Association between colon diverticula and hemoglobin, triglyceride and uric acid levels

MINORU TOMIZAWA[1], FUMINOBU SHINOZAKI[2], RUMIKO HASEGAWA[3], YOSHINORI SHIRAI[3], YASUFUMI MOTOYOSHI[4], TAKAO SUGIYAMA[5], SHIGENORI YAMAMOTO[6] and NAOKI ISHIGE[7]

Departments of [1]Gastroenterology, [2]Radiology, [3]Surgery, [4]Neurology, [5]Rheumatology, [6]Pediatrics and [7]Neurosurgery, National Hospital Organization Shimoshizu Hospital, Yotsukaido, Chiba 284-0003, Japan

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Abstract. Colon diverticula cause bleeding and acute diverticulitis. The present study analyzed laboratory test variables, aiming to predict the presence of diverticula. Patient records from between April 2011 and March 2014 were analyzed retrospectively (1,520 patients) and a one-way analysis of variance was performed to analyze the association between the presence of diverticula and each variable. A χ^2 test was then used to assess the correlation between the prevalence of diverticula and the percentage of patients with uric acid (UA) levels ≥5.1 mg/dl. A receiver operating characteristic (ROC) analysis was performed to determine the threshold values required to predict the presence of diverticula. Hemoglobin (Hb) levels were lower in patients with diverticula than in those without diverticula (P=0.0027), and compared with patients without diverticula, UA and triglyceride (TG) levels were higher in patients with diverticula (P=0.0066 and P=0.0136, respectively). The patients were divided into two groups, as follows: Patients with UA levels ≥5.1 mg/dl (the median value) and those with UA levels <5.1 mg/dl. The prevalence of diverticula was significantly higher in patients with UA levels ≥5.1 mg/dl than in those with UA levels <5.1 mg/dl (P=0.0004). ROC analysis demonstrated that the threshold values of Hb, TG and UA were 12,400, 146 and 5.1 mg/dl, respectively. The sensitivity of the Hb and UA levels at the threshold values was 76.5 and 71.0%, respectively. The prevalence of diverticula was associated with low Hb levels, and high TG and UA levels.

Introduction

Colon diverticula are outpouchings of the mucosa and muscularis mucosa. Diverticula develop where the colon wall is weak (1), the negative outcomes of which are bleeding and acute diverticulitis (2,3). Bleeding from diverticula accounts for 20-50% of lower gastrointestinal bleeding cases (4); this is usually self-limiting, but is occasionally fatal for patients taking non-steroidal anti-inflammatory drugs and anticoagulants (5-7). Acute diverticulitis is treated with antibiotics (8), which can cause complications, and surgery is required if diverticulum perforation occurs (9). The risk of bleeding and perforation may be reduced if the presence of diverticula is identified in advance.

Studies on the risks of diverticula predominantly focus on aging, genetic factors and dietary fiber. The odds ratio of siblings with diverticula is 7.15 for monozygotic twins and 3.2 for dizygotic twins (10). Among the cases of diverticula, 40% result from inherited factors and 60% from environmental factors (10). However, controversy remains over whether dietary fiber is one of the causes (11,12). Crowe *et al* (11) concluded that increased dietary fiber intake decreases the risk of diverticula, but Peery *et al* (12) reported that fiber intake does not affect the prevalence of diverticula. With regard to risk factors, Song *et al* (13) attributed aging, high-fat diets and high alcohol consumption as factors increasing the risk of diverticula.

If laboratory data that are correlated with the presence of diverticula were available, it would be possible to develop strategies to decrease the risk of developing diverticula; the present study therefore analyzed the laboratory data of patients who underwent colonoscopy in order to determine variables that predict the presence of diverticula.

Materials and methods

Patients. Patient records from between April 2011 and March 2014 were analyzed retrospectively. A total of 1,520 patients underwent colonoscopy and were included in the analysis, including 758 men (mean age ± standard deviation, 68.9±10.9 years) and 762 women (68.7±10.8 years). The current study was approved by the National Hospital Organization Shimshizu Hospital Ethics Committee (Yotsukaido, Japan) and was not categorized as a clinical trial as it was performed during routine clinical practice. Written informed consent was waived since the present study was retrospective. Patient anonymity was preserved.

Correspondence to: Dr Minoru Tomizawa, Department of Gastroenterology, National Hospital Organization Shimoshizu Hospital, 934-5 Shikawatashi, Yotsukaido, Chiba 284-0003, Japan
E-mail: nihminor-cib@umin.ac.jp

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Table I. Blood variable differences in patients with and without colon diverticula.

Variable	Total number of patients	Patients without colon diverticula, n	Variable level, mean ± SD	Patients with colon diverticula, n	Variable level, mean ± SD	P-value
WBC, μl	743	563	6.06±2.06	180	6.22±2.08	0.3514
Hb, g/dl	742	63	12.8±0.22	179	1.24±0.20	0.0027
CRP, mg/dl	392	303	0.95±3.11	89	0.69±1.63	0.4452
Plt, $10^4/\mu$l	734	554	2.23±0.73	180	2.20±0.69	0.6652
TP, g/dl	492	370	6.89±0.68	122	6.77±0.89	0.1268
Alb, g/dl	350	264	3.99±0.04	86	4.02±0.06	0.5985
T-Bil, mg/dl	499	378	0.76±0.42	121	0.75±0.33	0.9497
ALP, IU/l	255	196	2.38±1.02	59	2.23±0.59	0.2807
AST, IU/l	677	511	2.46±1.33	166	2.66±3.30	0.2617
ALT, IU/l	713	545	2.16±1.35	168	2.53±3.87	0.0591
γ-GTP, IU/l	290	225	0.51±2.24	65	0.45±0.56	0.8382
LDH, IU/l	379	297	2.06±1.04	82	1.97±0.49	0.4360
UA, mg/d)	282	213	5.13±1.46	69	5.66±1.28	0.0066
BUN, mg/dl	469	353	1.61±1.46	116	1.52±0.50	0.5124
Cre, mg/dl	713	545	0.84±0.39	168	0.86±0.26	0.6060
T-Chol, mg/dl	286	222	2.01±0.38	64	1.99±0.41	0.6999
TG, mg/dl	259	198	1.24±0.81	61	1.53±0.77	0.0136
HDL, mg/dl	197	145	5.97±1.75	52	5.68±1.59	0.2982
LDL, mg/dl	272	204	1.17±0.28	68	1.21±0.29	0.3834
BG, mg/dl	375	294	1.19±0.40	81	1.24±0.50	0.3211
HbA1c, %	180	139	6.17±0.94	41	6.27±1.35	0.5805
BMI, kg/m^2	273	212	2.25±0.36	61	2.29±0.40	0.4734
CEA, ng/ml	208	167	1.61±7.68	41	9.86±5.61	0.0669
CA19-9, U/ml	205	165	0.22±0.63	40	0.66±3.20	0.0984

'Total number of patients' indicates the number of patients subjected to each laboratory test. WBC, white blood cell count; Hb, hemoglobin; CRP, C-reactive protein; Plt, platelet; TP, total protein; Alb, albumin; T-Bil, total bilirubin; ALP, alkaline phosphatase; AST, aspartate aminotransferase; ALT, alanine aminotransferase; γ-GTP, γ-glutamyl transpeptidase; LDH, lactate dehydrogenase; UA, uric acid; BUN, blood urea nitrogen; Cre, creatinine; T-Chol, total cholesterol; TG, triglyceride; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; BG, blood glucose; HbA1c, hemoglobin A1c; BMI, body mass index; CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 19-9; SD, standard deviation.

Colonoscopy. A colonoscopy was performed for patients with abdominal symptoms, anemia or positive fecal occult blood. A colonoscopy was also performed for screening purposes. The colonoscopy devices used were CF-Q260DL/I and PCF-Q260AL/I (Olympus, Tokyo, Japan).

Blood variables. White blood cell count, platelet count, body mass index, and levels of hemoglobin (Hb), C-reactive protein, total protein, albumin, total bilirubin, alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase, γ-glutamyl transpeptidase, lactate dehydrogenase, uric acid (UA), blood urea nitrogen, creatinine, total cholesterol, triglyceride (TG), high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, blood glucose, HbA1c, carcinoembryonic antigen and carbohydrate antigen 19-9 were analyzed.

Statistical analysis. A one-way analysis of variance was performed to analyze the association between the presence of diverticula and each variable. A χ^2 test was used to determine the correlation between the presence of diverticula and age group, gender and UA levels ≥5.1 mg/dl. A receiver operating characteristic (ROC) analysis was performed to determine the threshold values able to predict the presence of diverticula. Specificity and sensitivity were automatically calculated using an ROC program in the statistical software. $P<0.05$ was considered to indicate statistical significance. JMP 10.0.2 software (SAS Institute, Cary, NC, USA) was used for the statistical analysis.

Results

To analyze the correlation between age and the presence of diverticula, the patients were divided into the following age groups: Group 20 (20-29 years old, 3 patients); group 30 (30-39 years old, 31 patients); group 40 (40-49 years old, 93 patients); group 50 (50-59 years, 125 patients); group 60 (60-69 years old, 508 patients); group 70 (70-79 years old, 597 patients); group 80 (80-89 years old; 154 patients) and group 90 (>90 years old; 9 patients) (Fig. 1). The incidence

Table II. Association between gender and the presence of colon diverticula.

	Colon diverticula, n		
Gender	Absent	Present	Total, n
Male	543	219	762
Female	605	153	758
Total	1148	372	1520

Table III. Association between uric acid level and the presence of colon diverticula.

	Colon diverticula, n		
Uric acid level	Absent	Present	Total, n
High (≥5.1 mg/dl)	99	49	148
Low (<5.1 mg/dl)	114	20	134
Total	213	69	282

Table IV. Threshold values to predict the presence of colon diverticula.

Blood variable	AUC	Threshold value, mg/dl	Sensitivity, %	Specificity, %
Hb	0.56926	12400	76.5	34.1
TG	0.63512	146	47.5	75.3
UA	0.62105	5.1	71.0	53.5

AUC, area under the (receiver operating characteristic) curve; Hb, hemoglobin; TG, triglyceride; UA, uric acid.

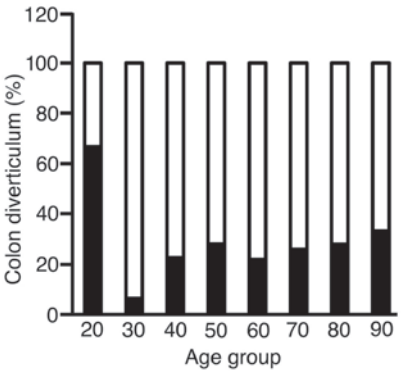

Figure 1. Prevalence of colon diverticula among different age groups. Patients were divided into different age groups. There were 3 patients in their twenties, which was significantly lower than the number of patients in the other age groups. White bar, patients without colon diverticula; black bar, patients with colon diverticula.

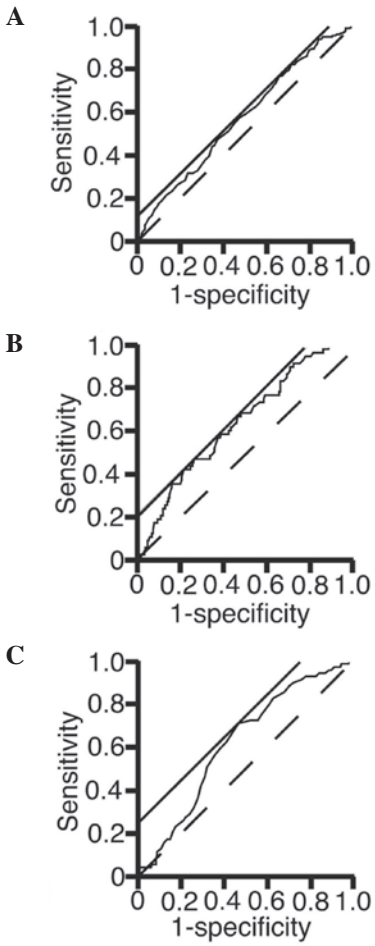

Figure 2. Receiver operating characteristic (ROC) analysis. The ROC analysis was performed to determine the threshold values of (A) hemoglobin, (B) triglycerides and (C) uric acid to predict the presence of colon diverticula. Solid straight line, a line with a slope of 45˚ used to calculate the threshold; dashed line, reference line.

of diverticula increased with advancing age, but no significant correlation was found by χ^2 test (P=0.0643).

The experimental variables were compared to determine significant differences between patients with and without diverticula (Table I). Hb levels were lower in patients with diverticula compared with those without diverticula (P=0.0027). UA and TG levels were also higher in patients with diverticula (P=0.0066 and P=0.0136, respectively).

Table II reports the χ^2 test results comparing the prevalence of diverticula between male and female patients. Diverticula were more frequent in male patients than in female patients (P=0.0001). The mean ages of the male and female patients with diverticula were 69.2±11.0 and 68.0±10.2 years, respectively.

Table I demonstrates that UA levels were significantly higher in patients with diverticula compared with those without diverticula. To confirm these results, the patients were divided into two groups according to UA level, as follows: Patients with UA levels ≥5.1 mg/dl and those with UA levels <5.1 mg/dl. In the patient sample of the current study, 5.1 mg/dl was the median UA level. The prevalence of diverticula was compared between the two groups (Table III); this was significantly higher in patients with UA levels ≥5.1 mg/dl than in those with UA levels <5.1 mg/dl

(P=0.0004; χ^2 test). Diverticula were markedly more frequent in patients with UA levels ≥5.1 mg/dl.

To address the possibility that the presence of diverticula could be predicted using laboratory test variables, an ROC analysis was performed (Fig. 2). The area under the curve, threshold value, sensitivity and specificity are presented in Table IV. The threshold values of the Hb, TG and UA levels were 12,400, 146 and 5.1 mg/dl, respectively. The sensitivity of the Hb and UA levels at the threshold values was 76.5 and 71.0%, respectively.

Discussion

The correlation between laboratory data, with the exception of age, and the presence of diverticula has not been previously reported. In the present study, the presence of diverticula was significantly associated with low Hb levels, and high TG and UA levels. A non-significant trend with increasing age was also revealed. The prevalence of diverticula may increase with advancing age due to structural changes in the colon wall (10,13,14). To the best of our knowledge, the present study is the first to report an association between diverticula and low Hb, high TG and high UA levels.

The current study revealed that the Hb levels were lower in patients with diverticula than in those individuals without; lower Hb levels were likely associated with the presence of diverticula as this is a major cause of lower gastrointestinal bleeding (15).

Higher TG levels are associated with metabolic syndrome (16,17) and TG level decreases as metabolic syndrome improves following lifestyle changes (18). In the present study, high TG levels were associated with diverticula. These previous data, alongside the data from the current study, indicate that diverticula may be associated with metabolic syndrome. Foster *et al* (19) compared the prevalence of diverticula between patients with and without ischemic heart disease and demonstrated that diverticula occurred in 57 and 25% of patients, respectively. This indicated an association with ischemic heart disease, which itself has a known association with high TG levels (20). Previous studies, together with the present data, thus indicate that high TG levels may be associated with diverticula.

The data in the current study clearly suggested that the prevalence of diverticula was associated with higher UA levels; to the best of our knowledge, the current study presents the first report of this association. The molecular details, however, are not known. The data on TG and UA presented in the current study may suggest that a reduction in TG and UA levels decreases the risk of diverticula.

Fernández *et al* (21) reported that predicting colonoscopic outcomes is challenging when based on blood examination results alone. The sensitivity of the Hb level at 12,400 mg/dl was 76.5% in the current study, suggesting that low Hb levels may be due to diverticulum bleeding. A notable finding was that the threshold value of UA was 5.1 mg/dl, the same value as the median.

To conclude, low Hb levels and high TG and UA levels are associated with the presence of diverticula. Therefore, colonoscopy may be recommended for patients with high TG and UA levels, in order to detect colon diverticula.

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