Development and Validation of a Novel Prognostic Scoring Model for Ischemic Colitis

Joo Won Chung

Department of Medicine

The Graduate School, Yonsei University

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Directed by Professor Jae Hee Cheon

The Master's Thesis submitted to the Department of Medicine, the Graduate School of Yonsei University in partial fulfillment of the requirements for the degree of Master of Medical Science

Joo Won Chung

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This certifies that the Master's Thesis of

Joo Won Chung is approved.

Thesis Supervisor : Jae Hee Cheon

Thesis Committee Member#1 : Tae Il Kim

Thesis Committee Member#2 : Kang Young Lee

The Graduate School

Yonsei University

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Joo Won Chung

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Development and Validation of a Novel Prognostic Scoring Model for Ischemic Colitis

Joo Won Chung

Department of Medicine
The Graduate School, Yonsei University

(Directed by Professor Jae Hee Cheon)

PURPOSE: The aim of this study was to identify the prognostic factors affecting the disease course of ischemic colitis and develop a prognostic scoring model.

METHODS: We analyzed the medical records of 153 patients who were diagnosed with and treated for ischemic colitis between October 2002 and September 2008 at Severance Hospital, Seoul, Korea. Patients were randomly assigned to a derivation or validation group and clinical, endoscopic, and laboratory data were analyzed to identify factors associated with poor outcome. A prognostic scoring model was derived from the derivation group and validated using the validation group.

RESULTS: Using the multivariate analysis of the derivation group (n=102), we found that the presence of tachycardia [adjusted odds ratio (AOR)=6.039], shock within 24 hours (AOR=6.46), and endoscopic evidence of ulcers

(AOR=10.451) were all significant independent risk factors predicting poor outcome. A novel scoring model with weighted factor gradations was developed. Using this scoring model, probability and risk index for severe ischemic colitis were determined, which classified patients into 3 risk groups: low risk (with risk index <9), intermediate risk (≥9 and < 40), and high risk (≥40). The area under the ROC in validation group (n=51) was 0.923 (95% CI, 0.848-0.999).

CONCLUSIONS: The results of this study demonstrate that endoscopic findings and instability of vital signs affect the disease course of ischemic colitis. Our new scoring model could be useful to physicians who treat ischemic colitis by providing a method for assessing patient prognosis.

Key words: ischemic colitis, prognosis, scoring model

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I. INTRODUCTION

Ischemic colitis is one of the most common gastrointestinal vascular diseases in the world. The incidence of ischemic colitis in the general population ranges from 4.5 to 44 cases per 100,000 person-years,[1] and accounts for 1 in 1000 hospitalizations among the general hospital population.[2] Previous studies have shown that ischemic colitis is more common in patients who have comorbid conditions such as cardiovascular disease, chronic kidney disease, or diabetes mellitus. Patients with ischemic colitis typically present with abdominal pain, abdominal distension, diarrhea, nausea, vomiting, and/or hematochezia. Because there are no known specific pathognomonic symptoms or laboratory findings that can identify ischemic colitis, abdominal computerized tomography (CT) scan or endoscopy should be performed when colonic ischemia is suspected.

The clinical disease course of ischemic colitis may vary from self-limiting to life-threatening. In general, most patients, their relevant symptoms and signs improve both clinically and endoscopically within 1 or 2 weeks with only bowel rest and hydration.[3] However, severe forms of the disease such as medically intractable massive bleeding, bowel wall perforation, panperitonitis, or stricture can occur as a result of severe transmural bowel necrosis. In these cases, surgical resection is often required and is associated with high morbidity and mortality. Therefore, many efforts have been made to identify the prognostic factors that affect the disease prognosis of ischemic colitis. According to previous studies, male gender, abdominal tenderness, age less than 80 years, and absence of lower intestinal bleeding have been shown to increase the risk of surgical intervention.[4] Furthermore, comorbidities such as rheumatoid arthritis, chronic renal failure, hemodialysis, right colon involvement, and total colon involvement have been demonstrated to necessitate surgical treatment and are associated with prolonged hospitalization.[5, 6] In addition, endoscopic findings such as ulceration or gangrenous changes is more common in patients with a severe form of ischemic colitis disease course.[7] Despite these results, there have been no studies concerning the development of a scoring system for predicting poor prognosis in an integrated manner. A scoring model that is predictive of an unfavorable ischemic colitis disease course could be helpful in clinical settings in which an appropriate decision needs to be made for selecting those

that need intensive treatment and the correct course of surgical treatment. Therefore, the aim of this study was to identify the factors associated with poor prognosis for ischemic colitis and develop a scoring model for assessing the probability of a severe disease course.

II. MATERIALS AND METHODS

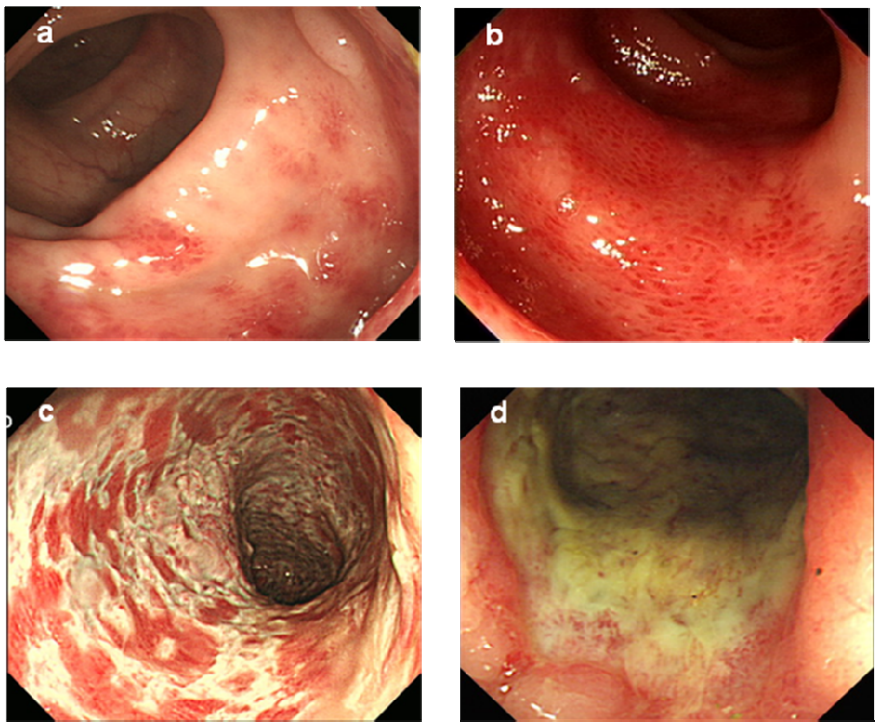
Patient population and data collection

We identified consecutive 173 patients who were diagnosed with and treated for ischemic colitis from the prospectively enrolled database at Severance Hospital, Seoul, Korea, between October 2002 and September 2008. For this study, the definition of ischemic colitis was essentially based on the criteria documented clinical and endoscopic findings of colonic ischemia without evidence of major vessel involvement.[8] Twenty of the 173 patients were excluded from the study due to unavailable endoscopic documentation regardless of their condition because they had not undergone endoscopy or they had been transferred to another hospital and we could not follow up with their clinical outcomes. Thus, a total of 153 patients were included in the sample and their clinical, endoscopic, and laboratory data were subsequently collected. These data included age, sex, comorbidities (hypertension, cardiovascular disease except hypertension, diabetes mellitus, chronic kidney disease, chronic pulmonary disease, chronic liver disease, cerebrovascular disease, and malignancy), medications [diuretics, digitalis, statin,

benzodiazepine, nonsteroidal anti-inflammatory drugs (NSAIDS), magnesium oxide], gastrointestinal symptoms or signs (abdominal pain, diarrhea, lower gastrointestinal bleeding, and peritoneal signs), laboratory findings [white blood cell count, hemoglobin, blood urea nitrogen (BUN), creatinine (Cr), and sodium levels], vital signs [systolic blood pressure (BP), heart rate (HR), body temperature (BT), and the presence of shock within 24 hours], pathology, radiologic findings, and endoscopic findings. The vital sign "shock within 24 hours" was defined as systolic blood pressure falling lower than 90 mmHg within 24 hours after admission or the development of symptoms.[9] All data were recorded at the time of diagnosis of ischemic colitis. Pathologic findings, such as infiltration of lymphocytes and neutrophilic granulocytes, epithelial erosion, ulceration, necrosis or gangrene represent ischemic mucosal change.[10] Segmental or circumferential wall thickening and homogenous or heterogenous wall enhancement with or without pericolic streakiness found on CT represent typical findings of ischemic colitis.[11] Two endoscopists (J. H. Cheon and J. J. Park) reviewed the endoscopic appearances of all patients. The resulting endoscopic patterns were classified into 2 stages: 1) "non-ulcer" for findings of pale, friable, or edematous mucosa with petechial hemorrhages, scattered erosion, segmental erythema, and bleeding; and 2) "ulcer" for findings of blue-black mucosal nodules, slough resulting in the loss of bowel wall integrity, or mucosal granularity with deep ulcerations (Figure 1).[10, 12] Severe ischemic colitis was defined as delayed improvement for more than 2

weeks, occurrence of complications requiring surgery, or death after admission due to complications of the disease.[13] The mild ischemic colitis group encompassed all of the remaining patients. Approval by the Institutional Review Board of our institute was obtained for this particular retrospective study.

Figure 1. Endoscopic findings of ischemic colitis



a. Non-ulcer stage: patchy erythema and mucosal edema.

b. Non-ulcer stage: submucosal hemorrhage and loss of vascularity.

c. Ulcer stage: multiple longitudinal ulcerations and mucosal granularity.

d. Ulcer stage: deep circumferential ulcerations covered with exudates encircling the lumen.

Derivation and validation of the scoring model for prediction of prognosis

A randomized selection procedure was performed to divide the 153 patients into 2 groups, namely, the derivation group for developing the scoring model (two-thirds of the patients in the study) and the validation group (the remaining one-third) for validating the model. A scoring model was constructed using the severity of ischemic colitis as the dependent variable and graded items as explanatory variables. Initially, explanatory items were selected using univariate analysis, and following individual item evaluation according to multiple regression analysis, explanatory items were subsequently weighted. Probability and risk index for all patients were calculated to classify them into 3 groups according to their risks for developing severe ischemic colitis.

To confirm the performance of the scoring model, we tested these variables on the validation group. The physicians who calculated the scores in the validation group followed the same instructions outlined in the scoring model derived from the derivation group. Based on this analysis, we calculated the area under the receiver operating characteristic (ROC) curve (AUC) as the discrimination accuracy.

Statistical analysis

Either Pearson's χ^2 test or Fisher's exact test was used for categorical variables while Student's *t* test or Mann-Whitney *U* test was used for

continuous variables. To identify independent factors associated with poor prognosis, multivariate logistic regression analysis was performed. Beginning with the variables that exhibited a *p* value of <0.05 in univariate analysis, a forward stepwise selection procedure was applied. We plotted the ROC curve of the scoring model in the derivation group; confidence intervals (CIs) were estimated for a 95% level. In all cases, a *p* value <0.05 was considered statistically significant. Statistical analysis was performed with SAS version 9.1 soft ware (SAS Institute, Cary, NC).

III. RESULTS

Patients' characteristics and outcomes

A total of 153 patients comprising 83 females (54.2%) and 70 males (45.8%) were included in this study with a median follow-up of 96 days from diagnosis. The mean age of all patients was 64.75±13.28 years. The most common comorbid disease was hypertension in 68 (44.4%) patients, followed by cardiovascular disease in 48 (31.4%), diabetes mellitus in 31 (20.3%), and malignancy in 29 (19.0%). The most common symptom was gastrointestinal bleeding, presenting in 94 (61.4%) patients, followed by abdominal pain in 85 (55.6%).

Pathologic confirmation was completed in 114 patients (74.4%), whereas the others were not examined due to bleeding tendency. Seventy four (80.4%) of

the 92 patients who had CT performed, showed typical findings of ischemic colitis. In two patients, who showed positive angiographic findings, there were 30% stenosis of celiac axis in one case and minimal stenosis of inferior mesenteric vein in the other. However distal blood flow was preserved in both cases.

Conservative treatment with bowel rest and parenteral nutrition was initiated for all patients. In the presence of any signs of infection such as fever or unstable vital signs, broad-spectrum antibiotics were administrated. Parenteral nutrition and fasting were continued until symptoms improved. All subjects included in the mild group recovered with the above management of treatment. In the severe group, four patients had symptomatic colonic stricture caused by chronic colitis from which two required segmental resection, and one underwent colonic stent insertion and endoscopic dilatation. Two patients who had experienced persistent diarrhea, hematochezia, and recurrent sepsis eventually underwent surgery. One patient also needed surgery as chronic colonic ischemia resulted in bowel perforation. A total of 14 (9.2%) patients expired. Of these, seven patients died of ischemic colitis while the remaining seven died of other underlying disease processes. Distributions of demographics and clinical features are described in Table 1.

Table 1. Demographic and clinical characteristics of the two study populations

Characteristics		Derivation group (n=102)	Validation group (n=51)
Age (years)	<60	27 (26.5%)	17 (33.3%)
	≥60	75 (73.5%)	34 (66.7%)
Gender	Male	54 (52.9%)	16 (31.4%)
	Female	48 (47.1%)	35 (68.6%)
Comorbidities	Hypertension	42 (41.2%)	26 (51.0%)
	Cardiovascular disease[a]	35 (34.3%)	13 (25.5%)
	Diabetes mellitus	17 (16.7%)	14 (27.5%)
	Chronic kidney disease	17 (16.7%)	3 (5.9 %)
	Chronic pulmonary disease	7 (6.9 %)	6 (11.8%)
	Chronic liver disease	5 (4.9 %)	6 (11.8%)
	Cerebrovascular disease	10 (9.8 %)	7 (13.7%)
	Malignancy	17 (16.7%)	12 (23.5%)
Medications	Diuretics[b]	23 (22.5%)	6 (11.8%)
	Digitalis	6 (5.9 %)	1 (2.0 %)
	Statins	18 (17.6%)	4 (7.8 %)
	NSAIDs	4 (3.9 %)	1 (2.0 %)
	Magnesium oxide	7 (6.9 %)	3 (5.9 %)
Clinical symptoms	Abdominal pain	60 (58.8%)	25 (49.0%)
	Diarrhea	23 (22.5%)	6 (11.8%)
	Hematochezia	62 (60.8%)	32 (62.7%)
	Peritoneal sign	1 (1.0 %)	1 (2.0 %)
Laboratory findings	WBC (mm^3)		
	Within normal	61 (59.8%)	31 (60.8%)
	≥12000, <4000	41 (40.2%)	20 (39.2%)
	Hemoglobin (g/dL)		
	≤10	34 (33.3%)	12 (23.5%)
	>10	68 (66.7%)	39 (76.5%)
	BUN (mg/dL)		
	≤25	75 (73.5%)	44 (86.3%)
	>25	27 (26.5%)	7 (13.7%)

	Creatinine (mg/dL)		
	≤1.4	76 (74.5%)	46 (90.2%)
	>1.4	26 (25.5%)	5 (9.8 %)
	Na (mmol/L)		
	Within normal	83 (81.4%)	42 (82.4%)
	>145, <135	19 (18.6%)	9 (17.6%)
Vital signs[c]	Systolic blood pressure (mmHg)		
	>90	95 (93.1%)	44 (86.3%)
	≤90	7 (6.9 %)	7 (13.7%)
	Heart rate (beats/min)		
	<90	80 (78.4%)	41 (80.4%)
	≥90	22 (21.6%)	10 (19.6%)
	Body temperature (℃)		
	<38	82 (80.4%)	41 (80.4%)
	≥38.0	20 (19.6%)	10 (19.6%)
	Shock within 24 hours[d]		
	No	87 (86.1%)	38 (74.5%)
	Yes	14 (13.9%)	13 (25.5%)
Endoscopic findings	Non ulcer	55 (53.9%)	30 (58.8%)
	Ulcer	47 (46.1%)	21 (41.2%)
Pathology	Not evaluated	24 (23.5%)	15 (29.4%)
	Positive[e]	78 (76.5%)	36 (70.6%)
CT correlation	Not evaluated	42 (41.2%)	19 (37.3%)
	Positive[f]	49 (48.0%)	25 (49.1%)
	Negative	11 (10.8%)	7 (13.7%)
Angiography	Not evaluated	100 (98.0%)	49 (96.0%)
	Vessel stenosis[g]	1 (1.0 %)	1 (2.0 %)
	Negative findings	1 (1.0 %)	1 (2.0 %)
Location	Rectum	29 (28.4%)	20 (39.2%)
	Left colon	84 (82.4%)	39 (76.5%)
	Transverse colon	17 (16.7%)	6 (11.8%)
	Right colon	9 (8.8 %)	4 (7.8 %)
Prognosis	Mortality	11 (10.8%)	3 (5.9 %)
	Surgery	5 (4.9 %)	2 (3.9 %)
	ICU care	13 (12.7%)	5 (9.8 %)

Severity		
Mild group	91 (89.2%)	42 (82.4%)
Severe group	11 (10.8%)	9 (17.6%)

WBC = white blood cell; BUN = blood urea nitrogen; Na = sodium; ICU = intensive care unit.

[a]Cardiovascular disease includes congestive heart disease, arrhythmia, valvular heart disease, coronary artery occlusive disease, and other heart problems (excluding hypertension).

[b]Diuretics include furosemide, spironolactone, hydrochlorothiazide and amiloride.

[c]Variables of vital signs, excluding shock within 24 hours, were collected at the time of diagnosis.

[d]Shock within 24 hours was defined as systolic blood pressure lower than 90 mmHg within 24 hours after admission or symptom development.

[e]Positive findings of pathology was defined as ischemic mucosal change such as infiltration of lymphocytes and neutrophilic granulocytes, epithelial erosion, ulceration, necrosis, or gangrene.

[f]Positive findings of CT was defined as segmental or circumferential wall thickening, homogenous or heterogenous wall enhancement with or without pericolic streakiness, and complications such as stricture, necrosis and perforation.

[g]Angiography showed 30% stenosis of celiac axis in one case and minimal stenosis of inferior mesenteric vein in another case, but distal blood flow was preserved in two cases.

2. Scoring model derivation

The 102 subjects in the derivation group were divided into 91 (89.2%) mild ischemic colitis patients and 11 (10.8%) severe ischemic colitis patients. Baseline characteristics of the severe and mild groups are listed in Table 2.

Table 2. Univariate analysis of variables associated with severe ischemic colitis

Characteristics		Mild ischemic colitis group (n=91)	Severe ischemic colitis group (n=11)	*P* value
Age (years)	<60	26 (28.6%)	1 (9.1 %)	0.197
	≥60	65 (71.4%)	10 (90.9%)	
Gender	Male	47 (51.6%)	7 (63.6%)	0.455
	Female	44 (48.4%)	4 (36.4%)	
Comorbidities	Hypertension	37 (40.7%)	5 (45.5%)	0.760
	Cardiovascular disease[a]	29 (31.9%)	6 (54.5%)	0.145
	Diabetes mellitus	15 (16.5%)	2 (18.2%)	0.887
	Chronic kidney disease	12 (13.2%)	5 (45.5%)	0.012
	Pulmonary disease	6 (6.6 %)	1 (9.1 %)	0.758
	Chronic liver disease	4 (4.4 %)	1 (9.1 %)	0.505
	Cerebrovascular disease	9 (9.9 %)	1 (9.1 %)	0.933
	Malignancy	15 (16.5%)	2 (18.2%)	0.887
Medications	Diuretics[b]	22 (24.2%)	1 (9.1%)	0.282
	Digitalis	6 (6.6 %)	0 (0 %)	0.999
	Statins	15 (16.5%)	3 (27.3%)	0.382
	NSAIDs	4 (4.4 %)	0 (0 %)	0.999
	Magnesium oxide	7 (7.7 %)	0 (0 %)	0.999
Clinical manifestations	Abdominal pain	52 (57.1%)	8 (72.7%)	0.329
	Diarrhea	21 (23.1%)	2 (18.2%)	0.715
	Bleeding	58 (63.7%)	4 (36.4%)	0.090
	Peritoneal sign	0 (0 %)	1 (9.1 %)	>0.999
Laboratory findings	WBC (mm^3)			
	Within normal	54 (59.3%)	7 (63.6%)	0.784
	≥12000, <4000	37 (40.7%)	4 (36.4%)	
	Hemoglobin (g/dL)			
	≤10	28 (30.8%)	6 (54.5%)	0.125
	>10	63 (69.2%)	5 (45.5%)	
	BUN (mg/dL)			
	≤25	70 (76.9%)	5 (45.5%)	0.034

	>25	21 (23.1%)	6 (54.5%)	
	Creatinine (mg/dL)			
	≤1.4	72 (79.1%)	4 (36.4%)	0.005
	>1.4	19 (20.9%)	7 (63.6%)	
	Na (mmol/L)			
	Within normal	77 (84.6%)	6 (54.5%)	0.023
	>145, <135	14 (15.4%)	5 (45.5%)	
Vital signs[c]	Systolic blood pressure (mmHg)			
	>90	86 (94.5%)	9 (81.8%)	0.139
	≤90	5 (5.5 %)	2 (18.2%)	
	Heart rate (beats/min)			
	<90	76 (83.5%)	4 (36.4%)	0.002
	≥90	15 (16.5%)	7 (63.6%)	
	Fever (℃)			
	<38	76 (83.5%)	6 (54.5%)	0.031
	≥38.0	15 (16.5%)	5 (45.5%)	
	Shock within 24 hours[d]			
	No	83 (91.2%)	5 (45.5%)	<0.001
	Yes	8 (8.8 %)	6 (54.5%)	
Endoscopic findings	non ulcer	54 (59.3%)	1 (9.1 %)	0.012
	ulcer	37 (40.7%)	10 (90.9%)	

WBC = white blood cell; BUN = blood urea nitrogen; Na = sodium.

[a]Cardiovascular disease included congestive heart disease, arrhythmia, valvular heart disease, coronary artery occlusive disease, and other heart problems (excluding hypertension).

[b]Diuretics include furosemide, spironolactone, hydrochlorothiazide, and amiloride.

[c]Variables of vital signs, excluding shock within 24 hours, were collected at the time of diagnosis.

[d]Shock within 24 hours was defined as systolic blood pressure lower than 90 mmHg within 24 hours after admission or symptom development.

Using univariate regression, the presence of chronic kidney disease, elevation of BUN or Cr, hypo- or hypernatremia, tachycardia (HR ≥90 beats/min), fever (BT ≥38℃), shock within 24 hours, and the presence of ulcer on endoscopy were found to be associated with severe colitis. There was no statistically significant multicollinearity between variables in multiple regression. According to multivariate regression analysis, tachycardia (HR, AOR=6.039, 95% CI, 1.322-27.596), shock within 24 hours (SHOCK, AOR=6.46, 95% CI, 1.373-30.462), and the presence of ulcer (ULCER, AOR=10.451, 95% CI, 1.126-97.006) were identified as independent significant factors for prediction of a severe disease course (Table 3). Using the coefficients of the estimated logistic model, we calculated a scoring model with three clinical variables: Y = 1.867 × SHOCK + 1.798 × HR +2.347 × ULCER - 5.001.

Table 3. Multivariate analysis of variables associated with severe ischemic colitis

	Coefficient	Standard error	*P* value	Adjusted odds ratio	95% CI
Tachycardia (≥90 beats/min)	1.798	0.775	0.020	6.039	1.322-27.596
Shock within 24 hours[a]	1.867	0.791	0.018	6.46	1.373-30.462
Presence of ulcer	2.347	1.137	0.039	10.451	1.126-97.006

CI = confidence interval.

[a]Shock within 24 hours was defined as systolic blood pressure lower than 90 mmHg within 24 hours after admission or symptom development.

Using the scoring model described above, probability [Probability = $e^{Y}/(1+e^{Y})$] and risk index [Risk index = $\{e^{Y}/(1+e^{Y})\}/\{e^{-5.001}/(1+e^{-5.001})\}$] for severe ischemic colitis were calculated in the derivation group (Table 4).

Table 4. Distribution of probability and risk index for severe ischemic colitis in the derivation group

Probability	Patients	Risk index
0.007	46 (45.1%)	1.000
0.039	6 (5.9 %)	5.840
0.042	1 (1.0 %)	6.241
0.066	27 (26.5%)	9.832
0.208	2 (2.0 %)	31.134
0.298	9 (8.8 %)	44.596
0.313	6 (5.9 %)	46.784
0.733	5 (4.9 %)	109.660

Probability = $e^{Y}/(1+e^{Y})$, Risk index = $\{e^{Y}/(1+e^{Y})\}/\{e^{-5.001}/(1+e^{-5.001})\}$

$Y = 1.867 \times SHOCK + 1.798 \times HR + 2.347 \times ULCER - 5.001$

SHOCK indicates "shock within 24 hours," which was defined as systolic blood pressure lower than 90 mmHg within 24 hours after admission or symptom development.

HR indicates "tachycardia," which was defined as heart rate ≥90 beats/min.

ULCER indicates "presence of ulcer" on endoscopy.

Furthermore, patients were classified into 3 risk groups according to risk index. The low-risk group was set as patients with a risk index <9, intermediate risk as those with an index ≥9 and <40, and high risk as those with an index ≥40 (Table 5).

Table 5. Classification of risk group according to the scoring model for the derivation group

	Low	Intermediate	High
Risk index	<9	≥9, <40	≥40
Total patients	53 (52%)	29 (28.4%)	20 (19.6%)
Severe patients	0 (0%)	2 (6.9%)	9 (45%)

Risk index = $\{e^{Y}/(1+e^{Y})\}$ /$\{e^{-5.001}/(1+e^{-5.001})\}$

Y = 1.867 × SHOCK + 1.798 × HR + 2.347 × ULCER - 5.001

SHOCK indicates "shock within 24 hours," which was defined as systolic blood pressure lower than 90 mmHg within 24 hours after admission or symptom development.

HR indicates "tachycardia," which was defined as heart rate ≥90 beats/min.

ULCER indicates "presence of ulcer" on endoscopy.

3. Validation of scoring model

Using the scoring model described above, a validation test was performed using the validation group. The median risk index was 5.84 (range, 1-109.660). Three of 12 (25%) patients in the intermediate-risk group and six of 10 (60%) in the high-risk group progressed to severe ischemic colitis (Table 6).

Table 6. Classification of risk group according to the scoring model for the validation group

	Low	Intermediate	High
Risk index	<9	≥9, <40	≥40
Total patients	29 (56.9%)	12 (23.6%)	10 (19.6%)
Severe patients	0 (0%)	3 (25%)	6 (60%)

Risk index = $\{e^{Y}/(1+e^{Y})\}/\{e^{-5.001}/(1+e^{-5.001})\}$

Y = 1.867 × SHOCK + 1.798 × HR + 2.347 × ULCER – 5.001

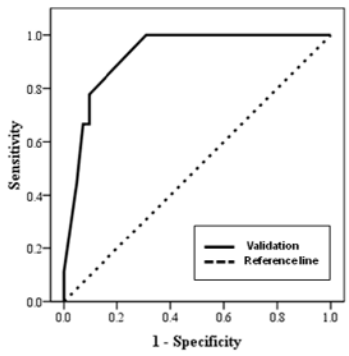
SHOCK indicates "shock within 24 hours," which was defined as systolic blood pressure lower than 90 mmHg within 24 hours after admission or symptom development.

HR indicates "tachycardia," which was defined as heart rate ≥90 beats/min.

ULCER indicates "presence of ulcer" on endoscopy.

In the high-risk group of validation, sensitivity, specificity, negative predictive value and positive predictive value were 66.7%, 90.5%, 60.0% and 92.7% respectively. The ROC curve in validation group is shown in Figure 2. The area under the ROC was 0.923 (95% CI, 0.848-0.999).

Figure 2. ROC curve of scoring model for the validation group



ROC = receiver operating characteristic.
Area under the curve was 0.923 (95% CI, 0.848-0.999).

IV. DISCUSSION

Ischemic colitis is considered a self-limiting disease, and conservative management proves sufficient in most patients. However, in some cases, persistent bowel hypoxia may result in delayed recovery and lethal complications. The two most important interventions that can improve the outcome of ischemic colitis are prompt diagnosis and adequate treatment.[3] However, there are no standard criteria for the diagnosis of ischemic colitis; therefore, clinicians make *ad hoc* treatment decisions based on observations of clinical manifestations and laboratory and imaging studies. A recent study demonstrated high accuracy for predicting the development of ischemic colitis among patients with lower abdominal pain and more than three of 6 factors (age >60 years, hemodialysis, hypertension, hypoalbuminemia <3.5 g/dL, diabetes mellitus, and constipation-inducing medications).[14] Importantly, early prediction of poor prognosis and intensive treatment in selected patients is also essential to design and implement adequate procedures. Even in cases where ischemic colitis is diagnosed early, clinicians occasionally find it difficult to treat patients requiring intensive interventions. Several clinical and laboratory factors have been identified as risk factors for surgery or prolongation of hospitalization.[4-6, 15-20] However, not only do these factors lack

general consensus among clinicians; furthermore, but also they are not consistent among studies. Thus, a scoring model to systematically predict disease course is needed but currently unavailable. To solve this problem, we aimed to develop a novel prognostic scoring model for ischemic colitis.

We first analyzed the clinical factors and disease course of 110 patients who were diagnosed with and treated for ischemic colitis at a single tertiary medical center. We found that the presence of chronic kidney disease, elevation of BUN or Cr, hypo- or hypernatremia, tachycardia (HR ≥90 b/min), fever (BT ≥38℃), shock within 24 hours, and the presence of ulcer on endoscopy were all associated with a severe ischemic colitis disease course. In multivariate regression, tachycardia, shock within 24 hours, and the presence of ulcer on endoscopy were identified as independent significant factors for the prediction of a severe disease course. Renal function appeared to be a very important prognostic factor in univariate analysis but not in multivariate analysis, which can be explained in part by the multicollinear relationship between the exacerbation of renal function and massive bleeding or intravascular volume loss.

According to our scoring model, tachycardia, shock within 24 hours, and ulcer on endoscopy can be early signs of poor progress. Our findings are consistent with several previous studies. Specifically, Añón, R et al. also divided ischemic colitis into 2 groups of mild and severe ischemia and reported “no evidence of hematochezia,” “peritonisism (positive Blumberg’s sign),”

“anemia,” “hyponatremia,” and “tachycardia (HR >90 b/min)” as predictors for severe ischemic colitis.[15] Moreover, it was reported in another study that initial hemodynamic instability is an important predictor of operative management.[16] Unstable vital signs due to underlying diseases per se can result in severe colonic ischemia by reduced blood flow of bowel wall. Conversely, it may be a consequence of severe sepsis or blood loss induced by severe colonic ischemia. Regardless of whether it is a cause or an effect of severe ischemia, there is no doubt that vital instability is of paramount importance in predicting a poor prognosis of ischemic colitis. In our study, we categorized endoscopic findings into two stages of ulcer and non-ulcer. A Japanese study also reported that duration of fasting and admission were significantly longer in the ulcer group (7.9 days vs. 4.4 days, *p* value=0.0057 and 17.9 days vs. 10.7 days, *p* value 0.0001).[17] In another study, confluent circumferential colon wall erythema with exudates and/or ulceration, dusky appearance, cyanosis or necrosis appeared in the moderate to late stage of ischemia due to which there was a significantly increased the need of surgery.[18] Together, these results suggest that the presence or degree of ulcers is related to the severity of tissue hypoperfusion and hypoxemia. Specifically, as ischemia progresses, ulcers become deeper and larger and intestinal mucosa is broken down, resulting in bacterial translocation and sepsis.[21]

Our scoring model has several advantages over previous models in that the variables included are simple and easy to evaluate and calculate, allowing

clinicians to quickly predict the severity of ischemic colitis and make appropriate decisions for the course of treatment. Our scoring model showed high specificity and negative predictive value, with low sensitivity and positive predictive value. Considering the dramatic course of ischemic colitis, the low positive predictive value of our scoring model was deemed acceptable.

Additional factors beyond the three suggested in this model may affect the progress of ischemia. Several studies have shown that the location or extension of colonic ischemia is significantly associated with poor prognosis.[5, 19, 22] However, in this study, we did not find these factors to be significant. In some cases, sigmoidoscopy instead of colonoscopy was performed urgently, and as a result, the location and extension of colonic ischemia could not be evaluated in all patients. Furthermore, if patients did not undergo endoscopy because of hemodynamic instability or emergent operation, they were excluded from this study, even if they were confirmed as having ischemic colitis on CT. Colonoscopic or sigmoidoscopic data are required in order to use our scoring model properly, but extremely unstable patients are not suitable for colonoscopy or sigmoidoscopy. In this regard, we have analyzed the 20 excluded patients' medical records again as there was a possibility that a significantly high number of patients with severe cases of ischemic colitis might be included in them. Of the excluded 20 cases, three (15%) had severe ischemic colitis. This figure is consistent with the proportion of patients

allocated in the severe group within the study population.

Some medications are also related with colonic ischemia. NSAIDS may cause vascular insufficiency and increase mucosal permeability by arachidonic acid metabolism.[23] The mechanism of the tissue ischemia induced by diuretics and digitalis are thought to cause mesenteric precapillary vasoconstriction.[24] Statin increases peripheral perfusion which in turn results in hypoperfusion of mesenteric vasculature.[25] In our study, a considerable portion of patients (39.6%) had taken those medications. However they had no significant relationships with the severity of ischemic colitis, suggesting that medications probably play some roles in the occurrence of ischemic colitis but not in the prognosis.

Our study has several limitations, namely the sample size was relatively small, and although the data were obtained prospectively, the analyses were performed retrospectively, which may have affected the study due to the limitations of such an investigational design. In order to reduce bias, we analyzed the data (between clinical and endoscopic variables and outcomes) in a blind fashion. Future studies utilizing larger samples sizes and prospective designs are warranted. Finally, external or internal validation by bootstrapping has yet to be performed to assess the power of the scoring model.

V. CONCLUSION

Our results demonstrate that endoscopic characteristics and vital instability can affect the disease course of ischemic colitis. A novel scoring model comprising these variables should prove useful to physicians who treat ischemic colitis by providing a method for assessing patient prognosis of ischemic colitis.

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< ABSTRACT(IN KOREAN)>

허혈성 대장염 환자에서 내시경 소견과 임상 양상을 이용하여 만든 예후 측정 점수 모형

<지도교수 : 천 재 희 >

연세대학교 대학원 의학과

정 주 원

<목적>허혈성 대장염은 대장에서 발생하는 가장 흔한 혈관 질환 중의 하나이다. 대부분의 환자들에서 자연 치유되어 양호한 경과를 보이나, 일부 환자에서는 치료 기간이 오래 걸리고, 과다 출혈, 협착, 복막염 등의 합병증이 발생하여 수술을 필요로 하거나 이로 인해 사망에 이르기도 한다. 본 연구는 허혈성 대장염의 경과를 예측할 수 있는 요인을 분석하여 점수체계를 만들었고 이를 실제 환자에 적용하여 보았다.

<대상 및 방법> 2002년 10월부터 2008년 9월까지 허혈성 대장염을 진단받고 치료 받은 환자 153명을 대상으로 후향적으로 조사하였다. 진단을 위하여 모든 환자에게 대장 내시경이나 직장내시경을 시행하였다. 무작위 추출 방법으로, 점수체계를 만들 모형군과 이를 적용할 검증군으로 나누었다. 모형군의 환자를 대상으로 경증의 허혈성 대장염 환자와 중증의 허혈성 대장염 환자를 분류하여 임상적, 내시경적 양상의 차이점을 분석하였다.

<결과> 모형군(102명)에서 다변량회귀분석 결과, 빈맥 [adjusted

odds ratio (AOR)=6.039], 쇼크 (AOR=6.46), 내시경상 궤양 소견 (AOR=10.451)이 중증의 허혈성 대장염과 의미 있는 연관성을 보였다. 이 변수를 이용하여 점수 모형을 만들고, 위험 확률와 위험지표를 구하였다. 환자들은 위험지표에 따라 저위험군 (<9), 중간위험군 (≥9 and < 40), 고위험군 (≥40)으로 나누었다. 점수모형을 검증군에 적용한 결과 ROC 곡선하면적은 0.923 (95% CI, 0.848-0.999)이었다.

<결론> 본 연구를 통하여 환자의 기저 질환 및 임상 양상, 내시경 소견으로 허혈성 대장염 환자의 중증의 경과를 예측할 수 있는 점수체계를 만들 수 있었고, 이를 임상에 적용하여 환자의 경과를 예측하고 설명하는데 도움이 될 수 있다.

핵심되는 말 : 허혈성 대장염, 예후, 점수모형