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Ischemic colitis: risk factors for eventual surgery

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Abstract

BACKGROUND: Ischemic colitis is a common disorder often without clear indications for surgical management. The aim of this study was to identify risk factors that predict the need for surgery.

METHODS: Patients were identified retrospectively based on International Classification of Disease codes and admission over an 8-year period.

RESULTS: A total of 253 patients presented with ischemic colitis. A total of 205 patients were managed nonsurgically, 12 underwent immediate surgery (within 12 hours of presentation), and 36 had delayed surgery. On univariate analysis, risk factors that predicted delayed surgery were peripheral vascular disease, atrial fibrillation, hypotension, tachycardia, absence of bleeding per rectum, free intraperitoneal fluid on computed tomography scan, intensive care unit admission, vasopressors, mechanical ventilation, and increased lactate level on admission. Intraperitoneal fluid on computed tomography scan and absence of bleeding per rectum were predictive of surgical intervention on multivariate analysis.

CONCLUSIONS: In patients with ischemic colitis, several risk factors were associated with the need for subsequent surgery during the same admission. These factors could be used to select patients for immediate surgery before worsening of their clinical condition.

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Ischemic colitis is the most common ischemic disorder of the gastrointestinal tract.[1] Because it typically affects elderly people, the incidence is increasing owing to the aging of the population. Colonic ischemia has been reported in approximately 3 patients per 1,000 hospital admissions in a tertiary care center.[2] Significant mortality rates up to 50% have been described in the literature.[1,3,4] Late diagnosis, delayed treatment, and coexisting comorbidities may be important contributing factors to complications and mortality of ischemic colitis. The clinical course ranges from mild self-limiting forms to severe gangrenous colitis. In the milder forms, only the mucosa and submucosa are involved with edema, submucosal hemorrhage, and ulcerations. Clinically, these patients have lower gastrointestinal bleeding that improves either spontaneously or with conservative measures. In contrast, the severe forms of colon ischemia are marked by transmural necrosis of the bowel, often require surgery, and may be life-threatening. The initial clinical presentation may be similar in both mild and severe forms and is not predictive of the severity of the ischemic insult. Therefore, it is difficult to forecast which patients will need surgery. The purpose of this study was to identify risk factors that predict the need for surgery and are detectable on admission in patients with ischemic colitis.

Methods

Data collection

A retrospective review included all patients admitted at Yale New Haven Hospital for ischemic colitis over a period

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of 8 years (2000–2007). Patient identification was based on the International Classification of Disease Codes. This study was approved by the Yale University Human Investigation Committee. Diagnosis was based on clinical, radiographic, endoscopic, and pathologic data. Patients with colon ischemia caused by trauma, bowel obstruction, volvulus, or hernia were excluded.

Patient demographics (age, sex), comorbidities, social history, American Society of Anesthesiologists class, clinical findings (symptoms, physical examination, vital signs on admission), laboratory data on admission (white blood cell count, hematocrit, serum lactic acid, serum bicarbonate, serum creatinine levels), and radiologic, endoscopic, and pathologic data were recorded. Hypotension was defined as systolic blood pressure lower than 90 mm Hg, and tachycardia as heart rate greater than 100 beats/min. The location and extension of ischemia was documented according to endoscopic, surgical, and pathologic findings. Treatment (nonsurgical or surgical), outcomes (complications and mortality), and follow-up evaluation after discharge were analyzed.

Classification of patients

Patient treatment was classified as immediate surgery (surgical treatment within 12 hours from admission or surgical consultation), delayed surgery (surgery performed more than 12 hours after admission owing to worsening clinical condition), and nonsurgical (limited to medical and supportive measures). Nonsurgical management included intravenous antibiotics, bowel rest, intravenous fluid resuscitation, serial abdominal examinations, and daily laboratories.

Statistical analysis

All variables were evaluated with univariate and multivariate analysis to determine if they were associated with delayed surgery or mortality. The data were analyzed using the statistical package SPSS 16.0 for Windows (SPSS, Chicago, IL). Univariate statistical analysis used the Mann–Whitney U test, the Fisher exact test, and the chi-square test ·here appropriate. Multivariate analysis was with reverse ɔwise logistic regression including all variables from the ıvariate analysis with a P value of less than .2.

Results

A total of 253 patients were admitted and treated for ischemic colitis during the 8-year study period. The mean age was 68.4 years (standard deviation, 15.9 y); 182 patients were female (72%), and 71 were male (28%). A total of 218 patients (86%) presented to the Emergency Department with their primary complaint related to ischemic colitis. Thirty-five patients (14%) developed ischemic colitis while they were hospitalized for other reasons: 6 patients were admitted for acute coronary syndrome, 4 for respiratory failure, 2 for retroperitoneal hematoma, 5 developed ischemic colitis after coronary artery bypass, 3 developed ischemic colitis after abdominal aortic aneurysm repair, 3 developed ischemic colitis after abdominal surgical procedures, and the remaining 12 were admitted for different other medical reasons.

Table 1 Patient characteristics

Characteristics	No. of patients (%)
Women	182 (72)
Men	71 (28)
Mean age ± SD, y	68.4 ± 15.9
Comorbidities	
Hypertension	166 (66)
Coronary artery disease	94 (37)
Diabetes mellitus	62 (25)
Peripheral vascular disease	52 (21)
Chronic renal failure	45 (18)
Dialysis	18 (7)
Atrial fibrillation	37 (15)
Smokers (active)	34 (13)
Alcohol (active)	17 (7)
Symptoms	
Abdominal pain	188 (74)
Bleeding per rectum	157 (62)
Diarrhea	80 (32)
Nausea/vomiting	65 (26)
Presyncope/syncope	24 (10)
Fever	8 (3)
Total patients	253 (100)

Hypertension was the most common comorbidity (Table 1): it was reported in 166 patients (66%). Other comorbidities were coronary artery disease, diabetes mellitus, peripheral vascular disease, chronic renal failure, and atrial fibrillation. Thirty-four patients (13%) were active smokers and 17 (7%) were active drinkers. The most common symptom was abdominal pain (74% of patients), followed by bleeding per rectum (62%), diarrhea (32%), and nausea/vomiting (26%).

A total of 165 patients were diagnosed with ischemic colitis by colonoscopy and biopsy. The remaining 88 patients underwent computed tomography (CT) of the abdomen and pelvis. Forty-one of 88 patients underwent exploratory laparotomy and colectomy: the diagnosis was confirmed by the pathology on specimen. In the remaining 47 of 88 patients the diagnosis was based on CT findings (bowel wall thickening in 47, free fluid in the abdomen in 7, and pneumatosis intestinalis in 2), negative *Clostridium difficile* tests, and negative stool cultures.

The distribution of disease along the large bowel is reported in Table 2. The distribution was determined based on colonoscopy and biopsy in 168 patients, CT scan in 158 patients, and surgical findings in 48 cases. The location in the left colon was defined as extensive involvement of the splenic flexure, descending colon, and sigmoid. The distri-

Table 2 Location of ischemic colitis

Location	N patients (%)
Sigmoid colon	53 (20.9)
Left colon	48 (19.0)
Right colon	45 (17.8)
Splenic flexure	32 (12.6)
Descending colon	25 (9.9)
Total colonic	24 (9.4)
Transverse colon	9 (3.6)
Cecum	6 (2.4)
Left colon and rectum	5 (2.0)
Hepatic flexure	4 (1.6)
Ascending colon	2 (0.8)
Total	253 (100)

bution in the right colon was defined as involvement of the ascending colon and hepatic flexure.

Twelve of 253 patients (5%) underwent immediate surgery (within 12 hours of admission or surgery consultation) and were excluded from the study group. A total of 241 patients initially were managed nonsurgically and formed the study group. Thirty-six of 241 patients underwent delayed surgery owing to worsening of clinical conditions or no response to conservative therapy. The median time to delayed surgery was 36 hours. Ninety-four percent of patients had surgery within 72 hours. The remaining 205 patients were treated nonsurgically (Fig. 1). The group of patients who initially were managed nonsurgically were studied to identify risk factors predicting the need for delayed surgery. On univariate analysis (Table 3), risk factors that predicted delayed surgery included peripheral vascular disease, atrial fibrillation, hypotension, tachycardia, absence of bleeding per rectum, intensive care unit admission, vasopressors, mechanical ventilation, free intraperitoneal fluid on CT scan, and increased serum lactate on presentation. Intraperitoneal fluid on CT scan (odds ratio, 50.000; 95% confidence interval, 6.757–333.333; $P < .001$) and absence of bleeding per rectum (odds ratio, 14.085; 95% confidence interval, 1.626–125.0; $P = .016$) were predictive of delayed surgery on multivariate analysis.

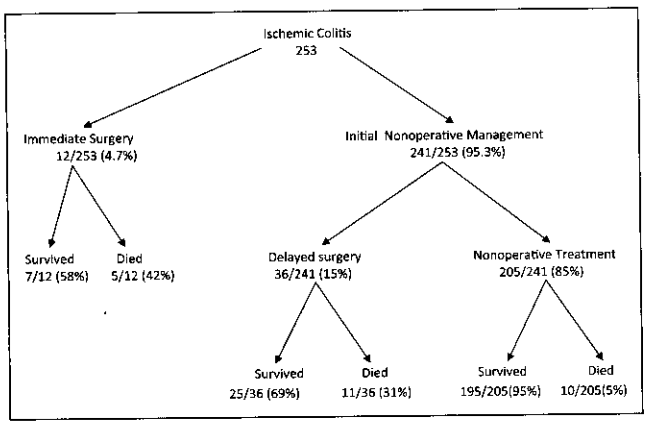


Figure 1 Outcomes of 253 patients with ischemic colitis

Table 3 Predictive factors of delayed surgery in ischemic colitis by univariate analysis

Variables	Odds Ratio [95% CI]	P
Peripheral Vascular Disease	2.700 [1.216–5.993]	$P = 0.012$
Atrial Fibrillation	3.504 [1.483–8.280]	$P = 0.006$
Coronary Artery Disease	1.754 [0.823–3.736]	$P = 0.142$
Chronic Renal Failure	1.778 [0.736–4.296]	$P = 0.197$
Hypotension (SBP < 90)	8.599 [3.380–21.875]	$P < 0.001$
Tachycardia (HR > 100)	4.148 [1.880–9.151]	$P < 0.001$
Fever > 101.5 F	3.417 [0.600–19.467]	$P = 0.182$
Absence of bleeding per rectum	3.700 [1.127–12.195]	$P = 0.043$
ICU admission	9.219 [4.107–20.695]	$P < 0.001$
Vasopressors	22.444 [8.033–62.707]	$P < 0.001$
Mechanical ventilation	19.744 [7.033–55.428]	$P < 0.001$
Free peritoneal fluid on CT	9.343 [3.279–26.619]	$P < 0.001$
Serum lactate >3.5 mMol/L on admission	12.505 [4.302–36.346]	$P < 0.001$

Twenty-six of 253 patients (10.3%) died during the index admission: 5 (19%) had immediate surgery, 11 (42%) had delayed surgery, and 10 (39%) were managed nonsurgically. The patients treated nonsurgically were evaluated to identify risk factors predicting mortality. On univariate analysis, factors associated with death were peripheral vascular disease, chronic renal failure, aspirin, clopidogrel (Plavix, Bristol-Myers Squibb/Sanofi Pharmaceuticals, New York, NY), hypotension, tachycardia, intraperitoneal free fluid on CT, intensive care unit admission, vasopressors, mechanical ventilation, low serum bicarbonate level, high serum lactate level, and increased serum creatinine level on admission. On multivariate analysis, lower serum bicarbonate level on admission ($P = .039$) and use of clopidogrel (odds ratio, 11.596; 95% confidence interval, 1.567–85.838; $P = .016$) were predictive of mortality in patients managed nonsurgically. Myocardial infarction, cardiac arrhythmias, and congestive heart failure were significant complications that contributed to the death in most of the patients on clopidogrel.

A total of 48 patients underwent surgery for ischemic colitis: 14 patients had subtotal colectomy and 34 patients had segmental colonic resections (right hemicolectomy in 24, left hemicolectomy in 7, cecectomy in 2, and transverse colectomy in 1). The mortality rate was 43% for patients who underwent subtotal colectomy and 35% for patients who underwent segmental colectomy. In the group of segmental colectomy patients, only 1 required a subtotal colectomy that was performed during a second-look laparotomy. A primary anastomosis was performed in 17 patients: 13 had right hemicolectomy, 2 left hemicolectomy, and 2 subtotal colectomy.

Follow-up data were available on 190 patients with a median follow-up period of 50 months. A recurrence was observed in 25 of 190 patients (13%), the mean time to recurrence was 16 months. Two patients with a recurrence

required surgical resection. All recurrences, but one, occurred in patients who were treated nonsurgically.

Comments

Ischemic colitis is the most common form of ischemic disorder of the large bowel. The incidence of ischemic colitis in the general population ranges from 4.5 to 44 cases per 100,000 person-years in different reports.[5] Although it can occur in young patients, ischemic colitis is considerably more common in the elderly. In our study, the mean age was 68 years and the prevalent sex was female (72%). Because the mean age of the American population is increasing, the incidence of ischemic colitis likely will increase in the near future.[6]

Most patients (86%) developed ischemic colitis and presented to the Emergency Department with main complaints of abdominal pain and bleeding per rectum. Fourteen percent of patients developed colonic ischemia as a complication during hospitalization for other reasons. The etiology of ischemic colitis likely is related to an imbalance between blood supply and metabolic demands of the large bowel.[7] In most cases, however, no major mesenteric vascular occlusion is found. Angiogram often shows no abnormalities in the major trunks of the mesenteric vasculature.[8] Risk factors associated with ischemic colitis were hypertension, coronary artery disease, diabetes mellitus, peripheral vascular disease, chronic renal failure, hemodialysis, and atrial fibrillation. Most of these factors are associated with medium and small artery pathology that could explain a reduction of the reserve of blood supply to the large bowel. Furthermore, hemodialysis may predispose to low-flow states with decreased bowel perfusion.[1] In the group of patients that developed ischemic colitis while hospitalized for other reasons, shock, low perfusion states, and ligation of the inferior mesenteric artery were the most common suspected causes of colonic ischemia.

The clinical presentation of ischemic colitis covers a wide spectrum from mild self-limiting forms to severe, fulminant, life-threatening courses. Mild forms consist of transient ischemia involving only mucosa and submucosa; these usually resolve with nonsurgical treatment. Full-thickness colonic necrosis is present in most severe cases—prognosis may be poor and surgical treatment is the rule. The rate of severe ischemic colitis ranges between 8% and 50% in different series.[1,2,9] This variation of rates is related to the different definition of severe ischemic colitis in different studies and to selection bias depending if it was a medical or a surgical series. The widespread use of colonoscopy as the gold standard diagnostic test allows more accurate diagnosis because many mild forms that in the past generally were diagnosed as indeterminate colitis now are identified as ischemic colitis.[1]

Absolute indications for surgery in the acute phase include peritonitis and pneumoperitoneum. However, the initial clinical presentation is not always straightforward: patients often present with abdominal pain, tenderness, and dehydration without peritoneal signs. In these cases, it is difficult to predict the severity of the clinical course and the need for surgical intervention. A retrospective series showed that male sex, age younger than 80 years, absence of bleeding per rectum, and abdominal tenderness were associated with severe form of ischemic colitis.[9] Chronic renal failure and hemodialysis also have been identified as risk factors for morbidity and mortality from ischemic colitis.[10,11] The extent of disease is an important criteria in the assessment of this disorder. Total colonic ischemia carries a higher mortality rate when compared with segmental ischemic colitis.[10] A recent retrospective study showed that right colon ischemia is associated with a 5-fold higher frequency of surgery and 2-fold higher mortality than other locations of ischemic colitis.[2]

In the present multivariate analyses, we identified risk factors for 2 outcomes: need for surgery and death. The absence of bleeding per rectum and the presence of intraperitoneal free fluid on CT were associated with a significant risk for delayed surgery in patients initially treated nonsurgically. The absence of bleeding per rectum was found as a negative prognostic factor also in 2 previous series.[9,12] The presence of intraperitoneal free fluid on CT is probably a marker of transmural ischemia of the colonic wall causing peritoneal inflammation. Low serum bicarbonate level on admission and a history of use of clopidogrel were predictors of mortality in the nonsurgical group. The serum bicarbonate level provides a good estimation of acidosis and tissue ischemia. The use of an antiplatelet drug is likely a marker of systemic arterial disease implying a compromise of the intestinal vascular supply. If one can better predict who will eventually require surgery early in the clinical course of the patient, perhaps an outcome benefit may be realized. Because many patients with ischemic colitis are elderly, they have limited physiologic reserve and cannot tolerate bacterial translocation, sepsis, and shock that occur when ischemic colitis progresses into transmural necrosis.

In cases with limited extension of disease and no hemodynamic instability, a segmental colon resection seems to be an effective option.[8,13] In our series, segmental colectomy did not carry worse results when compared with subtotal colectomy. During surgery, the mucosa should be examined to obtain mucosal margins free of ischemia. In cases with questionable resection margins or hemodynamic instability, a temporary abdominal closure and second-look laparotomy should be considered. In patients with right-sided ischemic colitis where the ileum and transverse colon are well vascularized, a primary anastomosis usually is performed with good results. In contrast, patients with left-sided ischemic colitis or pancolitis usually undergo resection and colostomy during the first surgery.[13]

Despite the advances in surgical techniques, anesthesia, and critical care the mortality rate after surgery for ischemic colitis is reported as 40% to 50%.[1,2,9,14,15] In our series the mortality rate after surgery was 33%. It is reasonable to conclude that avoiding delay in treatment and performing

surgery before deterioration of a patient's clinical condition may be a good strategy to decrease this mortality rate.

Few studies have evaluated follow-up and recurrence rate in patients after a first episode of ischemic colitis. In a previous series of 58 patients, the recurrence rate of ischemic colitis was 8.6% in 4 years. In our study, 190 patients were followed up for 5 years and the recurrence rate was 13%. Only 2 patients (1%) required surgery for recurrence, all the other cases resolved with nonsurgical treatment.

In conclusion, ischemic colitis is the most common mesenteric ischemic disorder. It is more prevalent in elderly patients and females. It is commonly associated with hypertension, atherosclerosis, diabetes mellitus, and renal failure. Clinical management and surgical indications are not always straightforward. Factors predictive of failure of nonsurgical management include history of clopidogrel use, lack of bleeding per rectum, presence of intraperitoneal fluid on CT, and low serum bicarbonate level on admission. All these factors could be used to identify patients who may benefit from early surgical intervention before deterioration of their condition. If patients successfully can be managed nonsurgically through discharge it is unlikely they will ever require surgical resection.

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