

# Elevated C-reactive protein level predicts lower gastrointestinal tract bleeding

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**Abstract.** Lower gastrointestinal (GI) bleeding can be caused by colorectal polyps or cancer. The aim of the present study was to identify blood test variables and medications that can predict lower GI bleeding, which would allow for appropriate colonoscopy. The medical records of patients who underwent colonoscopy from September 2014 to September 2015 were retrospectively analyzed. The selected patients included 278 men (mean age, 67.0±11.5 years) and 249 women (mean age, 69.6±12.0 years). The diagnosis, medications, and blood test variables were compared between patients with and without bleeding. Logistic regression analysis was performed to determine the factors associated with lower GI bleeding. The presence of colorectal polyp and cancer was associated with lower GI bleeding ( $P=0.0044$ ) with an odds ratio of 6.71 ( $P=0.0148$ ). No lower GI bleeding was observed in patients taking non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, or anticoagulants. The C-reactive protein (CRP) levels were significantly higher in patients with lower GI bleeding ( $P=0.0227$ ). The Hb levels were lower in patients with lower GI bleeding, however this finding was not statistically significant ( $P>0.05$ ). No blood test variable was associated with lower GI bleeding. Elevated CRP was associated with lower GI bleeding, while there was no association between the medications and lower GI bleeding.

## Introduction

Lower gastrointestinal (GI) bleeding occurs if the bleeding source is located distally to the Treitz ligament (1). It can

be caused by colorectal polyps, colorectal cancer (CRC), or colonic diverticulum (2) and can be lethal in some patients, particularly the elderly (3). It is diagnosed and treated with colonoscopy (4,5).

Lower GI bleeding is usually chronic and stops spontaneously (6). The identification of the bleeding site is important in its management (7). Lower GI bleeding is usually diagnosed with screening colonoscopy. If the risk factors are known, it is possible to perform colonoscopy for such patients. The risk factors of patients hospitalized for severe lower GI bleeding include medication with non-steroidal anti-inflammatory drugs (NSAIDs) and anticoagulants (8). It is not clear whether NSAIDs and anticoagulants are related to lower GI bleeding diagnosed using screening colonoscopy. Corticosteroids, used in the treatment of autoimmune disease such as rheumatoid arthritis (9), are associated with bleeding from peptic ulcer (1). However, whether corticosteroids are associated with lower GI bleeding remains to be determined.

Blood test variables are easy to obtain and quantitate. These variables can be useful in distinguishing upper from lower GI bleeding, which can aid the clinical diagnosis (10).

In this study, we analyzed the diagnosis of screening colonoscopy and compared medication intake (i.e., NSAIDs, corticosteroids, and anticoagulants) between patients with or without lower GI bleeding. Blood test variables were also analyzed.

## Materials and methods

**Ethics statement.** The National Hospital Organization Shimoshizu Hospital Ethics Committee approved this study. This study was not considered a clinical trial because the procedures were performed as part of routine clinical practice; thus, written informed consent for inclusion into the study was not required. Patient records were anonymized and retrospectively analyzed. Written informed consent was obtained from all the patients who underwent colonoscopy.

**Patients.** The selected patients included 278 men (mean age, 67.0±11.5 years) and 249 women (mean age, 69.6±12.0 years) who underwent colonoscopy. Twelve patients were diagnosed with lower GI bleeding. The causes of lower GI bleeding of these patients are presented in Table I.

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**Key words:** colonoscopy, colorectal cancer, colorectal polyp, C-reactive protein

Table I. Diagnosis of lower GI bleeding.

Diagnosis	No. of patients
CRC	10
Colorectal polyp	1
Ulcerative colitis	1
Total	12

GI, gastrointestinal; CRC, colorectal cancer.

**Study design.** The medical records of patients who underwent colonoscopy from September 2014 to September 2015 were retrospectively analyzed.

The patient characteristics included in the analysis were the presence of CRC, polyp, and diverticulitis and the intake of NSAIDs, corticosteroids, or anticoagulants. The presence of CRC and polyp were analyzed because they are major causes of lower GI bleeding (11). Colonic diverticulum is another cause of lower GI bleeding (12).

**Colonoscopy.** Patients underwent colonoscopy for screening, examination of symptoms, or when the fecal occult blood test was positive. The colonoscopy devices used were CF-Q260 and PCF-Q260AI (Olympus, Tokyo, Japan).

**Blood test variables.** Blood examination was performed before colonoscopy. The blood test variables analyzed were white blood cell (WBC) and platelet (Plt) counts and hemoglobin (Hb), C-reactive protein (CRP), blood urea nitrogen (BUN), and creatinine (Cr) levels.

**Statistical analysis.** The Chi-square test was used to compare the diagnosis and medication intake. One-way analysis of variance was used to analyze the blood test variables. A logistic regression analysis was performed to identify the factors associated with lower GI bleeding.  $P < 0.05$  was determined to be statistically significant. The JMP 10.0.2 program (SAS Institute, Cary, NC, USA) was used for all the statistical analyses.

## Results

To determine whether a relationship exists between each factor (CRC and polyp, diverticulum, NSAIDs, corticosteroid, and anticoagulants) and lower GI bleeding, the number of subjects of those with and without lower GI bleeding were compared (Table II). The presence of CRC and polyp were related to lower GI bleeding ( $P = 0.0044$ ). No lower GI bleeding was observed among the patients taking NSAIDs, corticosteroids, or anticoagulants.

To determine whether the blood test variables were related to lower GI bleeding, the variables were compared between the patients with and without lower GI bleeding (Table III). The CRP levels were significantly higher in patients with lower GI bleeding ( $P = 0.0227$ ). The Hb levels were lower in patients with lower GI bleeding; however, this finding was not statistically significant.

Table II. Characteristics of patients with or without lower GI bleeding.

Variables	Bleeding (-)	Bleeding (+)	Total	P-value
Total	515	12	527	
Patient no. (men/women)	249/266	6/6	255/272	0.8470
CRC, polyp	219	10	229	0.0044
Diverticulum	87	1	88	0.3932
NSAIDs	10	0	10	0.4952
Corticosteroids	42	0	42	0.1555
Anticoagulants	12	0	12	0.4546

GI, gastrointestinal; CRC, colorectal polyp; diverticulum, colonic diverticulum; NSAIDs, non-steroidal anti-inflammatory drugs; PPI, proton pump inhibitor; H2RA, histamine type-2 receptor antagonist.

Table III. Blood test variables of patients with or without lower GI bleeding.

Variables		Bleeding (-)	Bleeding (+)	P-value
WBC ( $\times 10^3$ )	3.50-8.50	6.556 $\pm$ 3.51	8.56 $\pm$ 4.76	0.1264
Hb	13.5-17.0	12.9 $\pm$ 2.1	11.3 $\pm$ 3.5	0.0708
Plt	15.0-35.0	23.2 $\pm$ 7.5	26.3 $\pm$ 10.7	0.2683
CRP	0.00-0.30	0.51 $\pm$ 0.81	3.13 $\pm$ 4.84	0.0227
BUN	8.0-22.0	15.2 $\pm$ 4.8	22.3 $\pm$ 26.2	0.1803
Cr	0.40-0.70	0.79 $\pm$ 0.18	1.00 $\pm$ 0.87	0.1609

GI, gastrointestinal; WBC, white blood cell; Hb, hemoglobin; Plt, platelet; CRP, C-reactive protein; BUN, blood urea nitrogen; Cr, creatinine.

Table IV. Logistic regression analysis of factors in lower GI bleeding.

Variables	Odds ratio	$\chi^2$	P-value
CRC, polyp	6.71	5.94	0.0148
Diverticulum	2.48	0.74	0.39
NSAIDs	0.00	0.00	1.00
Corticosteroids	0.00	0.00	0.99
Anticoagulants	0.00	0.00	1.00

GI, gastrointestinal; CRC, colorectal cancer; diverticulum, colonic diverticulum; NSAIDs, non-steroidal anti-inflammatory drugs; PPI, proton pump inhibitor; H2RA, histamine type-2 receptor antagonist.

The logistic regression analysis result of the factors involved with lower GI bleeding is shown in Table IV. The presence of CRC and polyp was significantly related to lower GI bleeding, with an odds ratio of 6.71 ( $P = 0.0148$ ). The odds ratios of diverticulum and medication intake (i.e., NSAIDs, corticosteroids, or anticoagulants) were not reliable because

Table V. Logistic regression analysis of blood test variables in lower gastrointestinal bleeding.

Variables	Odds ratio	$\chi^2$	P-value
WBC	1.00	0.15	0.7026
Hb	1.56	1.86	0.1730
CRP	0.76	0.12	0.7305
Plt	1.05	0.16	0.6849
BUN	1.04	0.03	0.8620
Cr	0.14	0.10	0.7524

WBC, white blood cell; Hb, hemoglobin; CRP, C-reactive protein; Plt, platelet; BUN, blood urea nitrogen; Cr, creatinine.

their P-values were not significant ( $P>0.05$ ). It was suggested that the presence of CRC and polyp was related to lower GI bleeding. These results were consistent with those of previous studies (11).

The logistic regression analysis result of the blood test variables and lower GI bleeding is shown in Table V. No blood test variables had a P-value  $<0.05$ . Thus, no blood test variable was related to lower GI bleeding.

## Discussion

CRP is an acute-phase response protein and its serum level is elevated during inflammation (13). In the present study, the CRP levels were higher in patients with lower GI bleeding than those without. Koseoglu *et al* analyzed the CRP levels of patients admitted to the emergency room for GI bleeding and found that the CRP levels were elevated (14). These results suggested that elevated CRP levels were associated with lower GI bleeding. The mechanism of CRP elevation in these patients is not clear. One hypothesis is that CRP elevation may have been caused by the inflammation around the bleeding area (15). In our study, 10/12 patients with lower GI bleeding had CRC or polyp. In a previous study, abdominal ultrasonography findings of patients with elevated CRP levels were analyzed (16). CRC was included in the diagnosis of the patients. Aleksandrova *et al* analyzed the serum CRP levels of patients with CRC and found that the levels were elevated (17). The abovementioned studies indicated that elevated CRP was associated with CRC. This may be explained by the fact that cancerous tissue can cause inflammation in the affected organ (18).

There are few studies available on the relationship between medication and lower GI bleeding. NSAIDs cause mucosal ulceration and inflammation in the lower GI tract (19). However, it is not well-documented whether the lower GI bleeding is caused by NSAIDs. There are no studies on the relationship between corticosteroids and lower GI bleeding. Anticoagulant intake is a risk factor of bleeding following polypectomy (20). It is not clear whether anticoagulants are related to lower GI bleeding diagnosed using screening colonoscopy. In the present study, no relationship was found between lower GI bleeding and intake of NSAIDs, corticosteroids, or anticoagulants. Owing to the

small number of patients, it cannot be safely concluded that the medications had no association with lower GI bleeding. Nonetheless, care should be taken for the management of patients with lower GI bleeding when they are prescribed with NSAIDs and anticoagulants (21).

One limitation of the present study was the limited number of patients. In this study, no relationship was identified between lower Hb and lower GI bleeding, which may be due to the small number of patients. Our study did not include patients with bleeding due to vascular ectasia or inflammatory bowel disease (22). In the future studies, more patients are to be recruited to evaluate the relationship between CRP levels and bleeding due to various causes.

In conclusion, an elevated CRP level was related to lower GI bleeding. Elevated CRP can potentially predict lower GI tract bleeding.

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