

Risk factors associated with recurrent hemorrhage after the initial improvement of colonic diverticular bleeding

Hiroki Nishikawa, Takanori Maruo, Takehiko Tsumura, Akira Sekikawa, Takashi Kanesaka, Yukio Osaki

Department of Gastroenterology and Hepatology, Osaka Red Cross Hospital, Osaka, Japan.

Abstract

We elucidated risk factors contributing to recurrent hemorrhage after initial improvement of colonic diverticular bleeding. 172 consecutive hospitalized patients diagnosed with colonic diverticular bleeding were analyzed. Recurrent hemorrhage after initial improvement of colonic diverticular bleeding is main outcome measure. We analyzed factors contributing to recurrent hemorrhage risk in univariate and multivariate analyses. The length of the observation period after improvement of colonic diverticular bleeding was 26.4 ± 14.6 months (range, 1-79 months). The cumulative recurrent hemorrhage rate in all patients at 1 and 2 years was 34.8% and 41.8%, respectively. By univariate analysis, age > 70 years ($P = 0.021$), BMI > 25 kg/m² ($P = 0.013$), the use of anti-coagulant drugs ($P = 0.034$), the use of NSAIDs ($P = 0.040$), history of hypertension ($P = 0.011$), history of smoking ($P = 0.030$) and serum creatinine level > 1.5 mg/dL ($P < 0.001$) were found to be significant risk factors for recurrent colonic diverticular bleeding. By multivariate analysis, age > 70 years (Hazard ratio (HR), 1.905, 95% confidence interval (CI), 1.067-3.403, $P = 0.029$), history of hypertension (HR, 0.493, 95% CI, 0.245-0.993, $P = 0.048$) and serum creatinine level > 1.5 mg/dL (HR, 95% CI, 0.288-0.964, $P = 0.044$) were shown to be significant independent risk factors. Close observation after the initial improvement of colonic diverticular bleeding is needed, especially in elderly patients or patients with history of hypertension or renal deficiency. (*Acta gastroenterol. belg.*, 2013, 76, 20-24).

Key words : colonic diverticular bleeding, recurrent hemorrhage, risk factors, initial improvement.

Introduction

Colonic diverticular bleeding is a common cause of lower gastrointestinal bleeding (LGIB) in adults (1,2,3), affecting 3% to 15% of individuals with diverticular disease (4,5). While 70% to 90% of colonic diverticular hemorrhage cases resolve spontaneously after treatment (6,7,8), approximately 10% to 40% of patients will experience recurrent hemorrhage (8-12). Severe hemorrhage can be fatal and, in older patients, recurrent hemorrhage is associated with significant comorbidity (3). Therefore, it is essential to identify risk factors that contribute to recurrent hemorrhage in patients who initially improve after treatment for colonic diverticular bleeding, to prevent or reduce the risk of rebleeding and improve patient outcomes. To our knowledge, there are few studies that have identified the risk factors contributing to recurrent hemorrhage after initial improvement.

The pathogenesis of diverticular bleeding involves an asymmetric intimal proliferation and segmental weakening of the associated vas rectum, arising from trauma within the diverticular or colonic lumen. Bleeding is

thought to be the result of an acute rupture of the altered vasa recta close to the diverticulum (13). Bleeding from the diverticulum can occur anywhere in the colon (14), and localization of the bleeding source is determined once the patient has been stabilized. The primary localization modalities include nuclear scintigraphy, angiography and colonoscopy. If the source of the bleeding is identified, colonic diverticular bleeding can be treated with endoscopic medical therapy or clipping (3). If the bleeding source is not identified, further imaging and surgical procedures may be necessary (3). Hemodynamically unstable patients who do not respond to medical treatment will require surgical intervention. The goal of our study was to identify the risk factors associated with recurrent bleeding after treatment of colonic diverticulitis to ensure appropriate post-treatment monitoring and improve patient outcomes. We performed a retrospective study of 172 patients diagnosed with colonic diverticular bleeding who were treated as inpatients at our institution to determine the risk factors for experiencing recurrent hemorrhage following treatment and initial improvement.

Patients and methods

Patients

In the present study, we retrospectively analyzed the medical records of consecutive 172 hospitalized patients diagnosed with colonic diverticular bleeding in the Gastroenterology department at Osaka Red Cross Hospital between January, 2004 and January, 2011. Colonoscopy was performed in all patients within 48 hours of arrival to the hospital, at which time written informed consent was obtained from all patients. In most of them, colonoscopy was performed after using polyethylene glycol-containing lavage solution for colon preparation and in no patient, somatostatine derivatives

Correspondence to : Hiroki Nishikawa, M.D., Department of Gastroenterology and Hepatology, Osaka Red Cross Hospital, 5-30 Fudegasaki-cho, Tennoji-ku, Osaka 543-0027, Japan. E-mail : h-nishikawa@osaka-med.jrc.or.jp

Submission date : 12/07/2012

Acceptance date : 09/08/2012

were not used. This study protocol was complied in adherence with all of the provisions of the Declaration of Helsinki.

Patients with two types of diagnoses of colonic diverticular bleeding were included in the study. The former type patients had a definite diagnosis of colonic diverticular bleeding, with at least one of the following findings after vigorous irrigation of diverticula : active bleeding, a nonbleeding visible vessel, or an adherent clot. In the latter type patients, the bleeding source was probably a diverticulum, with presumptive diverticular hemorrhage in which diverticula had no evidence of bleeding but no other major colonic lesions or bleeding sites were identified on colonoscopy. When an upper gastrointestinal source for bleeding was considered to be the differential diagnosis, esophagogastroduodenoscopy (EGD) was performed.

Treatments

All treatments were conducted at the discretion of the treating physician in an open-label manner. When active bleeding, a nonbleeding visible vessel, or adherent clot was not identified on colonoscopy, only medical treatment was administered. Endoscopic clipping was performed when the bleeding source was identified on colonoscopy. When the bleeding source was not identified because of heavy bleeding, emergent angiography or surgical resection was performed after discussion with the radiologist or surgeon. On emergent angiography, injection of vasopressin via microcatheters or selective embolization of bleeding vessels identified on angiography using microcoils was performed.

Patient education

After treatment and improvement of hemorrhage, patients were instructed at discharge to return to the hospital as soon as possible in the event of a bloody stool.

Statistical analysis

Recurrent hemorrhage after initial improvement of colonic diverticular bleeding was considered as the main outcome measure. Medical records data were analyzed using univariate and multivariate analyses. The cumulative recurrent hemorrhage rate was calculated using the Kaplan-Meier method, and tested using the log-rank test. Cox proportional hazard model was used for multivariate analyses of factors that were considered significant in univariate analysis. These statistical methods were used to estimate the interval from the improvement of colonic diverticular bleeding to recurrent hemorrhage. Data were analyzed using SPSS software, version 9.0 (SPSS Inc., Chicago, IL, USA) for Microsoft Windows. Data are expressed as means \pm standard deviation (SD). Values of $P < 0.05$ were considered to be statistically significant.

Table 1. — Clinical characteristics of study patients (N = 172)

Category	Number or mean \pm SD
Gender (male/female)	116/56
Age (years)	70.1 \pm 12.8
Observation period (months)	26.4 \pm 14.6
Hospitalization (days)	11 \pm 7.1
Treatment method	
Medical	136
Endoscopic	18
Angiographic	8
Surgical	10
Body mass index (kg/m ²)	23.1 \pm 3.3
Use of anticoagulant drugs (yes/no)	39/133
Use of NSAIDs (yes/no)	32/140
History of hypertension (yes/no)	133/39
History of heart disease (yes/no)	40/132
History of diabetes mellitus (yes/no)	19/153
History of hyperlipidemia (yes/no)	20/152
History of smoking (yes/no)	41/131
History of drinking (yes/no)	72/100
Laboratory data on admission	
Hemoglobin (g/dL)	10.8 \pm 2.5
Platelet (cells/mm ³)	19.1 \pm 6.6
Prothrombin time (%)	94.6 \pm 18.6
Blood urea nitrogen (mg/dL)	23.5 \pm 12.7
Serum creatinine level (mg/dL)	2.1 \pm 2.9
Vital signs on admission	
Systolic blood pressure (mm Hg)	137.2 \pm 23.6
Heart rate (beats/minute)	78.8 \pm 14.0

SD, standard deviation; NSAID, nonsteroidal anti-inflammatory drug.

Results

Patient characteristics and rate of recurrent hemorrhage

Baseline characteristics of all patients are shown in Table 1. A total of 69 patients (40.1%) experienced a recurrent hemorrhage. The average length of the initial hospital stay and the average length of the post-discharge observation period were 11 \pm 7.1 days (range, 4-33 days) and 26.4 \pm 14.6 months (range, 1-79 months), respectively. The cumulative recurrent hemorrhage rate in all patients at 1 and 2 years was 34.8% and 41.8%, respectively (Fig. 1).

Total Colonoscopy and distribution of colonic diverticula

Total Colonoscopy was performed in 160 patients (93.0%), of these 43 patients had diverticular disease on the right side, 19 on the left side and 98 on both sides of the colon.

Patients treated by therapeutic interventions

Endoscopic clipping was performed in 18 patients, all patients were treated successfully and no complications

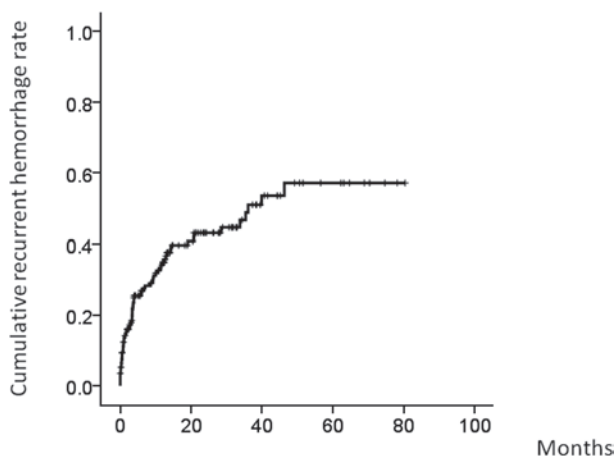


Fig. 1. — Cumulative recurrent hemorrhage rate in all patients. The cumulative recurrent hemorrhage rate at 1 and 2 years was 34.8% and 41.8%, respectively.

were observed. The bleeding sites in the patients who were treated endoscopically were in the ascending colon (14 patients), transverse colon (2 patients), descending colon (1 patient) and sigmoid colon (1 patient). Angiographic interventions were performed in 8 patients with severe colonic hemorrhage within 48 hours after initial colonoscopy, again, all patients were successfully treated and no complications – such as colonic ischemia – were observed. The bleeding sites in the patients who were treated angiographically were in the ascending colon (6 patients), transverse colon (1 patient) and sigmoid colon (1 patient). Ten hemodynamically unstable patients due to the severe hemorrhage underwent surgery within 48 hours after initial colonoscopy: right hemicolectomy

was performed in 7 patients, descending colectomy in 1 patient and sigmoidectomy in 2 patients. No major complications were observed after surgery.

Univariate analysis of factors contributing to recurrent hemorrhage risk

In our univariate analysis, age > 70 years ($P = 0.021$), body mass index > 25 kg/m² ($P = 0.013$), the use of anti-coagulant drugs ($P = 0.034$), the use of NSAIDs ($P = 0.040$), history of hypertension ($P = 0.011$), history of smoking ($P = 0.030$) and serum creatinine level > 1.5 mg/dL ($P < 0.001$) were found to be significant risk factors for recurrent colonic diverticular bleeding (Table 2).

Multivariate analysis of factors contributing to recurrent hemorrhage risk

In a multivariate analysis involving the 7 factors that were found to be significant in the univariate analysis, age > 70 years, history of hypertension and serum creatinine level > 1.5 mg/dL were found to be significant independent risk factors for recurrent colonic diverticular hemorrhage after initial improvement. The hazard ratios and P values for the seven factors are detailed in Table 3.

Discussion

Consistent with previous studies, we found that colonic diverticular bleeding often recurs, with 69 patients (40.1%) experiencing recurrent hemorrhage after initial improvement. McGuire reported that 38.4% of patients with bleeding diverticula had recurrence of bleeding (9),

Table 2. — Univariate analysis of recurrent hemorrhage risk factors in patients treated for colonic diverticular bleeding (N = 172)

Category	n	P value ^a
Gender (male/female)	116/56	0.595
Age > 70 years (yes/no)	79/93	0.021
Medical treatment (yes/no)	136/36	0.313
Body mass index > 25 kg/m ² (yes/no)	116/56	0.013
Use of anticoagulant drugs (yes/no)	39/133	0.034
Use of NSAIDs (yes/no)	32/140	0.04
History of hypertension (yes/no)	133/39	0.011
History of heart disease (yes/no)	40/132	0.097
History of diabetes mellitus (yes/no)	19/153	0.098
History of hyperlipidemia (yes/no)	20/152	0.878
History of smoking (yes/no)	41/131	0.03
History of drinking (yes/no)	72/100	0.127
Hemoglobin > 10 g/dL (yes/no)	103/69	0.482
Platelet > 15 cells/mm ³ (yes/no)	132/40	0.225
Prothrombin time > 90 seconds (yes/no)	110/62	0.807
Blood urea nitrogen > 20 mg/dL (yes/no)	88/84	0.152
Serum creatinine > 1.5 mg/dL (yes/no)	33/139	< 0.001
Systolic blood pressure > 140 mm Hg (yes/no)	72/100	0.941
Heart rate > 80 beats/minute (yes/no)	63/109	0.095

^a Kaplan-Meier method; NSAID, nonsteroidal anti-inflammatory drug.

Table 3. — **Multivariate analysis of recurrent hemorrhage risk factors in patients treated for colonic diverticular bleeding (N = 172)**

Variable	Hazard Ratio	95% confidence interval	P value ^a
Age (years)			
> 70	1.905	1.067-3.403	0.029
≤ 70	1.000		
Body mass index (kg/m ²)			
> 25	1.854	0.869-3.955	0.110
≤ 25	1.000		
Anticoagulant medication			
Yes	1.383	0.605-3.160	0.442
No	1.000		
NSAID medication			
Yes	1.423	0.580-3.492	0.441
No	1.000		
History of hypertension			
Yes	1.000		0.048
No	0.493	0.245-0.993	
History of smoking			
Yes	1.519	0.860-2.681	0.149
No	1.000		
Serum creatinine level (mg/dL)			
> 1.5	1.000		0.044
≤ 1.5	0.564	0.288-0.964	

^a Cox proportional hazard model; NSAID, nonsteroidal anti-inflammatory drug.

and Niikura *et al.* reported that recurrence occurred in 27 (38%) of 72 patients in their study (11). In our study, definite bleeding sites were identified in 36 patients, and in 30 patients, bleeding sites were located on the right side of colon. In Westernized populations, diverticular bleeding is most commonly found in the left side of colon, however, in Japan, diverticular bleeding is most commonly found in the right side of colon (15,16).

In the univariate analysis, age > 70 years, body mass index > 25 kg/m², the use of anticoagulant drugs, the use of NSAIDs, history of hypertension, history of smoking and serum creatinine level (> 1.5 mg /dL) were shown to be significant factors linked to recurrent hemorrhage. Others have reported that the risk of colonic diverticular rebleeding increases with age (16,17), and diverticular bleeding is thought to be the result of a rupture of an arteriosclerotic altered diverticular vessel (13,18,19).

Atherosclerosis and associated diseases such as the metabolic syndrome could play an important role in the pathogenesis of recurrent diverticular hemorrhage. Among the 7 significant risk factors identified in the univariate analysis, body mass index, history of hypertension, history of smoking and serum creatinine level are related to an increased risk of atherosclerosis. It is not surprising that the use of anticoagulant drugs was identified as a risk factor for recurrent hemorrhage, and the use of NSAIDs have been already identified as a risk factor for colonic diverticular bleeding and recurrent hemorrhage (11,12,15,20,21). NSAIDs reduce mucosal prostaglandin production, which leads to enhanced mucosal permeability and reduced microcirculation, which leads

to mucosal bleeding (22,23). Niikura *et al.* reported that patients with colonic diverticular bleeding show high recurrence rates within a short period after treatment, and that risk factors for recurrence included the use of NSAIDs or antiplatelet drugs and hypertension (11). Especially concerning risk factors of recurrent hemorrhage, their study results seemed to correlate with our results using univariate analysis.

In our multivariate analyses, age > 70 years, history of hypertension and serum creatinine level > 1.5 mg/dL were found to be significant independent factors linked to recurrent hemorrhage after initial treatment. Our results suggest that elderly patients or patients with a history of hypertension or renal insufficiency are at elevated risk for recurrent hemorrhage after treatment for colonic diverticular bleeding. Therefore, these high-risk patients should be provided post-treatment education concerning their risk of recurrent hemorrhage and what should be done if bleeding recurs, and they should be closely followed after discharge.

There are several limitations of the present study. The study was a retrospective chart review performed in a single center, and the post-discharge observation period was relatively short compared with previous studies. However, our study provides useful information on the post-discharge rate of recurrent hemorrhage in patients who initially improved after treatment for colonic diverticular bleeding. Our results suggest that special attention should be paid to the elderly, patients who have risk factors for atherosclerosis – such as hypertension – or renal insufficiency, to reduce the morbidity and mortality

associated with recurrent hemorrhage after treatment for colonic diverticular bleeding.

In conclusion, close observation of elderly patients or patients with history of hypertension or renal deficiency that show initial improvement of colonic diverticular bleeding is needed to reduce the risk and complications of recurrent hemorrhage.

Conflict of interest disclosure

The authors declare that they have no competing interests.

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