Population-Based Study of the Clinical Characteristics and Risk Factors of Ischemic Colitis

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ABSTRACT

Background: *Ischemic colitis (IC) is a common ischemic disorder of the colon caused by insufficient blood supply to the colonic mucosa. This study aimed to identify the clinical characteristics, comorbidities, and risk factors in patients with IC.*

Methods: *We performed a retrospective population-based study using electron video-colonoscopy imaging and pathological biopsies from 168 patients diagnosed with IC. A retrospective controlled study was used to analyze differences between a young to middle-aged patient group (78 cases) and an elderly patient group (90 cases) on the basis of clinical characteristics and risk factors.*

Results: *The primary symptoms in the 168 patients with IC were abdominal pain, diarrhea, and hematochezia. White blood cells (WBC), neutrophilic granulocyte percentage (NEUT%), C-reactive protein (CRP), and D-dimer were significantly elevated in elderly patients. The sigmoid colon and descending colon were the most common lesion locations (57.1% and 33.9%, respectively). Hypertension, cerebral infarction, and coronary heart disease were the most common comorbidities in elderly patients, while smoking history was the most common risk factor in young to middle-aged patients.*

Conclusion: *The sigmoid colon and descending colon are the most affected locations in IC. Hypertension, diabetes mellitus, and cerebral infarction are the most common risk factors and comorbidities.*

Keywords: *Ischemic colitis, young and middle-aged people, elderly people, clinical characteristics, risk factors*

INTRODUCTION

Ischemic colitis (IC) is the most common form of gastrointestinal ischemia, accounting for approximately 50% of cases of compromised intestinal vasculature,[1] which is one of the main causes of hematochezia.[2] The majority of IC patients in many studies,[3,5] including ours, are female. The clinical symptoms of IC manifest mostly as abdominal pain, diarrhea, and rectal bleeding.[6] Some less frequently observed symptoms include nausea, vomiting, fever, shock, abdominal distension, and peritoneal signs.[3,7] Boley et al.[8,9] described IC as representing an ischemic injury to the gastrointestinal tract. However, differences in symptoms and locations of IC lesions between young to middle-aged patients and elderly patients remain unclear.

Predisposing factors for IC include vascular and bowel-specific factors.[6] IC may occur in elderly individuals with multiple co-existing medical conditions, including hypertension, atherosclerotic disease, heart failure, and renal failure.[5,10,11] This condition usually presents in younger individuals with conditions such as hypercoagulable disorders (including gene mutations, coagulation factor overexpression, and deficiencies in proteins that prevent clotting),[12,13] vascular collagen diseases, cardiac emboli, long-distance running, cigarette smoking, constipation, and use of certain drugs (including digoxin, diuretics, estrogen, and nonsteroidal anti-inflammatory drugs).[14,15] Differences in IC treatment efficacy between young to middle-aged patients and elderly patients remain unclear.

The aims of this study were to record our experiences with IC, identify clinical characteristics and risk factors associated with the development of IC, compare hospitalized patients by age cohort (young to middle-aged patients vs. elderly patients), and further analyze therapeutic efficacy among hospitalized patients with a confirmed diagnosis of IC in the hospital.

METHODS

Clinical Samples

Medical records were obtained for 168 patients diagnosed with IC during the period from January 2013 to

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January 2018 in the hospital. Written informed consent for research purposes were obtained from all patients for study participation. Patients were diagnosed with IC according to clinical symptoms, features seen by electron video-endoscopy, and pathological characteristics. Exclusion criteria were (i) age less than 18 years, (ii) colonic ischemia caused by trauma or mechanical factors such as bowel obstruction, volvulus, or hernia, (iii) positive results for enteric pathogens including bacteria, viruses, parasites, etc., (iv) infectious colonic inflammation, and (v) incomplete clinical data (such as records of patients automatically discharged during hospitalization).

Patient Classification

This study included 168 patients (110 women and 58 men) with a mean age of 65.64 ± 12.096 years (range 37-88 years). IC patients were assigned to a young to middle-aged group (age range 18-59 years) or an elderly group (≥60 years).

Data Collection

A retrospective study was undertaken that analyzed patient characteristics including demographics (age and gender), comorbidities, social history, clinical findings (symptoms, physical examination, and vital signs on admission), and radiologic, endoscopic, and pathologic data. In addition, medical records were reviewed for date of IC diagnosis, method of diagnosis, ischemia subsite within the bowel, dates of hospitalization, date(s) and type(s) of surgery, and date of last follow-up or death. Laboratory data on admission, including white blood cells (WBC), neutrophilic granulocyte percentage (NEUT%), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and D-dimer were also assessed. Location and extent of ischemia were recorded based on endoscopic, surgical, and pathologic findings. Treatment (nonsurgical or surgical), outcomes (complications and mortality), and follow-up evaluation after discharge were also analyzed.

Main Points

- *The primary symptoms in the 168 patients with IC were abdominal pain, diarrhea, and hematochezia.*
- *White blood cells (WBC), neutrophilic granulocyte percentage (NEUT%), C-reactive protein (CRP), and D-dimer were significantly elevated in elderly patients.*
- *The sigmoid colon and descending colon were the most common lesion locations.*
- *Hypertension, cerebral infarction, and coronary heart disease were the most common comorbidities in elderly patients, while smoking history was the most common risk factor in young to middle-aged patients.*

Risk Factors

Follow-ups were performed by questionnaire to obtain details about long-term results. We defined risk factors as underlying or recurring conditions with a sustained effect on patients. The following 14 conditions were included as risk factors: hypertension, diabetes mellitus, cerebral infarction, coronary heart disease, chronic gastritis, fatty liver, hepatic cyst, intestinal polyps, biliary tract disease stone or polyp, history of bone fracture, history of abdominal surgery, history of oral medication, history of smoking, and history of drinking.

Statistical Analyses

All variables were analyzed to determine their association with time to surgery or mortality. Statistical analyses were performed using GraphPad Prism software (version 8.0.1) (Graphpad Software Inc, USA) and SPSS statistics 22.0 (IBM Corp.; Armonk, NY, USA). The results were expressed as means ± standard deviations (SD). Differences between demographic and clinicopathological ratios were tested for significance by c^2 test, Fisher's exact test, and the Mann–Whitney *U* test. Exact 95% CI limits for binomial proportion were computed by the *F* distribution method of Collett. Statistical significance is defined as $P < .05$.

RESULTS

Clinical Characteristics

During the study period, a total of 191 patients were diagnosed with IC by electron video-colonoscopy combined with pathological biopsy. Among the 191 cases reviewed, 23 patients were excluded due to characteristics such as other organic bowel diseases (n = 11), incomplete admission data (n = 8), and automatic discharge during treatment (n = 4). A total of 168 patients (110 women and 58 men) were included in the study (65.5 vs. 34.5%, ratio; 1.9:1.0). The average age at the time of diagnosis was 65.46 ± 12.09 years (range 37-88 years) (Table 1). Among the patients enrolled, 86.2% were older than 60 years; 55 (61.1%) of these were female and 35 (38.9%) were male. The most common symptoms on admission were abdominal pain (94.6%), bloody diarrhea (86.9%), nausea and vomiting (26.8%), diarrhea (26.3%), and change in bowel habits (12.5%). Most patients exhibited multiple symptoms. Incidence of diarrhea, hematochezia, nausea, and vomiting was significantly lower in the young to the

Table 1. Clinical Characteristics of all Patients with Ischemic Colitis (IC)

Clinical Characteristics	Patients (*n* = 168)
Mean age, years (mean ± SD)	65.64 ± 12.096
Age range	37-88
Gender, *n* (%)	
Male	58 (34.5%)
Female	110 (65.5%)
Laboratory tests, *n* (%)	
WBC↑	40 (23.8%)
NEUT%↑	40 (23.8%)
CRP↑	54 (32.1%)
D-dimer ↑	60 (35.7%)
ESR↑	55 (32.7%)
Predisposing factors, *n* (%)	
Diet	30 (17.9%)
Exercise	7 (4.2%)
Alcohol	25 (14.9%)
Other	6 (3.6%)
Clinical manifestations, *n* (%)	
Abdominal pain	159 (94.6%)
Diarrhea	44 (26.2%)
Hematochezia	146 (86.9%)
Nausea and vomiting	45 (26.8%)
Changes in stool behavior	21 (12.5%)
Location of the lesion, *n* (%)	
Descending colon	57 (33.9%)
Sigmoid colon	96 (57.1%)
Transverse colon	28 (16.7%)
Junction of sigmoid colon and descending colon	21 (12.5%)
Rectal	12 (7.1%)
Splenic flexure	7 (4.2%)
Hepatic flexure	5 (3.0%)
Total colon	2 (1.2%)
Ascending colon	2 (1.2%)
Other	16 (9.5%)
Concomitant chronic disease, *n* (%)	
Hypertension	81 (48.2%)
Cerebral infarction	19 (11.3%)
Diabetes mellitus	30 (17.9%)
Coronary artery disease	43 (25.6%)
Heart arrhythmias	25 (14.9%)

Data are available in 168 patients.
WBC, white blood cells; NEUT %, neutrophilic granulocyte percentage; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate.

Table 2. Clinical Manifestations in IC Patients

	Young and Middle-Aged (*n* = 78)	Elderly People (*n* = 90)	*P*
Abdominal pain	74 (94.9%)	85 (94.4%)	.902
Nausea and vomiting	13 (16.7%)	32 (35.6%)	<.01
Hematochezia	62 (79.5%)	84 (93.3%)	<.01
Changes in stool behavior	12 (15.4%)	9 (10.0%)	.293
Diarrhea	14 (17.9%)	30 (33.3%)	.024

middle-aged group than in the elderly group ($P < .05$) (Table 2).

Laboratory Diagnostic Studies

To identify the laboratory diagnostic indicators, we compared young to middle-aged IC patients with elderly IC patients by differential indicators analysis (Table 3). Among the 168 IC patients, frequently seen indicators included abnormal D-dimer (35.7%), ESR (32.7%), CRP (32.1%), WBC (23.8%), and NEUT% (23.8%). Importantly, the prevalence of abnormal WBC, NEUT%, CRP, and D-dimer was significantly lower in the young to the middle-aged group than in the elderly group ($P < .05$). The prevalence of ESR was not significantly different between

Table 3. Laboratory Tests for IC Patients

	Young and Middle-Aged (*n* = 78)	Elderly People (*n* = 90)	χ^2	*P*
WBC				
Normal	66 (84.6%)	62 (68.9%)	5.697	.017
Increased	12 (15.4%)	28 (31.1%)		
NEUT%				
Normal	67 (85.9%)	61 (74.4%)	7.563	<.01
Increased	11 (14.1%)	29(25.6%)		
ESR				
Normal	52 (66.7%)	61 (67.8%)	0.023	.878
Increased	26 (33.3%)	29 (32.2%)		
CRP				
Normal	62 (79.5%)	52 (57.8%)	9.029	<.01
Increased	16 (20.5%)	38 (42.2%)		
D-dimer				
Normal	59 (75.6%)	49 (54.4%)	8.177	<.01
Increased	19 (24.2%)	41 (45.6%)		

Table 4. Diseased Tissue Locations Among IC Patients

	Young and Middle-Aged (n = 78)	Elderly People (n = 90)	χ^2	P
Transverse colon	13 (16.7%)	15 (16.7%)	0.000	1.000
Descending colon	19 (24.4%)	38 (42.2%)	5.948	.015
Sigmoid colon	38 (48.7%)	58 (64.4%)	4.220	.040
Junction of sigmoid and descending colon	10 (12.8%)	11 (12.2%)	0.014	.907
Rectum	7 (9.0%)	5 (5.6%)	0.736	.391
Other	6 (7.7%)	10 (11.1%)	0.567	.452

the 2 groups (P > .05). These results suggest that WBC, NEUT%, CRP, and D-dimer are likely to be IC diagnostic indicators.

Location of the Disease

To further analyze the prognosis among IC patients, we performed a statistical analysis of the main site of disease among different IC patients. Among the 168 total patients, multiple different sections were affected. Overall, we found that more than half of the IC patients had 2 or more affected colon segments. A total of 10 commonly affected locations were identified. Endoscopy indicated that lesions in young to middle-aged IC patients usually occurred in the sigmoid colon (48.7%), descending colon (24.4%), transverse colon (16.7%), sigmoid colon and descending colon (12.8%), rectum (9.0%), and others (7.7%). The lesions in elderly patients mainly occurred in the sigmoid colon (64.4%), descending colon (42.2%), transverse colon (16.7%), sigmoid colon, descending colon (12.2%), rectum (5.6%), and others (11.1%). Interestingly, the prevalences of lesions of the sigmoid colon and descending colon were significantly lower in the young to middle-aged group (P < .05), while lesions in the transverse colon, sigmoid colon, descending colon, and other colon sites displayed no differential prevalence between groups (P > .05). The allocation of risk factors to IC sites is shown in Table 4.

Comorbidities

Chronic diseases accompany IC mainly in elderly patients, with fewer incidences in young to middle-aged IC patients. The most common comorbidities in young to middle-aged IC patients were hypertension (35.9%), diabetes mellitus (10.3%), cerebral infarction (3.8%), coronary heart disease (17.9%), and arrhythmia (11.5%). The most common comorbidities among elderly patients included hypertension (58.9%), diabetes (24.4%), cerebral infarction (17.8%), coronary heart disease (32.2%), and arrhythmia (17.8%). The comorbidities of hypertension, diabetes mellitus, cerebral infarction, and coronary heart disease were significantly lower among young to middle-aged patients than among the elderly group (P < .05), and incidence of arrhythmia displayed no difference between age cohorts (P > .05). The distributions of chronic diseases among young to middle-aged patients and elderly patients are shown in Table 5.

Risk Factor Analyses

We analyzed risk factors and their associations with conditions or events. The prevalence of putative IC risk factors among 78 young to middle-aged patients and 90 elderly patients is shown in Table 6. As expected, an evident history of risk-associated oral medication was found in 103 IC patients (61.3%). Hypertension was the next most common risk factor, found in 81 patients (48.2%), followed by a history of abdominal surgery in 72 patients (42.9%), chronic gastritis in 66 patients (39.3%), biliary tract disease stones or polyps in 54 patients (32.1%), intestinal polyps in 43 patients (25.6%), and coronary heart disease in 43 patients (25.6%). Additional precipitating factors were seen in the patient data of 44 IC patients. The main factors included unhealthy diet and alcohol abuse. The odds of developing IC were higher in cigarette smokers (current or ever) (P < .05) than in those

Table 5. Comorbidities Among IC Patients

	Young and Middle-Aged (n = 78)	Elderly People (n = 90)	χ^2	P
Hypertension	28 (35.9%)	53 (58.9%)	10.943	<.01
Cerebral infarction	3 (3.8%)	16 (17.8%)	10.110	<.01
Diabetes mellitus	8 (10.3%)	22 (24.4%)	5.734	.017
Coronary heart disease	14 (17.9%)	29 (32.2%)	4.470	.034
Arrhythmia	9 (11.5%)	16 (17.8%)	1.284	.257

Table 6. Risk Factors Among IC Patients

	Patients (n = 168)			
Risk Factors	Young and Middle-Aged (n = 78)	Elderly People (n = 90)	χ^2	P
Hypertension, n (%)				
Yes	28 (35.9%)	53 (58.9%)	10.943	<.01
No	50 (64.1%)	37 (41.1%)		
Diabetes mellitus, n (%)				
Yes	8 (10.3%)	22 (24.4%)	4.470	.034
No	70 (89.7%)	68 (75.6%)		
Cerebral infarction, n (%)				
Yes	3 (3.8%)	16 (17.8%)	8.086	<.01
No	75 (96.2%)	74 (82.2%)		
Coronary heart disease, n (%)				
Yes	14 (17.9%)	29 (32.2%)	7.897	<.01
No	64 (82.1%)	68 (67.8%)		
Chronic gastritis, n (%)				
Yes	35 (44.9%)	31 (34.4%)	1.905	.168
No	43 (55.1%)	59 (65.6%)		
Fatty liver, n (%)				
Yes	10 (12.8%)	12 (13.3%)	0.01	.922
No	68 (87.2%)	78 (86.7%)		
Hepatic cyst, n (%)				
Yes	10 (12.8%)	14 (15.6%)	0.255	.613
No	68 (87.2%)	76 (84.4%)		
Intestinal polyps, n (%)				
Yes	14 (17.9%)	29 (32.2%)	4.470	.034
No	64 (82.1%)	61 (67.8%)		
Biliary tract disease stone or polyp, n (%)				
Yes	26 (33.3%)	28 (31.3%)	0.095	.758
No	52 (66.7%)	62 (68.7%)		
History of bone fracture, n (%)				
Yes	4 (5.1%)	15 (16.7%)	5.932	.026
No	74 (94.9%)	75 (83.3%)		
History of abdominal surgery, n (%)				
Yes	28 (35.9%)	44 (48.9%)	2.88	.09
No	50 (64.1%)	46 (51.1%)		
History of oral medication, n (%)				
Yes	40 (51.3%)	63 (70.0%)	6.997	<.01
No	38 (48.7%)	27 (30.0%)		
History of smoking, n (%)				
Yes	20 (25.6%)	11 (12.2%)	5.000	.025
No	58 (74.4%)	79 (87.8%)		
History of drinking, n (%)				
Yes	6 (7.7%)	7 (7.8%)	0.000	.984
No	72 (92.3%)	83 (92.2%)		

who had never smoked. Smoking as a factor was obviously higher among young to middle-aged patients than among elderly patients. An unhealthy diet was also significantly higher among young to middle-aged patients than among elderly patients ($P < .01$). No difference was observed between the younger and elderly in exercise ($P > .05$). The proportion of young and middle-aged IC patients with a history of alcohol abuse was significantly higher than that among elderly patients ($P < .01$). No differences were seen in other factors ($P > .05$). Risk factor analyses comparing age cohorts are displayed in Table 6.

DISCUSSION

IC refers to inflammation of the colon secondary to vascular insufficiency and ischemia. The etiology of IC is multifactorial, and clinical presentation is variable.[16] In this study, patients with IC were more likely to be elderly and female. These results reflect those of Sherid et al.[17,] who found that the incidence of IC in women is significantly higher than that in men. This result is likely to be related to dysregulated hormone levels and blood hypercoagulability in women as a result of taking birth control pills. Other relevant data indicate that oral contraceptives and abdominal surgery are related risk factors for IC.[17,18] In this study, one patient's IC was induced by oral contraceptives. In recent years, many women are willing to reduce labor pain by accepting cesarean section, which may increase the incidence of IC among females. Therefore, women can reduce the incidence of this disease in some ways by lifestyle choices.

Previous research has established that acute infection indicators such as WBC, NEUT%, and CRP have clinical potential for early diagnosis of IC.[19,20] In this study, WBC, NEUT%, CRP, and D-dimer were abnormally increased in elderly patients. These acute infection indicators may be regulated by the body's own immune system. The elderly have slower metabolisms, lower immunity, and weaker resistance, priming these acute infection indicators for more sensitive responses. In recent years, studies have found that D-dimer can contribute to early diagnosis and prognosis of acute mesenteric ischemia.[21,22] Prognosis worsens in proportion to D-dimer elevation.[23] The proportions of elderly IC patients with elevated indicators were D-dimer (45.6%) > CRP (42.2%) > ESR (32.2%)> WBC (31.1%). D-dimer may become a serological indicator for early diagnosis of IC in the elderly. Among the 168 IC patients studied, 68 patients had elevated ESR. However, there was no difference between age cohorts. The reason may be complex etiology and lack of specificity.

Diagnosis may be difficult given the non-specific presenting symptoms which may be similar to those seen with other colonic diseases.[24] Abdominal pain, hematochezia, and diarrhea were the most common symptoms in IC patients.[25] Sridhar et al.[6] demonstrated that the left colon was the most affected segment in IC. In our study, the sigmoid colon and descending colon were the most commonly affected segments, and the rectum and ascending colon were the least affected segments, consistent with previously reported data.[17,26] In observational studies, there is a potential for bias due to age-related differences in the site of presentation. For instance, the descending colon and sigmoid colon were significantly more common presentation sites in the elderly cohort than in the young to the middle-aged cohort. These results indicate that IC lesions in the elderly are likely to be found in the descending colon and/or sigmoid colon, but such lesions need to be distinguished from other inflammatory bowel diseases to achieve an accurate diagnosis.

Among the 168 IC patients, 40.6% had predisposing factors; 57.7% of those with predisposing factors were young to middle-aged patients. Hyun Il Seo[27] has confirmed that hypertension (54.7%), diabetes mellitus (19.5%), and constipation (17.6%) are common risk factors, consistent with our study. Improper diet could induce IC in both elderly patients (11.1%) and young to middle-aged patients (25.6%). Recent evidence suggests that a history of abdominal surgery is a risk factor for IC,[28] which may be exacerbated under certain conditions. We found no difference in the history of abdominal surgery between the different age cohorts. We found that smoking is an independent risk factor for young to middle-aged IC patients, possibly related to harmful substances in tobacco. Most studies show that chronic constipation and irritable bowel syndrome are independent risk factors for IC in young to middle-aged people.[29,30] There were insufficient cases with relevant medical history in this study; thus, no analyses of these conditions were performed.

Many questions regarding ischemic bowel disease remain unanswered, and its incidence is increasing. At present, there are few studies on clinical manifestations, diagnosis, treatment, or prevention, and further prospective research is needed to guide clinical treatment and prevention efforts.

CONCLUSION

Our study has demonstrated, despite its limitations, that the descending colon and sigmoid colon were the most affected segments in IC patients. Some IC risk factors

may correlate with age. IC was more frequently induced in young to middle-aged patients by alcohol and smoking, while elderly IC patients were more prone to chronic diseases. Abnormal levels of acute infection indicators WBC, CRP, and D-dimer were higher in the elderly group, suggesting that these biomarkers may serve as early indicators of IC in elderly patients.

Ethics Committee Approval: This study was approved by the Shanghai Huadong Hospital Human Investigation Committee. Written informed consent for research purposes was obtained from all patients for study participation.

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