

Hospitalization costs were lower in the conservative treatment group ($2,068±681) compared to the urgent hemostasis group ($3,228±2,992, *P*=0.0101), while the median length of hospital stay did not differ between the two groups (8 days vs. 8 days, *P*=0.0932). Additionally, there was no significant difference in the early rebleeding rate after hospitalization (14.6% vs. 33.3%, *P*=0.0733) and the overall 1-year cumulative late rebleeding rate (9.2% vs. 23.1%, *P*=0.2271) between the two groups.

Factors related to early and late rebleeding

The early rebleeding rate within 30 days after hospitalization was 16.3% across all patients, with a 95% CI of 11.5–22.5%. No significant difference was observed between the conservative treatment group (14.6%) and the urgent hemostasis group (33.3%, *P*=0.0733). Additionally,

multivariate logistic analyses showed that no clinical backgrounds, except that all patients were male, significantly relate to early rebleeding. Late rebleeding, occurring after 30 days of hospitalization, was observed in 32 patients (18.6%, 95% CI: 13.5–25.1) during an observation periods of 45.9±22.7 months. The cumulative late rebleeding rate at 1, 3 and 5 years was 10.3%, 19.6% and 22.5%, respectively, with no significant difference between the two groups. Multivariable analyses using the Cox proportional hazard model, as shown in Table 5, identified a previous history of diverticular bleeding (hazard ratio 2.66, 95% CI 1.30–5.40, *P*=0.0082), patients on hemodialysis (hazard ratio 4.40, 95% CI 1.57–10.66, *P*=0.0070), and oral administration of thienopyridine derivatives (hazard ratio 2.49, 95% CI 1.03–5.43, *P*=0.0432) as significantly related factors to late rebleeding.

Discussion

Although early intervention for colonic diverticular bleeding has been extensively discussed, this is the first report of a prospective study using spontaneous hemostasis as the primary endpoint. The rate of spontaneous hemostasis in the conservative treatment group in this study was 94.3%, which is consistent with the results of our previous observational study [20]. Conversely, all patients in the urgent hemostasis group required hemostatic intervention, suggesting that this approach might be a useful strategy for identifying patients who need hemostatic intervention.

Even though recent studies on diverticular bleeding have been designed to perform early colonoscopy as soon as possible after hospital admission (e.g., within 24 h) [8,9], our hemostatic results were comparable to those studies. In most previous studies of endoscopic intervention, the primary endpoint was the identification rate of SRH, and cases with identified SRH were considered eligible for treatment. However, the identification rate of SRH varies from institution to institution, ranging from 15% to 47% [7,8,16-19], and there is a relatively large discrepancy compared to the spontaneous hemostasis rates reported in the past [4-6]. This suggests that SRH might not always indicate the necessity for endoscopic hemostasis.

Because the colon is less exposed to digestive fluids than the upper gastrointestinal tract, hemostatic intervention is not required as often as it is for upper gastrointestinal bleeding. In addition, most diverticular bleeding, generally thought to be caused by a breakage in the vulnerable part of the vasa recta located deep within the diverticulum cave [22], is inherently difficult to identify. Moreover, SRH, which is considered an indication for endoscopic hemostasis, is defined as active bleeding, visible vessel, or adherent clot [7]. While there is no dispute that the first two are indications that hemostatic intervention is necessary, the finding of adherent clot varies from observer to observer and, above all, represents a state of spontaneous hemostasis. Furthermore, the presence of a clot does not necessarily indicate a bleeding site. In other words, the high rate of spontaneous hemostasis might imply that endoscopic hemostasis is not necessary for adherent clots. This might explain why several previous reports have shown

that hemostatic intervention for SRH did not prevent early rebleeding [8,23]. At least in this study, all patients in the early colonoscopy group were found to have active bleeding or visible vessels, suggesting that a no-treatment observational study should be used for adherent clots in the future.

Next, cases requiring hemostatic intervention in diverticular bleeding are those with persistent bleeding that cannot be expected to stop spontaneously, leading to circulatory instability. From this perspective, our strategy was to use CECT as an indicator of persistent bleeding and blood pressure at presentation as an indicator of hemodynamic instability as criteria for early colonoscopy, and to perform early colonoscopy only when both criteria are met. In other words, if only one of the criteria is met, hemostatic intervention is not considered necessary. For instance, if extravasation is observed on CECT, it indicates persistent bleeding at the time of imaging, but if the blood pressure is stable, the bleeding is likely to be of a level that does not affect hemodynamics. This is because CECT can detect blood flow as low as 0.5 mL/min [24], and if the bleeding does not affect circulation, there is a high possibility that it would stop spontaneously. Conversely, even in cases of temporary hemodynamic instability, the absence of extravasation on CECT suggests that spontaneous hemostasis has already been achieved. Additionally, hypotension may be due to vagal reflex and cannot necessarily be attributed to hypovolemic shock. Regarding the Shock Index, heart rates in elderly patients may not increase

as much as younger patients because they may be taking drugs that affect this, such as β-blockers and calcium channel blockers, or they may have decreased sensitivity to catecholamines. There are some reports indicating that the Shock Index is not a valid indicator for gastrointestinal bleeding in a high proportion of elderly patients [25]. Moreover, in our previous retrospective study, heart rates was not associated with urgent hemostasis. Therefore, we selected blood pressure as a simple and more sensitive indicator. Given the high rate of spontaneous hemostasis, this strategy appears appropriate; in fact, 94.3% of patients in the conservative treatment group achieved spontaneous hemostasis. Similar validation in a multicenter study is needed in the future.

There was no significant difference in early rebleeding rates between the conservative treatment group and the urgent hemostasis group. In the urgent hemostasis group, early rebleeding after endoscopic hemostasis occurred only after using clipping methods, and no patients rebled after OTSC. This suggests that early rebleeding might be preventable if the bleeding point is identified and a reliable hemostatic method is used. Various recent reports have shown the effectiveness of EBL, which is certainly an effective and less costly treatment [26-28]. However, there have been reports of delayed perforation in a very small number of cases [29-31]. In this regard, the efficacy and safety of OTSC have recently been reported [11,32]. Although the cost of OTSC needs to be addressed, it is expected to become widely used as a safe

hemostatic treatment device.

As with previous reports, this study did not find any benefit of early colonoscopy and endoscopic hemostasis in reducing the late rebleeding rate [33,34]. Diverticular bleeding often occurs in patients with multiple colonic diverticula, making it difficult to identify the bleeding point. Late rebleeding may also occur even after successful endoscopic hemostasis, suggesting the possibility of bleeding from another diverticulum. Given these factors, preventing late rebleeding is currently challenging. With the increasing number of patients taking antithrombotic drugs and those on dialysis, the total number of diverticular bleeding cases is likely to rise further, presenting a major issue for the future.

This study has several strengths. First, this strategy reduces the burden not only on medical personnel but also on patients. Urgent endoscopic procedures, especially at night, cause significant physical and psychological stress to medical staff, and even more to the patient, who must undergo bowel preparation while in a poor general condition. Considering that nearly 90% of diverticular bleeding achieves hemostasis spontaneously and the identification rate of SRH by early colonoscopy is low, this strategy, which aims to identify only life-threatening bleeding, could be useful in clinical practice. Second, it is cost-effective in cases of diverticular bleeding. Diverticular bleeding is known to recur in approximately one-third of patients [33,35], often within a few months. Additionally, a large proportion of patients are older, and repeated

endoscopic examinations are costly and physically demanding. In the absence of preventive measures for diverticular bleeding, once other bleeding sources have been ruled out by colonoscopy, cases with repeated spontaneous hemostasis can be managed with conservative treatment alone, in accordance with this strategy.

However, this study also presents two limitations. First, the use of CECT for the evaluation of active bleeding. While CECT is quick and allows evaluation of blood flow throughout the body, it poses challenges due to radiation exposure and the risk of contrast nephropathy in patients with severe renal dysfunction. Magnetic resonance imaging is also difficult to use in the presence of severe renal dysfunction and does not allow dynamic study of the entire intestinal tract. Although ultrasonography contrast agents can be used regardless of renal function, they make it difficult to evaluate intestinal blood flow. Currently, real-time evaluation of intestinal blood flow is only possible with CECT, and the development of contrast agents that can be used even in renal impairment is a major challenge. Second, this is a single-center, single-arm study. Although a randomized controlled trial is desirable to clarify the usefulness of a treatment strategy, we have confirmed the usefulness of this strategy in a retrospective study. Given the most cases of colonic diverticular bleeding achieve spontaneous hemostasis, performing colonoscopy in all cases is burdensome for both the medical staff and patients. A multicenter study is necessary to further validate the usefulness of this strategy.

In summary, most colonic diverticular bleeding can stop spontaneously. However, there are a small number of cases requiring hemostatic intervention, and it is important to detect these cases. We believe that the widespread use of this strategy is expected to provide efficient medical care that is less burdensome physically, psychologically, and economically, not only for patients but also for healthcare professionals.

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Tables

Table 1. Characteristics of patients

Patients (n=172)		
Age (years, mean±SD)		70.0±12.6 (34–97)
Sex (male/female)		125/47
Localization of diverticulum	Right-sided	51 (29.7%)
	Left-sided	12 (7.0%)
	Bilateral	109 (63.3%)
Previous history of diverticular bleeding		44 (25.6%)
Hypertension		106 (61.6%)
Diabetes		22 (12.8%)
Dyslipidemia		36 (20.9%)
Hemodialysis		11 (6.4%)
Chronic kidney disease		39 (22.7%)
Liver cirrhosis		3 (1.7%)
Medications		
Antithrombotic drugs (total)		59 (34.3%)
Aspirin		28 (16.3%)
Thienopyridine derivative		21 (12.2%)
Dual antiplatelet therapy		10 (5.8%)
Anticoagulants		25 (14.5%)
Nonsteroidal anti-inflammation drugs		14 (8.1%)
Systolic Blood Pressure (mmHg, mean±SD)		122.9±31.1
Less than 90mmHg		32 (18.6%)
Heart rate (bpm, mean±SD)		88.4±18.9
Loss of consciousness		16 (9.3%)
Extravasation on CECT		42 (24.4%)

SD, standard deviation; *CECT*, contrast-enhanced computed tomography

Table 2. Treatment outcomes of the study

	Total (n=172)	**Urgent hemostasis** (n=15)	**Conservative treatment** (n=157)	***P*-value**
Hemostatic intervention	24 (14.0%)	15 (100%)	9 (5.7%)	<.0001
Mortality	1 (0.6%)	0 (0%)	1 (0.6%)*	.9128

Early rebleeding	28 (16.3%)	5 (33.3%)	23 (14.6%)	.0733
Late rebleeding	32 (18.6%)	4 (26.7%)	28 (17.8%)	.2955
Cumulative late rebleeding				.2271
1-year	10.3%	23.1%	9.2%	
3-year	19.6%	30.8%	18.5%	
5-year	22.5%	30.8%	21.7%	
Blood transfusion	75 (43.6%)	12 (80.0%)	63 (40.1%)	.0032
Units of blood (mean±SD)	2.9±4.8	8.5±8.7	2.4±3.9	.0002
Periods of fasting (days, mean±SD, median)	3.2±1.5 (3)	3.1±1.8 (3)	3.3±1.5 (3)	.6029
Length of stay (days, mean±SD, median)	9.2±6.8 (8)	13.9±20.2 (8)	8.8±3.5 (8)	.0932
Hospitalization costs (USD, mean±SD)	2190±1124	3228±2992	2068±681	.0101

SD, standard deviation; *USD*, United States dollar; one dollar was converted to 145 Japanese yen.

*One patient died due to sepsis from phlegmon of the lower extremities after achieving spontaneous hemostasis.

Table 3. Treatment outcomes of hemostatic intervention

		Rebleeding rate after initial hemostasis	Second hemostasis for rebleeding
Urgent hemostasis group (n=15)			
Clipping	Direct placement (6)	33.3% (2)	Direct placement (1), OTSC (1)
	Zipper fashion (2)	100% (2)	OTSC (1), IVR (1)
OTSC (4)		0%	
IVR (3)		33.3% (1)	IVR (1)
Conservative treatment group (n=9)			
Clipping	Direct placement (4)	0%	-
OTSC (4)		0%	-
Elective surgery (1)		0%	-
Total (n=29, including second hemostasis)		Rebleeding rate after hemostasis	
Clipping	Direct placement (11)	18.2% (2)	
	Zipper fashion (2)	100% (2)	
OTSC (10)		0%	
IVR (5)		20.0% (1)	
Elective surgery (1)		0%	

OTSC, over-the-scope clip; *IVR*, interventional radiology

Table 4. Factors requiring hemostatic intervention

	Requiring intervention (n=24)	Spontaneous hemostasis (n=148)	Univariate analysis	Multivariate analyses		
			P-value	OR	95% CI	*P*-value
Age (years, mean±SD)	72.5±10.7	69.6±12.8	.2830			
Sex (male)	21 (87.5%)	104 (70.3%)	.0596			
Hypertension	18 (75.0%)	88 (59.5%)	.1085			
Diabetes	5 (20.8%)	17 (11.5%)	.1704			
Dyslipidemia	6 (25.0%)	30 (20.3%)	.3848			
Hemodialysis	4 (16.7%)	7 (4.7%)	.0494	1.15	0.19-6.86	.8767
Liver cirrhosis	0 (0%)	3 (2.0%)	.6353			
Medications						
Antithrombotic (total)	11 (45.8%)	48 (32.4%)	.1468			
Aspirin	7 (29.2%)	21 (14.2%)	.0670			
Thienopyridine	3 (12.5%)	18 (12.2%)	.5899			
Dual antiplatelet therapy	3 (12.5%)	7 (4.7%)	.1478			
Anticoagulants	5 (20.8%)	20 (13.5%)	.2536			

NSAIDs	2 (8.3%)	12 (8.1%)	.6115			
Systolic blood pressure <90 (mmHg)	15 (62.5%)	17 (11.5%)	<.0001	21.39	6.83-66.99	<.0001
Heart rate (bpm, mean±SD)	86.5±23.9	88.7±18.0	.5884			
Loss of consciousness	5 (20.8%)	11 (7.4%)	.0519			
Extravasation on CECT	14 (58.3%)	28 (18.9%)	.0001	5.84	1.87-18.21	.0024
Laboratory data						
Hemoglobin level (g/dL, mean±SD)	10.9±3.0	11.0±2.5	.8984			
White blood cells count ($\times 10^3/mm^3$, mean±SD)	7.6±2.3	7.7±3.0	.9286			
Platelet count ($\times 10^4/mm^3$, mean±SD)	20.6±5.8	22.2±9.2	.4152			
UN/Cre ratio (mean±SD)	19.6±10.1	21.2±8.0	.3895			
Albumin level (g/dL, mean±SD)	3.5±0.5	3.7±0.5	.1388			
PT-INR (mean±SD)	1.1±0.2	1.0±0.2	.4272			

OR, odds ratio; *CI*, confidence interval; *SD*, standard deviation; *NSAIDs*, nonsteroidal anti-inflammation drugs; *CECT*, contrast-enhanced computed tomography; *UN/Cre*, urea nitrogen/creatinine; *PT-INR*, international normalized ratio of prothrombin time

Table 5. Factors associated with cumulative late rebleeding

	Univariate analysis			Multivariate analysis		
	HR	**95% CI**	***P*-value**	**HR**	**95% CI**	***P*-value**
Male	1.33	0.61–3.37	.4969			
Previous history of diverticular bleeding	2.95	1.46–5.93	.0013	2.66	1.30–5.40	.0082
Hypertension	1.20	0.59–2.59	.6177			
Diabetes	0.66	0.16–1.84	.4807			
Dyslipidemia	0.75	0.25–1.79	.5484			
Hemodialysis	4.51	1.68–10.26	.0003	4.40	1.57–10.66	.0070
Medications						
Antithrombotic (total)	1.83	0.90–3.67	.0831			
Aspirin	1.45	0.58–3.18	.3799			

Thienopyridine	2.81	1.18–6.01	.0079	2.49	1.03–5.43	.0432
Dual antiplatelet therapy	1.65	0.40–4.66	.3999			
Anticoagulants	1.74	0.70–3.83	.1859			
Nonsteroidal anti-inflammation drugs	0.31	0.02–1.46	.0824			
Systolic blood pressure <90 (mmHg)	1.83	0.80–3.82	.1174			
Loss of consciousness	0.58	0.09–1.91	.4451			
Extravasation on contrast-enhanced CT	2.10	1.01–4.25	.0371	1.33	0.61–2.80	.4587
Urgent hemostasis group	0.53	0.21–1.79	.2271			
Hemostatic intervention	1.57	0.63–3.45	.2140			

HR, hazard ratio; *CI*, confidence interval; *CT*, computed tomography