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Outcomes of patients with ischemic colitis causing severe hematochezia managed medically or surgically

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Abstract

Purpose To compare short- and long-term outcomes of hospitalized patients with ischemic colitis (IC) presenting with severe hematochezia and treated medically or colectomy and also those with inpatient vs. outpatient start of hematochezia. **Methods** A retrospective analysis of prospectively collected data for IC patients hospitalized for severe hematochezia from two teaching hospitals was done from 1994 to 2020, with the diagnosis of IC made colonoscopically and confirmed histologically.

Results Ninety-seven patients initially all had medical management for IC. Seventy-two (74.2%) were stable and had no further bleeding; 17 (17.5%) had colon resection; and 8 were critically ill and not surgical candidates. Surgical patients and non-surgical candidate had higher comorbidity scores; received more red blood cell (RBC) transfusion (median (IQR) 5 (3–10) vs. 4.5 (3–6.5) vs. 1 (0–4) units, p < 0.001); had significantly longer hospital and ICU days; had higher severe complication rates (35.3% vs. 100%. vs. 5.6%, p < 0.001); and had higher 30-day all-cause mortality rates (23.5% vs. 87.5% vs. 0, p < 0.001). Inpatients developing IC hemorrhage had more RBC transfusions, more complications, longer hospital stays, and higher mortality than patients whose IC bleeding started as outpatients.

Conclusions The majority of IC patients hospitalized for severe hematochezia were successfully treated medically. Patients who were not surgical candidate had the highest rates of severe complications and mortality. Surgical patients and those who were not surgical candidate had worse outcomes than the medical group. Patients with inpatient start of bleeding from IC had significantly worse outcomes than those with outpatient start of bleeding.

Keywords Ischemic colitis \cdot Hematochezia \cdot Lower gastrointestinal bleeding \cdot Colectomy \cdot Medical management \cdot Clinical outcomes

Introduction

Ischemic colitis (IC) is a very common colonic cause of severe hematochezia in referral centers [1]. IC with severe hematochezia is usually distinguishable from colon

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infarction or embolism where patients present to surgical services with severe abdominal pain, hypotension, fever, peritonitis, but not severe hematochezia [1]. IC is more prevalent in elderly patients with multiple comorbidities, e.g., atherosclerotic disease, congestive heart failure, chronic

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kidney disease, recent abdominal aortic aneurysm repair, or recent hypotension [2-5]. However, IC may occur in younger persons with other risk factors, e.g., cigarette smoking, cocaine use, hypercoagulable states, collagen vascular diseases, or with no predisposing factors [6-8].

IC with severe hematochezia without full-thickness necrosis is hypothesized to occur when the colonic blood flow is compromised due to acute, transient hypoperfusion, leading to ischemic mucosal injury, inflammatory changes, and reperfusion injury [9, 10]. Management of IC depends upon the etiology, location, and severity and extent of colonic wall injury [4, 11, 12]. Overall mortality in patients with severe IC remains high, ranging from 6 to 53% [4, 13]. However, 80% of patients with reversible colopathy and non-transmural IC are successfully managed with medical treatment. Colectomy is only required in those with severe bleeding, perforation, or recurrent sepsis from IC [9, 12, 14].

In this study, we compared 30-day and follow-up outcomes of medical management and colon resection in patients with ischemic colitis who initially presented with severe hematochezia without severe abdominal pain, peritonitis, or only radiologic evidence of ischemia. Our aim was to compare the clinical outcomes of 3 subgroups of IC patients with severe hematochezia: those managed medically, medical failures treated surgically, and those referred for surgery but not considered to be surgical candidates because of severe comorbidities. We also compared outcomes of those with inpatient (INPT) versus outpatient (OUTPT) start of hematochezia.

Materials and methods

Study design

This is a retrospective analysis of prospectively collected data of hospitalized patients with severe hematochezia and a confirmed diagnosis of IC by colonoscopy and histopathology. All eligible patients in this study had been enrolled in Institutional Review Board (IRB)–approved prospective studies of severe hematochezia between February 1994 and 2020 at Ronald Reagan UCLA Medical Center or the Veterans Administration (VA) Greater Los Angeles Healthcare System. Patients were identified from the Center of Ulcer Research and Education (CURE) Hemostasis Research group databases and any missing data were retrieved from study charts and/or medical records.

Outcome measures

Primary outcomes of the three subgroups of patients were 30-day morbidity and mortality. Secondary outcomes were recurrence of IC, development of colonic strictures, and all-cause mortality during long-term follow-up. Other secondary outcomes were 30-day morbidity and mortality of IC patients who had hematochezia starting as inpatients (after hospitalization for a non-gastrointestinal bleeding medical or surgical diagnosis) vs. outpatients.

Inclusion and exclusion criteria

Inclusion criteria were patients \geq 18 years old who (1) were hospitalized with severe hematochezia or had been hospitalized for other medical conditions but developed severe hematochezia during hospitalization; (2) were diagnosed with IC during initial urgent colonoscopy performed by the CURE Hemostasis Group; and (3) either had medical management and colectomy for IC or were not considered to be candidates for surgery.

We excluded patients who were diagnosed with IC by computed tomography (CT) scan or other abdominal imaging after hospitalization with IC presenting with other clinical symptoms other than presentations without severe hematochezia, such as severe abdominal pain, abdominal distension, or peritoneal findings. Other exclusion criteria were other causes of colonic bleeding than IC, such as acute or chronic occlusive mesenteric ischemia requiring vascular surgery, infectious colitis, inflammatory bowel disease, or pseudomembranous colitis. In addition, patients with less than 30 days of follow-up were also excluded.

Severe hematochezia, diagnosis, and classification

Severe hematochezia was defined as passage of red blood or clots per rectum along with the following criteria: (1) requiring hospitalization, (2) having clinical signs of severe hematochezia with hemodynamic instability, (3) decreasing hemoglobin at least 2 g/dL from the baseline, and/or (4) requiring 1 or more units of red blood cell (RBC) transfusions for bleeding.

The initial diagnosis of IC was made during urgent colonoscopy [1]. Final diagnosis of IC was confirmed with histopathology and negative stool cultures and/or viral assays [1]. In clinically ill patients with very severe IC, flexible sigmoidoscopy or limited colonoscopy was performed and computed tomography (CT) scan or magnetic resonance imaging (MRI) was used to confirm the distribution of ischemia and the presence of transmural infarction (presence of pneumatosis and portal or mesenteric venous gas) and to exclude other causes [9, 15].

The severity of colonoscopic IC findings was grouped according to Favier's classification as stage I: patchy erythema and ischemia limited to the mucosa; stage II: submucosal ischemia with nonnecrotic ulceration (Fig. 1); and stage III: transmural ischemia with necrosis, gangrene, and possible perforation (Fig. 2) [16]. Fig. 1 Colonoscopic findings of Favier's classification stage II ischemic colitis in the descending colon. A and B show nonnecrotic ischemic ulcers from the same patient with a longitudinal ulcer or a single-stripe sign (A) and large hemorrhagic ulceration (B). C shows edematous and ulcerated mucosa with pseudopolyp. D shows erythematous mucosa with interspersed ulcers

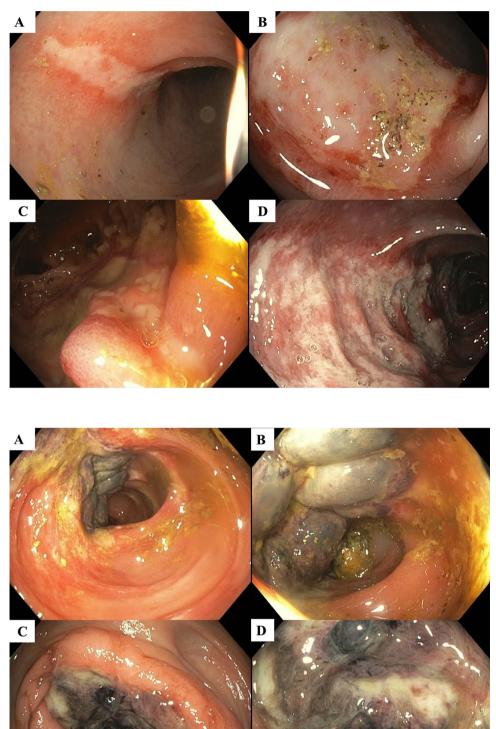


Fig. 2 Favier's classification stage III findings of ischemic colitis at the splenic flexure at colonoscopy. A and B show ischemic necrosis of the bowel wall with edematous mucosa and lumen narrowing. C and D show 60% circumferential deep necrotic ulceration with lumen stricture

After discharge and following complete resolution of the index IC when patients presented with recurrent hematochezia and a new diagnosis of IC was made, they were classified as having recurrent IC. The IC diagnosis of recurrent IC was confirmed by colonoscopy and histopathology, similar to the initial criteria. A colon stricture was defined as having obstructive symptoms and a reduction in colon diameter identified radiographically or colonoscopically.

Management for IC

Management for IC patients depended upon the severity of the bleeding at presentation, hemodynamic status, and preoperative risk stratification. In this study, all patients initially received medical management and were subsequently classified into 3 groups based upon their final treatment for IC including colon resection, medical treatment, and those who failed medical treatment but were not deemed to be surgical candidates as assessed by the surgical team.

Initial medical management included supportive treatment, intravenous fluids, RBC transfusion for severe bleeding with hemoglobin < 8 g/dl, bowel rest, treatment for precipitating factors, and avoidance of vasoconstrictors. In addition, those with severe IC who were not surgical candidates were treated medically as described and with antimicrobial therapy and/or arterial embolization to control severe active arterial bleeding in a few cases. Patients with major stigmata of recent hemorrhage (SRH) (active bleeding, nonbleeding visible vessel (NBVV), or adherent clot) in a focal ulcer on colonoscopy were treated with hemoclipping [1, 17]. All patients were treated by the same GI and/or surgical teams throughout the study period.

Surgical management was recommended to patients who failed medical and endoscopic treatment, including those with severe ongoing bleeding, peritoneal signs, or progressive hemodynamic instability. The extent of colectomy was determined by the severity, distribution, and location of IC. Colon viability was visually assessed during colonoscopy and intraoperatively prior to resection. In cases where IC was limited to one colonic segment, segmental colectomy such as hemicolectomy or sigmoidectomy with or without Hartmann's procedure and end colostomy was performed. In cases of severe pancolitis or when colon viability appeared to be poor, a total or subtotal colectomy with end ileostomy was performed. In patients with a severe recurrence of colon ischemia after an initial colon resection, a second-look laparotomy was recommended. All colon operations were performed by experienced colorectal or gastrointestinal (GI) surgeons.

Data management and statistical analysis

Baseline variables compared were demographics, comorbidities, the American Society of Anesthesiologists (ASA) classification, Center for Ulcer Research and Education (CURE) hemostasis prognosis scores [18], Glasgow-Blatchford bleeding scores (GBS) [19], Age-adjusted Charlson Comorbidity Index (ACCI) [20], laboratory values, and RBC transfusions. We also analyzed treatments, colonoscopic findings and hemostasis, lesion extent and location, type of operation performed, postoperative complications, length of hospital and intensive care unit (ICU) days, unplanned reoperation, readmission, recurrence of IC, development of symptomatic colonic strictures, and all-cause mortality.

Data management and statistical analysis were performed using the StataCorp LLC Stata Statistical Software version 17.0, TX, USA. For categorical variables, chi-square was used for the three-group comparisons and either chi-square or Fisher's exact tests were used for the two-group comparisons. For continuous variables, the Kruskal–Wallis test and post hoc Bonferroni correction with Dunn's test were performed for multiple group comparisons. Demographics and outcomes are presented in either median and interquartile range (IQR) or mean \pm standard deviation (SD) according to the data distribution. A p value of less than 0.05 was considered statistically significant.

Results

Patient demographics

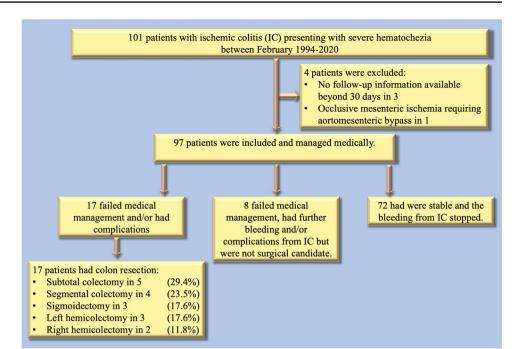
A total of 101 patients with IC were identified through the CURE database. Four patients were excluded and 97 patients were included. Twenty-five of 97 (25.7%) failed medical treatment. Of these, 17 (17.5%) required colectomy and 8 (8.2%) were managed conservatively because they were severely ill and not surgical candidate. Seventy-two (74.2%) receiving medical treatment were stable and the bleeding from IC stopped (Fig. 3).

For all 97 patients, the mean age (SD) was 65.3 (14.4) years old and 53.6% were male. The race and ethnicity of the patients were Caucasian (51.6%), Hispanic (16.5%), African American (15.5%), and Asian (15.5%). Most patients had ASA class III or IV (82.3%). The most common comorbidities were hypertension (68%), chronic kidney disease (57.7%), diabetes mellitus (40%), atherosclerotic cardiovascular diseases (35.1%), and atrial fibrillation or atrial flutter (35.1%).

The majority of patients (63%) had multifocal IC on urgent colonoscopy. The splenic flexure (55.7%) was the most common segment, followed by descending colon (47.4%) and sigmoid colon (45.4%).

Medical, endoscopic, and angiographic management

Among patients receiving medical or conservative management (72 in the medical group and 8 in the non-surgical candidate group), 67 (83.7%) had medical treatment alone, 10 (12.5%) had endoscopic hemostasis, and 3 (3.8%) had transcatheter arterial embolization for control of severe bleeding. **Fig. 3** Flow diagram of patients with ischemic colitis during the study period. A total of 97 included patients had medical management, 17 had colon resection, and 80 received medical management. Among 80 medical patients, 72 had no further bleeding and 8 were those who were severely ill and not surgical candidate



Indication for surgery and the extent of colon removed

In the surgical group of 17 patients, indications for colectomy were uncontrolled bleeding in 11 patients (64.7%) and peritonitis with severe sepsis in 6 cases (35.3%). All 6 peritonitis cases had emergency surgery. All colectomies were performed with an open approach. The types of colectomy performed are shown in Fig. 3. No intraoperative complications occurred and no patient required a second-look laparotomy. The mean operative time (SD) was 226 (83) min and the median estimated blood loss was 300 (range 150–1200) mL. Twelve (70.6%) patients had diverting stoma (5 end ileostomies and 7 end colostomies). One (8.3%) patient had subsequent closure of colostomy in 8 months. The other 11 patients did not have closure of stoma due to death in 8 and still having the ostomy during the study period in 3.

Comparison of baseline demographic characteristics for the surgical, medical, and non-surgical candidate groups

Baseline demographics of the three groups are shown in Tables 1 and 2. The surgical and non-surgical candidate groups had significantly worse CURE prognosis, Glasgow-Blatchford scores, and ACCI, and more had inpatient development of IC bleeding than the medical group. The surgical group also had more patients who were on prophylactic anticoagulants for a history of deep vein thrombosis (DVT). The non-surgical candidate group had a significantly higher proportion of patients with chronic kidney disease on dialysis or cirrhosis than the other two groups.

Potential causes of IC, colonoscopic findings, and colon hemostasis

The cause of IC in the majority of patients with surgical management and those who were not surgical candidate was hypotension or shock as documented in the hospital prior to start of inpatient hemorrhage. In the medical group, the causes of IC were not documented in almost half of the patients who started bleeding as outpatients, although hypoperfusion was suspected as the cause in all of them and was documented in those who had inpatient IC start of bleeding. The colonic distribution was not different for the three groups. However, the colonoscopic severity of IC was worse in the surgical group (Table 2).

Overall, 12 patients (12.5% of all) had colonoscopic hemostasis for SRH in focal ischemic ulcers, 2/17 (11.8%) in the surgery group, 10/72 (13.9%) in the medical group, and 1/8 (12.5%) in the non-surgical candidate group. The SRH in focal ischemic ulcers which were treated endoscopically were active bleeding in 6, non-bleeding visible vessel (NBVV) in 4, and adherent clot in 2.

Major 30-day outcomes in patients with IC hemorrhage

Surgical and non-surgical candidate patients received significantly more total units of RBC transfusions, had significantly longer hospital and ICU stays, and had higher severe

Table 1	Demographics and basel	ine characteristics of	patients with severe	hematochezia from	ischemic colitis

Variables	Surgery group $(n = 17)$	Non-surgical candidate group $(n=8)$	Medical group $(n=72)$	p value
Age, years old, mean (SD)	60 (47–72)	60.5 (52.5–66)	69.5 (57–76.5)	0.055
Sex, n (%)				
Female	7 (41.2)	1 (12.5)	37 (51.4)	0.104
Male	10 (58.8)	7 (87.5)	35 (48.6)	
Race and ethnicity, n (%)				
Caucasian	9 (52.9)	2 (25)	39 (54.2)	0.099
Hispanic	3 (17.6)	4 (50)	9 (12.5)	
African American	2 (11.8)	0	13 (18.1)	
Asian	2 (11.8)	2 (25)	11 (15.3)	
Native American	1 (5.9)	0	0	
Smoker, <i>n</i> (%)	7 (41.2)	2 (25)	20 (37.8)	0.804
Alcohol consumption, <i>n</i> (%)	0	0	8 (11.1)	0.870
ASA Classification, n (%):				
Class I	0	0	3 (4.2)	0.003
Class II	1 (5.9)	0	13 (18.1)	
Class III	4 (23.5)	0	33 (45.8)	
Class IV	12 (70.6)	8 (100)	23 (31.9)	
CURE prognosis, median (IQR)	4 (3–5)	4 (3.5–4.5)	2.5 (2-3)	< 0.001
Glasgow-Blatchford score, median (IQR)	13 (10–16)	15 (13–18)	8 (4–11)	< 0.001
ACCI, mean (SD)	7 (6–9)	8 (6–9.5)	6 (4–8)	0.043
Comorbidities, n (%)				
Diabetes mellitus	8 (47.1)	3 (37.5)	28 (38.9)	0.958
Hypertension	10 (58.8)	3 (37.5)	53 (73.6)	0.065
Dyslipidemia	6 (35.3)	3 (37.5)	25 (35.2)	> 0.99
Coronary artery disease	9 (52.9)	1 (12.5)	24 (33.3)	0.130
Congestive heart failure	4 (23.5)	2 (25)	14 (19.4)	0.756
Cardiac arrhythmia	6 (35.3)	4 (50)	24 (33.3)	0.741
Cerebrovascular disease	2 (11.8)	0	14 (19.4)	0.518
Peripheral vascular disease	4 (23.5)	0	8 (11.1)	0.300
History of AAA repair	2 (11.8)	0	3 (4.2)	0.641
DVT on anticoagulant	6 (35.3)	1 (12.5)	7 (9.7)	0.026
Hypercoagulable state	1 (5.9)	0	3 (4.2)	0.703
Chronic kidney disease	12 (70.6)	8 (100)	36 (50)	0.007
Currently on dialysis	9 (52.9)	7 (87.5)	21 (29.2)	0.002
Cirrhosis	6 (35.3)	6 (75)	8 (12.1)	< 0.001
Disseminated cancer	1 (5.9)	0	2 (2.8)	0.595
Medications, <i>n</i> (%)			· · ·	
Aspirin usage	5 (29.4)	0	33 (45.8)	0.020
Anticoagulants	7 (41.2)	1 (12.5)	23 (31.9)	0.712
Antiplatelet agents	2 (11.8)	0	4 (5.6)	0.601
NSAID use	0	0	5 (6.9)	0.729
Hormonal drug use	0	0	8 (11.1)	0.427
Diuretics use	7 (41.2)	3 (37.5)	21 (29.2)	0.611
Immunosuppressive drugs	2 (11.8)	2 (25)	8 (11.1)	0.421

n, number of patients; *SD*, standard deviation; *IQR*, interquartile range; *ASA*, American Society of Anesthesiologists; *CURE*, Center of Ulcer Research and Education; *ACCI*, Age-adjusted Charlton Comorbidity Index; *DM*, diabetes mellitus; *AAA*, abdominal aortic aneurysm; *DVT*, deep vein thrombosis; *NSAIDs*, nonsteroidal anti-inflammatory drugs

Adjusted *p* values for CURE prognosis: surgery group vs. non-surgical candidate group, p = 0.950; surgery group vs. medical group, p = 0.001; and non-surgical group vs. medical group, p = 0.002

Adjusted *p* values for Glasgow-Blatchford score: surgery group vs. non-surgical candidate group, p=0.215; surgery group vs. medical group, p=0.003; and non-surgical group vs. medical group, p<0.001

Adjusted p values for ACCI: surgery group vs. non-surgical candidate group, p > 0.99; surgery group vs. medical group, p = 0.0547; and non-surgical group vs. medical group, p = 0.136

- Gold probe with or without injection

- Gold probe with hemoclip

Table 2 Clinical presentations, colonoscopic findings, and colonoscopic treatments of patients with severe hematochezia from ischemic colitis

Variables	Surgery group (n=17)	Non-surgical candidates $(n=8)$	Medi- cal group (n=72)	p value
Initial bleeding setting, <i>n</i> (%)				
- Inpatient	13 (76.5)	8 (100)	27 (37.5)	< 0.001
- Outpatient	4 (23.5)	0	45 (62.5)	
Other clinical presentations along with hema- tochezia, n (%)				
- Abdominal pain	4 (23.5)	0	25 (34.7)	0.029
- Hypovolemic shock	1 (5.9)	1 (12.5)	1 (1.4)	
- Sepsis	1 (5.9)	0	0	
Suspected cause of ischemic colitis, n (%)				
- Systemic hypoperfusion	10 (58.8)	7 (87.5)	27 (37.5)	0.004
- Other cause	5 (29.4)	0	10 (13.5)	
- Unknown cause	2 (11.8)	1 (12.5)	35 (48.6)	
Endoscopic classification*, n (%)				
- Stage I	0	3 (37.5)	11 (15.5)	0.002
- Stage II	8 (61.5)	5 (62.5)	57 (80.3)	
- Stage III	5 (38.5)	0	3 (4.2)	
Anatomical segment of ischemic colitis, n (%)				
- Splenic flexure and distal colon	8 (47.1)	4 (50)	37 (51.4)	0.981
- Colon proximal to splenic flexure	4 (23.5)	2 (25)	19 (26.4)	
- Both anatomical segments	5 (29.4)	2 (25)	16 (22.2)	
Segmental involvement, n (%)				
- Multi-segmental	14 (82.4)	5 (62.5)	44 (61.1)	0.276
- Single-segmental	3 (17.6)	3 (37.5)	28 (38.9)	
Colonoscopic hemostasis, n (%)				
- None	15 (88.2)	7 (87.5)	63 (87.5)	0.646
- Hemoclip with or without injection	1 (5.9)	1 (12.5)	7 (9.7)	
- Injection alone	1 (5.9)	0	0	

n, number of patients; IQR, interquartile range. *The severity of endoscopic findings in the acute stage was classified according to Favier's classification as stage I: patchy erythema and ischemia limited to the mucosa; stage II: submucosal ischemia with nonnecrotic ulceration; and stage III: transmural ischemia with necrosis, gangrene, and possible perforation

0

0

1(1.4)

1(1.4)

0

0

complication rates than those treated medically (Table 3). There were no statistical differences in the 30-day rebleeding and readmission rates due to IC for the 3 groups.

Five surgical patients (29.4%), 5 (62.5%) non-surgical candidate patients, and 11 (15.3%) medical patients had rebleeding from IC within 30 days (Table 3). For the surgical patients, the rebleed rates from IC were 1 of 5 (20%) for the subtotal colectomy group and 4 of 8 (50%) for those with segmental colectomy (p > 0.99). Two patients who initially had segmental colectomy required reoperation due to bleeding from a different colon segment of IC on postoperative days 8 and 13. One patient in the medical group required angioembolization for recurrence of bleeding from IC. The rest of the patients with rebleeding were treated medically and the bleeding stopped.

The 30-day all-cause mortality rate was significantly higher in the non-surgical candidate group (87.5%), followed by the surgical group (23.5%), and none in the medical group. The median (IQR) time to death (within 30 days) was 19.5 (15-25) days in surgical patients and 12.6 (4-21) days in the non-surgical candidate group (p = 0.06). The causes of death in the surgical group were multiorgan failure in 2 and sepsis in 2. The causes of death in the non-surgical candidate group were multiorgan failure in 3, sepsis in 3, and end-stage liver disease in 1.

Severe complications

Severe complications in the surgical group were 1 death from multiorgan failure, 1 septic shock, 1 cardiac failure,

Outcome variables	Surgery group $(n=17)$	Non-surgical candi- dates $(N=8)$	Medical group $(n=72)$	p value
30-day outcomes				
Received RBC transfusion, n (%)	14 (82.4)	8 (100)	39 (54.2)	0.005
Total RBC transfusion (units), median (IQR)	5 (3–10)	4.5 (3-6.5)	1 (0-4)	< 0.001
Hospital stay (days), median (IQR)	22 (13-57)	12 (9–20)	4(1-14)	< 0.001
ICU stay (days), median (IQR)	20 (4-33)	11 (6–20)	0	< 0.001
Rebleeding rates, n (%)	5 (29.4)	5 (62.5)	11 (15.3)	0.635
Unplanned reoperation rates, n (%)	2 (11.8)	0	0	0.037
Severe complication rates, n (%)	6 (35.3)	8 (100)	4 (5.6)	< 0.001
Readmission rates, n (%)	0	-	2 (2.8)	> 0.99
All-cause mortality rates, n (%)	4 (23.5)	7 (87.5)	0	< 0.001
Follow-up outcomes after 30 days				
Follow-up intervals (months), median (IQR)	6 (2–14)	2	28.5 (2-85)	0.167
Recurrence of IC during follow-up*, n (%)	1/10 (10.0)	-	2/71 (2.8)	0.330
All-cause mortality rates (beyond 30 days)*, n (%)	9 (52.9)	1 (100)	17 (23.6)	0.109
Time to death (months)*, median (IQR)	2 (1.2–4.4)	2	27.0 (10.3-55.3)	0.024
Cumulative mortality rates, n (%)	9 (52.9)	8 (100)	17 (23.6)	< 0.001

Table 3	Thirty-day and mid-term outcomes	of surgery and med	lical management in patien	nts with severe hematochezia from ischemic colitis

n, number of patients; *IQR*, interquartile range; *RBC*, red blood cell transfusion; *IC*, ischemic colitis; *ICU*, intensive care unit. *Patients who expired in 30 days were not included

Adjusted *p* values for the pairwise comparisons for total RBC transfusion: surgery group vs. non-surgical candidate group, p > 0.99; surgery group vs. medical group, p < 0.001; and non-surgical group vs. medical group, p = 0.008

Adjusted p values for hospital stay: surgery group vs. non-surgical candidate group, p = 0.384; surgery group vs. medical group, p < 0.001; and non-surgical group vs. medical group, p = 0.184

Adjusted *p* values for ICU stay: surgery group vs. non-surgical candidate group, p > 0.99; surgery group vs. medical group, p < 0.001; and non-surgical group vs. medical group, p = 0.002

Adjusted *p* values for Time to death (after 30 days): surgery group vs. non-surgical candidate group, p=0.830; surgery group vs. medical group, p=0.035; and non-surgical group vs. medical group, p=0.119

p values for the pairwise comparisons between the surgical and medical groups: 30-day rebleeding rate = 0.361; 30-day readmission rate = 0.865; severe complication rate = 0.003; 30-day mortality = 0.001; mortality during follow-up = 0.261; and cumulative death = 0.017

1 liver failure, 1 pneumonia, and 1 wound dehiscence. No anastomotic leaks were observed.

All patients who were not surgical candidates had multiple severe complications including diffuse bowel ischemia in 1 patient, rebleeding from IC in 1, and other multiorgan complications (e.g., respiratory failure, renal failure, septic shock, severe coagulopathy with cerebrovascular hemorrhage, and death).

Severe complications in the medical group were renal failure in 2 patients and sepsis in 2 patients.

No complications occurred in patients having colonoscopic hemoclipping for hemostasis in either group.

Long-term follow-up and outcomes after 30 days

The duration of follow-up and outcomes after 30 days are shown in Table 3. The overall median (IQR) follow-up interval was 21 (2–75) months (n = 86). No symptomatic colonic strictures were noted during follow-up. For the 10 surgical patients who had long-term follow-up, one patient (10%) had

recurrence of IC presenting with peritonitis at 45 months from the index IC treatment and required segmental colectomy. Within 2 months, there were recurrences of IC hemorrhage in two (2.8%) patients in the medical group at the different colon segments. Both patients received medical management for the recurrent episode.

During the follow-up period, all-cause mortality in the surgical group was arithmetically higher than in the medical group. Time to death was also significantly shorter in the surgical group (Table 3). All deaths were related to patients' comorbidities and no patient died of GI bleeding.

Thirty-day outcome comparisons of outpatient vs. inpatient presentation of hematochezia from IC

Patients who had hematochezia starting as inpatients (after hospitalization for a non-bleeding medical or surgical diagnosis) had significantly worse comorbidity scores, received more RBC transfusions, had more severe complications, had longer ICU and hospital stays, and had higher 30-day allcause mortality (Table 4).

Discussion

In this study, we evaluated the clinical outcomes of patients with histologically confirmed IC who were hospitalized with severe hematochezia. Surgical patients and those who were not surgical candidate were sicker and the majority of them had inpatient start of bleeding. Systemic hypoperfusion was documented as the most common cause of IC. For more than half of patients in the medical group, IC developed as an outpatient and although suspected to be from hypoperfusion, this was not documented. Surgical patients and those who were not surgical candidates received significantly more RBC transfusions, had longer hospital and ICU stays, and had higher rates of severe complications. However, 30-day rebleeding rate was not significantly different for the three groups.

Similar to studies reported in literature, patients with surgical management of IC had a worse prognosis than those treated medically [21–24]. Poorer outcomes in IC

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patients with surgical treatment in other reports could be due to delays in a timely diagnosis, especially in those with development of severe inpatient hematochezia. Delays in diagnosis and treatment can result in gangrene and necrosis of the colonic wall [25]. However, diagnosis and management of IC are challenging because the clinical presentation is heterogeneous and often difficult to assess, especially in severely ill patients with multiple comorbidities. Furthermore, the extent of colon resection is also difficult to determine because of concern about worsening ischemia after resection or incomplete removal of the IC segment, which could result in further bleeding, as seen in 29.4% of surgical patients in our study. This could be a reason for refraining from aggressive surgical treatment in some cases. In addition, severe IC carries higher morbidity and mortality risks [12], as also seen in our surgical and non-surgical candidate groups. Most patients with severe IC have multiple, severe comorbidities, which worsen their prognosis and postoperative outcomes [26].

In our study, the 30-day all-cause mortality was significantly higher in the non-surgical candidate group (87.5%), followed by the surgical group (23.5%), with two major causes of death—multiorgan failure and sepsis. A

	Hematochezia from IC started as		p values
	Outpatient $(n=49)$	Inpatient $(n=48)$	
Baseline characteristics			
Age (years), mean (SD)	67.3 (13.5)	63.2 (15.0)	0.105
CURE prognosis, median (IQR)	2 (1–2)	3.5 (3-4)	< 0.001
Glasgow-Blatchford score, median (IQR)	6 (2–9)	13 (10–15)	< 0.001
ACCI, mean (SD)	5 (3–7)	8 (6–9)	< 0.001
Treatment received			
Medical management, n (%)	45 (91.8)	35 (72.9)	0.017#
Surgical management, n (%)	4 (8.2)	13 (27.1)	
30-day outcomes			
Total RBC transfusion (units), median (IQR)	0 (0–2)	4 (2–6)	< 0.001
Hospital stay (days), median (IQR)	2 (1–5)	21 (11-43)	< 0.001
ICU stay (days), median (IQR)	0	8.5 (0-30)	< 0.001
Severe complications, <i>n</i> (%)	1 (2.0)	17 (35.4)	< 0.001
Rebleeding from IC	6 (12.2)	15 (31.3)	0.052
Unplanned reoperation, n (%)	0	1 (2.0)	0.424#
All-cause mortality, n (%)	2 (4.1)	9 (18.8)	0.028#
Readmission, n (%)	1 (2.0)	0	0.836#
Follow-up outcomes after 30 days			
Follow-up intervals (months), median (IQR)	40 (10-121)	8 (1.5–32)	< 0.001
Recurrence of IC during follow-up, n (%)	2 (4.3)	1 (2.9)	> 0.99#
All-cause mortality rates, n (%)	11 (22.4)	23 (47.9)	0.567
Time to death (months), median (IQR)	29.4 (10.9-82.3)	8 (2.6–16.4)	0.047

n, number of patients; *IQR*, interquartile range; *CURE*, Center of Ulcer Research and Education; *ACCI*, Age-adjusted Charlson Comorbidity Index; *RBC*, red blood cell transfusion; *IC*, ischemic colitis; *ICU*, intensive care unit. [#]Fisher's exact

 Table 4
 Outcomes of inpatient

 vs. outpatient presentation of
 hematochezia in patients with

 ischemic colitis
 hematochezia

similar 30-day mortality rate (25.3%) in surgical patients was reported by Tseng et al., analyzing 4548 IC patients for various etiologies undergoing emergency colectomy [27]. In smaller studies of 115 or fewer cases, higher mortality rates of 36–50% were reported in surgical patients and the mortality rates of 9–24% were also reported in non-surgical patients [24, 28–30]. The mortality rates in patients undergoing colectomy are higher due to advanced age, poor functional status, and multiple comorbidities. Furthermore, delays in surgery due to preoperative resuscitation or delay in diagnosis can also increase the likelihood of clinical deterioration, sepsis, and multiorgan failure [27, 31, 32].

IC can reoccur in either surgically or medically treated patients. The rates of recurrent IC with hematochezia or other clinical symptoms in our study were low and not statistically different in the surgery or medical groups (10% vs. 2.8%). IC recurrence rates of 6.8–16% are reported during 5 years of follow-up [24, 33–35]. Removal of the affected colon segment can be curative in most patients. However, this does not prevent recurrence of IC in residual colon segments. Data regarding IC recurrence following subtotal colectomy are scarce.

A small percentage of patients with IC can develop other long-term complications, such as chronic IC or colonic stricture as a result of repetitive ischemic injury and circumferential deep ischemic ulceration [36]. Montoro et al. [11] reported that 20% (13/65) of patients developed colonic stenosis, which was identified during repeat colonoscopy and/or barium enemas in the first 6 months. However, 60% of their patients were asymptomatic. In our study, no patients had symptoms of colonic strictures during a median follow-up of 21 months. However, because our patients were asymptomatic, they did not have routine surveillance with radiologic imaging or colonoscopy for colonic strictures.

Whereas angioembolization of focal colonic bleeding sites is useful when active arterial bleeding is suspected, its diagnostic yield in patients with IC hemorrhage and lesser stigmata (e.g., visible vessel or adherent clot) or no stigmata would be low. To support this, on urgent colonoscopy of our patients with IC as a cause of severe colon hemorrhage, only 12.5% had some stigmata of recent hemorrhage (SRH) in focal ischemic ulcerations and those were treated with hemoclipping. Arterial bleeding as one of the IC SRH was seen in only 6% of all IC patients. CTAs or other types of angiography would only be expected to visualize active arterial bleeding in IC patients and not other non-bleeding SRH. In all, 87.5% of our patients had diffuse bleeding and no SRH on urgent colonoscopy. Therefore, neither CTA nor standard angiography with embolization would be positive studies for detection of a bleeding site or treatment of most patients with hemorrhage from IC. Based upon our results, the evidence supporting an expanded use of angioembolization for diagnosis or treatment of hospitalized patients with severe hemorrhage from IC is lacking. Only 3 of our patients had angioembolization for control of severe bleeding.

The major strength of our study was prospective data collection and follow-up by the same GI and surgery teams. The comparison of inpatient vs. outpatient start of hemorrhage is clinically important and should be included in an early diagnosis algorithm of severe colon hemorrhage. Our report on the safety and effectiveness of identifying and treating stigmata of hemorrhage on focal ulcers is also new. In addition, we report on a different subgroup of patients with mucosal/ submucosal injury who present to medical teams and gastroenterologists with severe painless hematochezia. These are in contrast to patients presenting to surgeons without severe colon hemorrhage who have abdominal pain, sepsis, and peritonitis from transmural injury and thromboembolism. The latter group is most often reported in the surgical literature.

This study has several limitations. First, it was not a randomized controlled trial and the sample size was small for the surgical and non-surgery candidate groups. Second, we only included a specific group of patients who initially presented with severe hematochezia from IC and had colonoscopic evaluation. A different group of IC patients who presented with other signs and symptoms such as severe abdominal pain, peritonitis, or perforation without severe colon hemorrhage and those with radiologic evidence of IC without severe hematochezia were not included in our study. Therefore, our study patients are not representative of all patients with severe IC. Third, because autopsies were not performed, we were not able to provide more details about patients who died and may have had an occult perforation. Last, there was a selection bias in our study as evidenced by the surgery group and the non-surgical candidate group which both failed initial medical treatment but had poorer prognosis than patients in the medical group.

Conclusion

The majority of patients with severe hematochezia from IC were successfully treated medically. For all patients with severe hematochezia, only 12.4% had focal ulcerations with stigmata of recent hemorrhage and were effectively and safely treated with colonoscopic hemostasis. Patients undergoing colectomy for IC and those who were not surgical candidates had poorer short-term clinical outcomes than those in the medical group due to more severe comorbidities and worse colon ischemia. Aggressive surgical treatment may be required in selected cases. However, optimal colon resection can be challenging as the IC segment may be incompletely removed or could later progress, resulting in further bleeding and complications. Regardless of treatment received, patients with inpatient start of hematochezia from

IC had significantly worse prognosis and outcomes than those whose hematochezia started as outpatients. Further research is warranted to facilitate early diagnosis, accurate risk stratification, better medical and surgical treatments, and improvement in primary prevention of ischemic colitis and severe hemorrhage.

Authors' contributions Thongsak Wongpongsalee: study design, acquisition of data, analysis and interpretation of the data, and drafting of the article. Usah Khrucharoen: acquisition of data, analysis and interpretation of the data, drafting of the article, and critical revision of the manuscript. Dennis M. Jensen: study conception and design, acquisition of data, interpretation of the data, and critical revision of the manuscript. Rome Jutabha: interpretation of the data and critical revision of the manuscript. Mary Ellen Jensen: analysis of the data and critical revision of the data and critical revision of the data and critical revision of the manuscript. Gail Thibodeau: interpretation of the data and critical revision of the manuscript.

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Availability of data and material The data are not publicly available due to the institutions' privacy restrictions.

Code availability Not applicable.

Declarations

Ethics approval All patients in this study had been enrolled in Institutional Review Board (IRB)–approved prospective studies of severe hematochezia at Ronald Reagan UCLA Medical Center or VA Greater Los Angeles Healthcare System.

Conflict of interest The authors declare no competing interests.

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