Clinical features and risk factors for ischemic colitis in young and middle-aged patients

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Abstract

Background and study aims: **Ischemic colitis (IC) is thought to occur more frequently in the elderly, but the incidence in young and middle-aged adults is increasing. This study determined the clinical characteristics of and risk factors for young and middle-aged IC patients.**

Patients and methods: **The medical records of 190 IC patients from 2010-2020 were reviewed. The clinical features of the young and middle-aged IC group (group A, < 60 years [n=70]) were compared to the elderly IC (group B, ≥60 years [n=120]) and age- and gender-matched colon polyp groups (group C, <60 years [n=272]). Independent risk factors for IC in group A were assessed using multivariate logistic regression analysis.**

Results: **There were no significant differences in groups A and B with respect to season of onset, symptoms, signs, treatment, or recurrences. The main symptoms of group A were abdominal pain (98.6%) and hematochezia (98.6%). Lesions commonly involved the left half of the colon (87.1%) and the clinical conditions were generally not severe. The percentage of patients with constipation (11.4% vs. 4.0%, P=0.034) and using a calcium channel antagonist (21.4% vs. 11.4%, P=0.028) was significantly higher in group A than group C. Regression analysis demonstrated that constipation (OR 2.831, P=0.037) and taking a calcium channel antagonist (OR 2.486, P=0.012) were closely associated with the occurrence of IC in group A.**

Conclusions: **Constipation and taking a calcium channel antagonist were independent risk factors for the onset of IC in young and middle-aged adults. Among young and middle-aged adults with abdominal pain and bloody stools who also have constipation or are taking a calcium channel antagonist to treat hypertension, the diagnosis of IC should be considered.** (Acta gastroenterol. belg., **2022,** 85, **283-290**).

Keywords: Ischemic colitis, young and middle-aged, clinical features, risk factors.

Introduction

Ischemic colitis (IC) is the most common intestinal ischemic disease, and is thought to be caused by a reduced intestinal blood supply, followed by blood flow reperfusion injury (1,2). IC may present with a number of transient symptoms (3). Hematochezia, acute abdominal pain, and vomiting are the most common manifestations of IC (1). The more benign manifestations of IC respond well to drug therapy, but the acute manifestations may present with more severe clinical symptoms and require surgical intervention (1,4). Systemic symptoms, such as sepsis, peritoneal irritation, and acute respiratory distress, should prompt the healthcare provider to suspect severe IC (1). A more accurate diagnosis can be obtained using computed tomography, CT angiography, or colonoscopy, and physical features are the foundation of the diagnosis (1,5).

Any part of the colon may be affected, but the left colon is the main site in approximately 75% of patients (6), while 10% experience right colon ischemia (7). The splenic flexure and recto-sigmoid junction may be vulnerable in a systemic low-flow state due to the Sudeck (intersection of the sigmoid and superior colonic arteries) and Griffith points (intersection of the middle colonic artery with the left colonic artery) (8,9). It is estimated that up to 17.7 per 100,000 people have IC, with a predominance in the elderly (1); however, we have found in our clinical work that it is not rare for young and middle-aged adults with lower gastrointestinal bleeding to be diagnosed with IC. The incidence of IC in young and middle-aged people is on the rise (1).

Risk factors associated with IC include female gender, > 65 years of age, hypertension, type II diabetes, chronic obstructive pulmonary disease, dyslipidemia, arrhythmias, coronary artery disease, heart failure, peripheral arterial occlusive disease, and renal failure (10). Multiple investigations have confirmed that use of certain drugs increase the risk for developing IC (11); however, it has also been reported among young adults without any related risk factors (12-14). Some medications are linked to IC; digitalis and aspirin are independent risk factors for IC occurrence (15). Proton pump inhibitors, H2 antagonists, and spasmolytic agents are also associated with IC (16); however, limited research is available on the clinical features of and risk factors for IC in young and middle-aged patients. Therefore, we conducted this retrospective evaluation comparing young and middle-aged IC patients with elderly IC patients to determine whether the two age groups of patients have unique disease characteristics and to compare the IC patients with age- and gender-matched colon polyp (CP) patients to identify independent susceptibility factors.

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Patients and Methods

Patient selection

A retrospective study was conducted involving 190 patients diagnosed with IC in the Department of Gastroenterology at the Second Affiliated Hospital of Soochow University from 2010-2020. The medical records of these patients were collected from the electronic medical record system. This study included 3 groups of patients: IC patients were divided into 2 groups based on age (group A, <60 years of age [n=70] and group B, ≥60 years of age [n=120]); and group C, age- and gender-matched patients with CP < 60 years of age.

During the 2010-2020 time period, a comparative analysis was performed. Endoscopic images were obtained from the hospital patient imaging archive system and re-examined for one or more IC endoscopic features, including hyperemia, edema, erosions, erythema, ulcerations, mucosal hemorrhage, stenosis, purple nodules, and necrosis. The criteria for selection were as follows: patients with a primary clinical, radiologic, and endoscopic diagnosis of IC that was confirmed by pathologic examination (17); no malignancy; and no mucosal inflammation under endoscopy in group C. A total of 928 patients with CP were selected. Then, a propensity score-matched (PSM) analysis was performed using a multivariable logistic regression model based on age and gender. A total of 272 CP patients were required based on 1:4 greedy nearest neighbor matching with a PS score of 0.01 (Table 1). None of the patients with IC had a history of long-term use (> 1 y) of proton pump inhibitors (PPIs), thus PPIs were not included as a study factor.

Table 1. — **Basic demographics between the IC and CP groups in young and middle-aged adults after propensity score matching**

	Group A (n=70) (IC patients, <60 years)	**Group C (n=272) (CP patients, <60 years)**	***P***
Age (y)	50.87±7.87	51.36±6.46	0.590
Gender, male	16 (22.9%)	65 (23.9%)	0.855

IC: ischemic colitis; CP: colon polyps.

Data collection

Basic clinical information was collected, including demographics, co-morbidities, abdominal surgery, and medications. Clinical features were collected, including season of onset, clinical signs and symptoms, treatment course, recurrences, and endoscopic findings. The basic clinical information and clinical features of group A was compared with groups B and C. Smoking was defined as lifetime smoking > 100 cigarettes and smoker was defined as smoking in the past year (18). Alcohol consumption was defined as 2 drinks or more in a day for men and 1 drink or more in a day for women (19).

The diagnosis of constipation was based on the Rome IV standard diagnosis of functional gastrointestinal disease (20). Abdominal surgery was defined as any operation involving abdominal and pelvic organs, such as a cholecystectomy, appendectomy, or hysterectomy. The medications mainly included antiplatelet drugs, anticoagulants, antihypertensives, and antidepressants. Patients had been taking the above medications for at least 1 year. The medication doses were taken in accordance with the conventional treatment dosage prescribed according to drug instructions.

We focused on the lesion manifestations and types during colonoscopy. We used the splenic flexure as the boundary point. The splenic flexure is the bend where the transverse and descending colons meet at the upper left quadrant of the abdomen, and the splenic flexure and colon below the splenic flexure are the left colon. The colon above the splenic flexure was defined as the right colon.

Statistical Analysis

SPSS statistics 26.0 (IBM, Armonk, NY, USA) was used for data analysis. Qualitative variables are expressed as numbers (percentages) and compared using a chi-square test. Quantitative data are presented as the median (range) and compared using the Mann-Whitney U test. The independent risk factors associated with the onset of IC in group A were determined by multivariate logistic regression analysis. All *P* values were based on a two-sided test. A *P* value < 0.05 indicated statistical significance.

Results

Comparison of basic clinical information

The basic clinical information is shown in Table 2. There was significantly fewer male than female patients. Compared with group B, the proportion of patients with hypertension in group A was significantly lower (35.7% vs. 64.2%, P<0.0001) and the proportion of patients with constipation was significantly higher (11.4% vs. 2.5%, P=0.020). Group B had a higher proportion of calcium channel antagonist (36.7% vs. 21.4%, P=0.029), angiotensin receptor blocker (11.7% vs. 2.9%, P=0.035), or diuretic (10.0% vs. 1.4%, P=0.034) use than group A.

Comparison of clinical features

There were no significant differences in groups A and B with respect to season of onset, symptoms, signs, treatment, or recurrences. The main symptoms in group A were abdominal pain and bloody stools, and the clinical course was generally mild (Table 3).

Table 2. — **Basic clinical information of the IC patients**

Variables	Group A (n= 70) (IC patients, <60 years)	Group B (n= 120) (IC patients, ≥60 years)	*P*
Demographics			
Age (yrs, ranges)	53.5 (21-59)	67.5 (60-88)	——
Gender, male	16 (22.9%)	33 (27.5%)	0.480
Smoking	5 (7.1%)	10 (8.3%)	0.769
Alcoholism	5 (7.1%)	8 (6.7%)	1.000
Co-morbidities			
Hypertension	25 (35.7%)	77 (64.2%)	0.000
Diabetes mellitus	6 (8.6%)	16 (13.3%)	0.322
Coronary heart disease	1 (1.4%)	6 (5.0%)	0.264
Hypertriglyceridemia	8 (11.4%)	14 (11.7%)	0.961
Hypercholesterolemia	5 (7.1%)	13 (10.8%)	0.402
Atrial fibrillation	0 (0.0%)	3 (2.5%)	0.298
Cerebral infarction	1 (1.4%)	10 (8.3%)	0.057
Hyperuricemia	3 (4.3%)	9 (7.5%)	0.540
Constipation	8 (11.4%)	3 (2.5%)	0.020
Abdominal surgery	20 (28.6%)	42 (35.0%)	0.362
Medications			
Aspirin	3 (4.3%)	5 (4.2%)	1.000
Clopidogrel	0 (0.0%)	1 (0.8%)	1.000
Warfarin	0 (0.0%)	1 (0.8%)	1.000
Calcium channel anta-gonist	15 (21.4%)	44 (36.7%)	0.029
Angiotensin converting enzyme inhibitor	3 (4.3%)	11 (9.2%)	0.214
Angiotensin receptor blocker	2 (2.9%)	14 (11.7%)	0.035
Beta receptor antagonist	4 (5.7%)	12 (10.0%)	0.305
Diuretic	1 (1.4%)	12 (10.0%)	0.034
Antidepressant drug	1 (1.4%)	3 (2.5%)	1.000

IC: ischemic colitis

Comparison of endoscopic findings

Manifestations of IC, such as congestion, edema, erosions, ulcerations, and necrosis, were detected during colonoscopy. The endoscopic findings did not differ between the two groups. These were also no significant differences with respect to lesion location and endoscopic types between groups A and B (Table 4).

Comparison of the clinic information between groups A and C

The percentage of patients with constipation (11.4% vs. 4.0%, P=0.034) and using a calcium channel antagonist (21.4% vs. 11.4%, P=0.028) was significantly higher in group A than group C. The percentage of patients with hypertriglyceridemia (11.4% vs. 29.0%, P=0.003) and hypercholesterolemia (7.1% vs. 18.4%, P=0.022) was significantly lower in group A than group C (Table 5).

Multivariate logistic regression analysis of IC-associated risk factors between groups A and C

The independent risk factors for IC in group A were determined by logistic regression analysis. Based on the basic clinical information between groups A and C, we selected the significant variables to carry out multivariate logistic regression analysis. The statistical results showed that constipation (OR, 2.831; 95% CI, 1.063-7.535; P=0.037) and calcium channel antagonist

Table 3. — **Clinical features of the patients**

Variables	Group A (n=70) (IC patients, <60 years)	Group B (n=120) (IC patients, ≥60 years)	*P*
Onset season			0.290
Spring	11 (15.7%)	30 (25.0%)	
Summer	16 (22.9%)	27 (22.5%)	
Autumn	17 (24.3%)	32 (26.7%)	
Winter	26 (37.1%)	31 (25.8%)	
Clinical symptoms			
Abdominal pain	69 (98.6%)	119 (99.2%)	1.000
Hematochezia	69 (98.6%)	116 (96.7%)	0.653
Bloody diarrhea	45 (64.3%)	66 (55.0%)	0.210
Emesis	30 (42.9%)	38 (31.7%)	0.121
Fever	3 (4.3%)	3 (2.5%)	0.671
Abdominal distention	2 (2.9%)	1 (0.8%)	0.240
Dizziness and/or palpitations	23 (32.9%)	37 (30.8%)	0.772
Clinical signs			
Tenderness	39 (55.7%)	78 (65.0%)	0.204
Treatment processes			
Hospital stay (days)	9 (6,12)	8 (6,10)	0.277
Symptoms subsided	70 (100.0%)	120 (100.0%)	——
Surgery	0 (0.0%)	0 (0.0%)	——
Mortality, n, (%)	0 (0.0%)	0 (0.0%)	——
Recurrence	1 (1.4%)	6 (5.0%)	0.264

IC: ischemic colitis

use (OR, 2.486; 95% CI, 1.217-5.709; P=0.012) were strongly associated with IC in young and middle-aged adults (Table 6).

Discussion

The present study elicited three main findings. First, the clinical features and endoscopic findings were similar between young and elderly patients. Second, the main symptoms among young and middle-aged IC patients were abdominal pain and hematochezia. The lesions often involved the descending and sigmoid colon and the clinical course was not severe. Third, young and middle-aged adults who had constipation or used a calcium channel antagonist were more prone to develop IC.

IC has been classified into gangrenous, structuring, and transient forms (21). In the past 20 years, however, studies have categorized IC patients into mild/moderate and severe groups based upon the need for surgery or death (22-24). These studies showed that lesions involving the right colon alone and signs of peritonitis predicted a severe outcome, which was also confirmed by additional studies (25,26). In the current study, although 22 patients presented endoscopically with stenosis or necrosis, only 3 patients in group A had lesions involving the right colon alone, no patients had peritonitis, and no patients required surgery or died, suggesting that all patients in our study had mild-to-moderate IC, which may further indicate that severe IC is uncommon in the Chinese population, regardless of age.

Several retrospective studies comparing IC between young and elderly adults have been published in the past 10 years (27-29). Although these 3 studies were grouped based on age (45, 50, and 65 years, respectively), all of the studies showed young IC patients had a shorter length of hospital stay than elderly IC patients. It is worth noting that no significant differences in endoscopic findings existed between the two groups in the three studies, which is consistent with the finding in our study.

No significant difference was observed between groups A and B in length of hospital stay. This finding might reflect the absence of severe IC cases in the two groups we studied. Additionally, according to the definition of elderly in China, our research set the age

Table 4. — **Endoscopic findings of the patients**

Variables	Group A(n=70) (IC patients, <60 years)	Group B (n=120) (IC patients, ≥60 years)	*P*
Endoscopic manifestations			
Congestion	51 (72.9%)	98 (81.7%)	0.154
Edema	38 (54.3%)	60 (50.0%)	0.569
Erosions	62 (88.6%)	101 (84.2%)	0.402
Erythema	6 (8.6%)	9 (7.5%)	0.792
Ulcerations	24 (34.3%)	45 (37.5%)	0.657
Mucosal hemorrhage	17 (24.3%)	20 (16.7%)	0.201
Strictures	1 (1.4%)	3 (2.5%)	1.000
Mauve nodules	4 (5.7%)	9 (7.5%)	0.771
Necrosis	1 (1.4%)	6 (5.0%)	0.264
Lesion sites			0.093
Left colon	61 (87.1%)	111 (92.5%)	
Right colon	3 (4.3%)	0 (0.0%)	
Both left and right hemi-colon involvement	4 (5.7%)	7 (5.8%)	
Entire colon	2 (2.9%)	2 (1.7%)	
Endoscopic types			0.558
Transient	64 (91.4%)	104 (86.7%)	
Strictures	4 (5.7%)	12 (10.0%)	
Gangrenous	2 (2.9%)	4 (3.3%)	

IC: ischemic colitis

cut-off point at 60 years, which could objectively reflect the disease characteristics of Chinese young and middle-aged IC patients. Our research demonstrated there was also no significant difference in the seasonal distribution of IC onset between groups A and B, which was the same as the study by Yamanouchi (30).

Research focusing on the risk factors for IC is gradually increasing. Hypertension (31,32), diabetes mellitus (15, 31), hyperlipidemia (15, 31), irritable bowel syndrome (IBS) (33,34), constipation (33), abdominal surgery (32), alcoholism (32,35), and medications (15,34,36) are thought to be susceptible factors for IC in the population at large; however, there are few studies involving the factors associated with IC in young and middle-aged adults. Several studies conducted at least 20 years ago reported that constipation and contraceptive pill use were contributors to IC in young people (14,37-39). A Japanese study published in 2012 concluded that smoking and hyperuricemia were closely related to the occurrence of IC in youth (27); however, these risk factors have not been verified in young people in China. The risk factors for IC in the elderly might differ from younger adults. Therefore, a multivariate logistic regression analysis was performed in the present study. We first compared the basic clinical information between groups A and C. Then, multivariate logistic regression analysis demonstrated that constipation is a risk factor for IC in group A; our finding is similar to an earlier study (28). Constipation increases the colonic intraluminal pressure, then leads to a decrease in blood supply to the intestinal wall and intestinal mucosal ischemia (28). Another important finding in our research was the strong association between calcium channel antagonist use and IC in group A, which can be explained by the side effects of calcium channel antagonists, such as constipation. Hypertension in group A patients was not an independent risk factor when compared to group C patients.

Unlike the Japanese study (28), our research did not show that IC in group A had a significant relationship with smoking. This finding may be related to the low percentage of subjects in our study who smoked. Hyperuricemia was also shown not to be an independent risk factor. We suggest that this finding might be associated with different dietary habits in geographic regions. In contrast to adults, the right colon is the most affected anatomic site in young people and remains unexplained for this specific location (15). The results of the close correlation between calcium channel antagonists and the occurrence

Table 5. — **Basic clinical information of IC and CP groups in young and middle-aged patients**

Variables	Group A (n= 70) (IC patients, <60 years)	Group C (n= 272) (CP patients, <60 years)	*P*
Demographics			
Smoking	5 (7.1%)	13 (4.8%)	0.384
Alcoholism	5 (7.1%)	9 (3.3%)	0.173
Co-morbidities			
Hypertension	25 (35.7%)	78 (28.7%)	0.252
Diabetes mellitus	6 (8.6%)	16 (5.9%)	0.416
Coronary heart disease	1 (1.4%)	0 (0.0%)	0.205
Hypertriglyceridemia	8 (11.4%)	79 (29.0%)	0.003
Hypercholesterolemia	5 (7.1%)	50 (18.4%)	0.022
Cerebral infarction	1 (1.4%)	3 (1.1%)	1.000
Hyperuricemia	3 (4.3%)	13 (4.8%)	1.000
Constipation	8 (11.4%)	11 (4.0%)	0.034
Abdominal surgery	20 (28.6%)	60 (22.1%)	0.251
Medications			
Aspirin	3 (4.3%)	3 (1.1%)	0.103
Calcium channel antagonist	15 (21.4%)	31 (11.4%)	0.028
Angiotensin-converting enzyme inhibitor	3 (4.3%)	3 (1.1%)	0.103
Angiotensin receptor blocker	2 (2.9%)	15 (5.5%)	0.541
Beta receptor antagonist	4 (5.7%)	6 (2.2%)	0.126
Diuretics	1 (1.4%)	5 (1.8%)	1.000
Antidepressant drugs	1 (1.4%)	2 (0.7%)	0.498

IC: ischemic colitis; CP: colon polyps.

Table 6. — **Multivariate logistic regression analysis of IC-related risk factors between groups A and C**

Variables	*β*	Wald	*P*	OR	95% CI
Constipation	1.041	4.339	0.037	2.831	1.063-7.535
Calcium channel antagonist	0.911	6.245	0.012	2.486	1.217-5.709
Hypertriglyceridemia	-1.056	6.727	0.009	0.348	0.157-0.773
Hypercholesterolemia	-0.927	3.409	0.065	0.396	0.148-1.059

IC: ischemic colitis

of IC in middle-aged and young adults suggest that there is a difference in the onset background between middle-aged and young IC patients, and elderly patients.

The present study had several limitations. First, due to the lack of complete data, we could not study the effects of contraceptive use and irritable bowel syndrome on the occurrence of IC in young and middle-aged adults. Second, our retrospective, comparative study involved only one center in China. Third, the sample size of this study was not large enough. In particular, smoking is usually considered to be an influencing factor for IC, but in this group, the proportion of smokers was only 8% (15/190) of the study population, so a statistical bias due to small sample size cannot be excluded. Further studies with larger sample sizes and more complete data are needed to confirm the results of this study.

In summary, constipation and the use of calcium channel antagonists are considered to be two independent risk factors related to IC development in young and middle-aged adults. IC should be included in the differential diagnosis of young and middle-aged adults with abdominal pain and hematochezia who have constipation or take calcium channel antagonists to treat hypertension. The use of calcium channel blockers

was higher in group B than group A (36.7% vs. 21.4%), suggesting that calcium channel blockers warrant further study as an important factor in the development of IC, both in the young and the elderly.

Data Availability Statement

The research data are related with patients involving privacy, so the data cannot be publicly available on ethical grounds. The data related to this study are available from the corresponding author based on reasonable request.

Conflicts of Interest Statement

The authors have no conflicts of interest to declare.

Author Contributions

Wei Cai did the study concept and drafting of the manuscript. All authors collected the clinical data. Jianwei Zhu performed the hyperspectral analysis. Duanmin Hu made critical revisions on the manuscript.

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None.

Statement of Ethics

The study was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. This retrospective study was granted by the ethics committee of the Second Affiliated Hospital of Soochow University (No. JD-HG-2020-21). The patients gave written informed consent to publish the study with their information.

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