

Severe acute ischemic colitis: What is the place of endoscopy in the management strategy?



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ABSTRACT

Background and study aims Ischemic colitis (IC) is potentially lethal. Clinical and biology information and results of computed tomography (CT) scan and/or colonoscopy are used to assess its severity. However, decision-making about therapy remains a challenge.

Patients and methods This was a retrospective, single-center study between 2006 and 2015. Patients with severe IC who underwent endoscopic evaluation were included. The aims were to determine outcomes depending on endoscopic findings and assess the role of endoscopy in the management.

Results A total of 71 patients were included (men=48 (68%), mean age=71 ± 13 years). There was hemodynamic instability in 29 patients (41%) and severity signs on CT scan in 18 (38%). Twenty-nine patients (41%) underwent surgery and 24 (34%) died. The endoscopic grades were: 15 grade 1 (21%), 32 grade 2 (45%), and 24 grade 3 (34%). Regarding patients with grade 3 IC, 55% had hemodynamic instability, 58% had severity signs on CT scan, 68% underwent surgery, and 55% died. The decision to perform surgery was based on hemodynamic status in 62% of cases, CT scan data in 14%, endoscopic findings in 10%, and other in 14%. Colectomy was more frequent in patients with grade 3 IC ($P<0.05$). A mismatch between mucosal aspect (necrosis) and serous (normal) was observed in 13 patients (46%). Risk factors for colectomy in univariate analysis were aortic aneurysm surgery, hemodynamic instability, no colic enhancement on CT scan, and endoscopic grade 3. Risk factors for mortality in multivariate analysis were hemodynamic instability, colectomy, and Charlson score >5 ($P<0.05$).

Conclusions This study suggests a low impact of endoscopy on surgical decision making. Hemodynamic instability was the first indication for colectomy. A discrepancy between endoscopic mucosal (necrosis) and surgical serous (normal) aspects was frequently noted.

Introduction

Ischemic colitis (IC) is the most common gastrointestinal ischemic disease and is potentially lethal [1–3]. Its incidence is estimated at 22.9 per 100,000 person-years and is increasing [4], mostly in people older than age 65 years [1–3, 5]. The identified risk factors are aortic surgery [6–8], cardiovascular disease [9, 10] and exposure to some drugs [11, 12]. The mortality

rate for IC in published studies ranges between 5% and 50%, depending on the severity of the patient's condition [4, 13, 14].

Many studies have been published on the management of IC, reflecting a very heterogeneous disease in terms of clinical pattern (edematous and gangrenous form), diagnostic strategy, evolution, and treatment [1, 3, 4]. They all reflect that the decision for the management strategy (conservative/medical treatment vs. surgery) is challenging [1]. Furthermore, the correlation between the endoscopic aspect of the mucosa and

clinical severity is not absolute, and even for patients with peaty and/or purple mucosa, IC may resolve ad integrum. The American consensus highlighted the need for assessing the entire clinical picture before deciding about an indication for surgical intervention [1].

Several studies have classified IC as “severe” or “not severe,” based on epidemiological, clinical, biological, endoscopic, and CT scan features, as well as the need for surgery and the death rate [1]. In 1976, Favier et al. created an endoscopic classification for IC: stage 1 (mucosal edema and erythema), stage 2 (mucosal ulcerations but not necrotic mucosa), and stage 3 (colonic necrosis) [15]. Stage 3 Favier is widely acknowledged to require surgical management, as does stage 2 with organ failure [1, 16, 17].

To date, no studies have evaluated the prognosis of IC according to the endoscopic stages and their correlation with imaging and surgical findings. Patients with severe IC who underwent endoscopic evaluation were included in this retrospective study, based on screening of patients who had endoscopy. We proposed this study to determine patient outcomes depending on the endoscopic findings and to assess the impact of endoscopy on therapeutic decision making. Secondary aims were to identify risk factors for mortality and surgery in this cohort.

Patients and methods

Data collection

This was a retrospective study conducted in a tertiary center from 2006 to 2015, in North Hospital, Marseille, France. The endoscopy unit database was searched for all patients in whom IC was suspected (FileMaker Pro v.9, FileMaker Inc. California, United States). A systematic search by keywords (hemorrhage, colitis, IC) facilitated identification of all endoscopies carried out for suspicion of IC. Files of all patients who underwent lower gastrointestinal endoscopy for suspected IC were reviewed. Patients who had IC and did not have endoscopy (mainly patients with a contraindication to endoscopy: signs of peritonitis or confirmed perforation) were not included in the study.

Ethics

This was a retrospective study and according to current French legislation, at the time of the study, there was no need for patient consent and Institutional Review Board approval. The data used were anonymized and collected from the APHM computer file which is declared to the Commission Nationale Informatique et Liberté (French National Commission for Data Protection). Moreover, all endoscopies were performed during a critical emergency, most before potential surgical resection, in patients informed about the therapeutic multidisciplinary decision.

Inclusion criteria

Only patients with IC considered as severe before endoscopy and/or confirmed by the endoscopic aspect were included in the analysis. The severity before endoscopy was defined clinically

as patients hospitalized in the Intensive Care Unit (ICU) and/or clinical condition with hemodynamic instability requiring an urgent colonoscopy (without delay) before potential surgery. The severity signs on CT scan were defined as peritoneal fluid collection and/or defect of enhancement and/or perforation.

A decision proceed with surgery theoretically had been made based on Favier grade 3 at endoscopy, grade 2 with hemodynamic instability, or CT scan severity criteria with hemodynamic instability. The therapeutic decision was made by surgeons, intensivists, and endoscopists.

We excluded patients suspected of having IC that was unconfirmed at endoscopy and with IC considered non-severe (no need to perform endoscopy quickly according to the doctor in a hemodynamically stable patient with no sign of peritoneal irritation).

Data collection

The data collected were age, comorbidities, Charlson comorbidity score, vascular disease, etiology including aortic surgery, clinical symptoms (diarrhea, abdominal pain, bleeding), organ failure (hemodynamic instability, respiratory failure, renal failure), hospitalization in the ICU, severity signs on CT scan (effusion, enhancing defect or perforation), delay of colonoscopy (always < 36 hours), Favier endoscopic stage, endoscopy complication, surgery findings, relapse, and death [15, 18]. Information on the main indication for surgery, such as clinical condition (hemodynamic status), CT scan severity signs or endoscopy findings, also was searched in the medical file and collected.

Study objectives

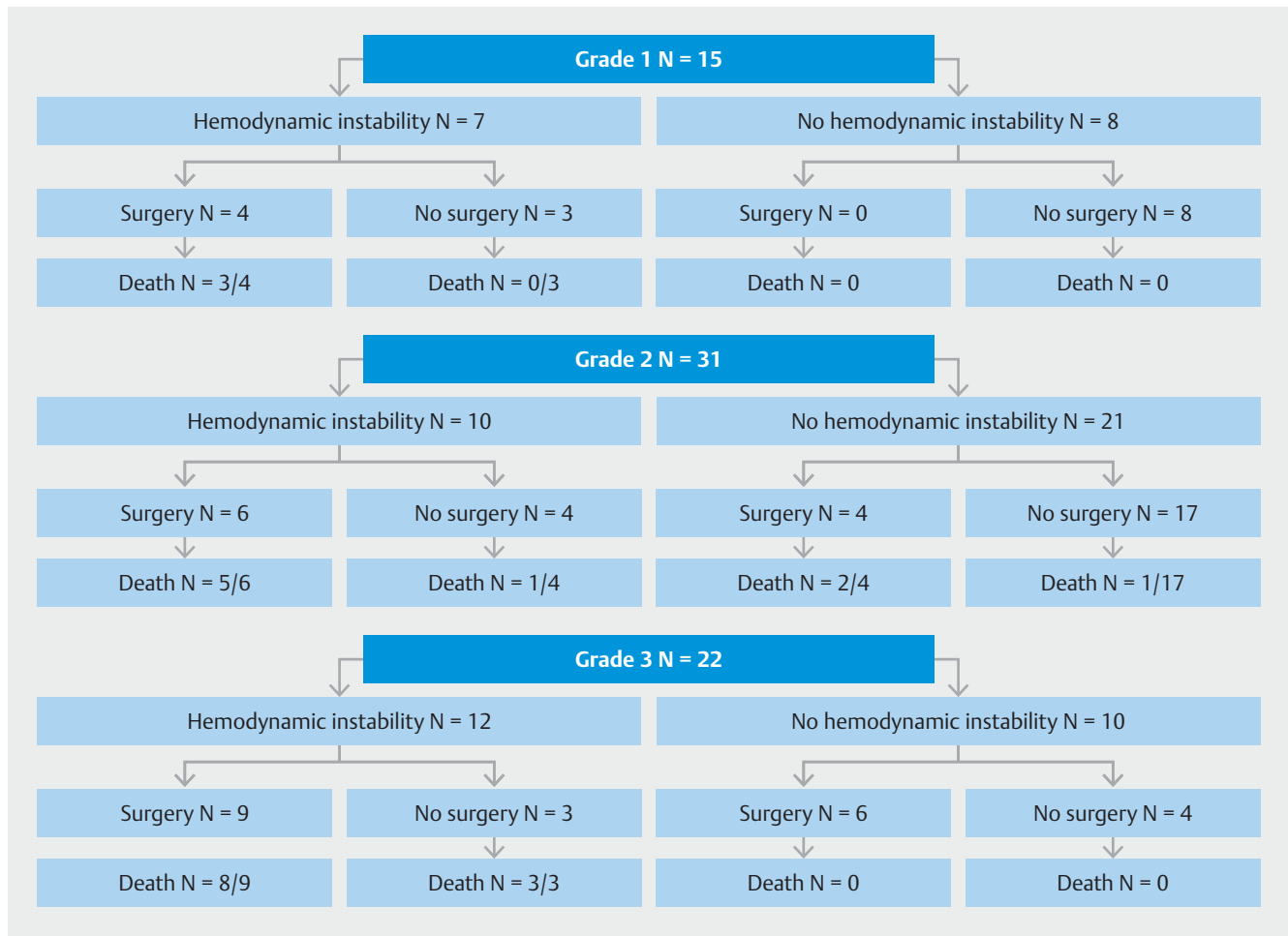
The primary objective was to document the outcomes depending on endoscopic stages. The secondary endpoints were to identify the impact of endoscopy on the therapeutic decision and to elucidate factors associated with colectomy and mortality in case of IC.

Endoscopic classification of patients

Patients were classified according to endoscopic grades of Favier (► **Fig. 1**) [15]: stage 1, mucosal edema and erythema; stage 2, mucosal ulcerations but not necrotic; stage 3, colonic necrosis.

Statistical analysis

Descriptive statistics were used to analyze patient characteristics. Data were expressed as mean ± standard deviation or median and interquartile range 25 to 75 (IQR25-75). Univariate and multivariate with descendant logistic regression analyses were used to identify risk factors for colectomy and mortality in patients with IC and factors significantly associated with endoscopic stage 3. A Student's *t* test for quantitative variables and the Chi-squared test or Fisher's exact tests for qualitative variables were used in the univariate analysis. Multivariate analysis was performed to determine the strength of associations. Odds ratios (ORs) and 95% confidence intervals (95%CI) were calculated using regression analysis. All statistical analyses



► **Fig. 1** Colonoscopic pictures showing the three endoscopic Favier's Stage of ischemic colitis.

were performed using the SPSS software program (version 18.3) (IBM, Armonk, New York, United States). A two-tailed $P < 0.05$ determined a statistically significant result.

Results

Epidemiological characteristics

Between 2006 and 2015, 118 patients were identified with potential IC undergoing a colonoscopy, 47 patients were excluded because their condition was not considered severe before endoscopy or questionable diagnosis of IC, and 71 patients were finally included. There were 48 men (68%) with a mean age of 71 ± 13 years old. The main epidemiological characteristics are detailed in ► **Table 1**.

Clinical features

All patients presented with severe IC as defined above. The mean Charlson score was 5.1 ± 2.2 . Fifty-six (80%) had a history of vascular disease. The etiologies of IC were aortic surgery ($n=26$; 37%), atherosclerotic disease of digestive arteries ($n=13$; 18%), gastrointestinal surgery ($n=8$; 11%), embolic cause ($n=7$; 10%), a state of hemodynamic instability/resuscitation ($n=4$; 6%), nonsteroidal anti-inflammatory drug use

($n=2$; 3%), others ($n=2$; 3%), and idiopathic ($n=9$; 13%). Fifty-six (79%) patients took antiplatelet or anticoagulant therapy before IC.

Forty patients (56%) had only left colitis. Seven patients (10%) had extensive colitis (beyond the left colon). Only one patient (1.4%) had an exclusively right injury. In 23 patients (32%), we could not know the exact involvement of IC. CT scan was not performed and emergency colonoscopy (often due to poor preparation) was not complete. Three patients developed small intestinal ischemia after IC during the same hospital stay and had to undergo surgery.

Among patients with a surgical risk factor (aortic or gastrointestinal surgery; $n=34$), 23 (68%) had undergone their surgery in context of emergency because of a critical condition. Twenty-nine patients (43%) presented with hemodynamic instability. Among them, 19 (66%) underwent surgery and 20 (69%) died.

In total, 24 patients (34%) died because of the IC. Among these patients, 18 (75%) had undergone surgery and all except one was hemodynamically unstable at the time of colonoscopy. Furthermore, in case of aortic surgery ($n=26$), 19 patients (73%) had hemodynamic instability, 16 (62%) had colectomy and 13 (50%) died. In the case of association including aortic

► **Table 1** Characteristics of patients with ischemic colitis (IC).

Characteristics	Total patients (%)	Patients <60 yrs	Patients >60 yrs
Total	71 (100%)	11	60
Age of diagnosis (mean ± SD)	71.1 ± 13.3		
Sex			
▪ Men	48 (68%)	8 (73%)	40 (67%)
▪ Women	23 (32%)	3 (27%)	20 (33%)
Charlson comorbidity score (mean ± SD) ¹	5.1 ± 2.2	5.6 ± 1.9 ¹	2.2 ± 1.6 ¹
Smoking	39 (55%)	6 (55%)	33 (55%)
Alcohol consumption	7 (10%)	0 (0%)	7 (12%)
History of vascular disease ¹	56 (80%)	6 (55%) ¹	50 (83%) ¹
End stage renal disease	0	0 (0%)	13 (22%)
Etiology of IC			
▪ Aortic surgery	26 (37%)	3 (27%)	23 (38%)
▪ Other surgery	8 (11%)	2 (18%)	6 (10%)
▪ Atherosclerotic disease	13 (18%)	1 (9%)	12 (20%)
Embolitic cause			
▪ Hemodynamic failure	7 (10%)	2 (18%)	5 (8%)
▪ NSAIDs	4 (6%)	1 (9%)	3 (5%)
▪ Others	2 (3%)	1 (9%)	1 (2%)
▪ No causes	2 (3%) 9 (12.5%)	0 1 (9%)	2 (3%) 8 (8%)
Clinical symptoms			
▪ Hemorrhage	48 (71%)	8 (73%)	40 (67%)
▪ Abdominal pain ²	48 (94%) ²	7 (100%) ²	41 (91%) ²
▪ Diarrhea	47 (70%)	6 (55%)	41 (68%)
Hemodynamic instability	29 (43%)	6 (55%)	23 (38%)
Endoscopic grade of Favier			
▪ Grade 1	15 (21%)	2 (18%)	13 (22%)
▪ Grade 2	32 (45%)	6 (55%)	26 (44%)
▪ Grade 3	24 (34%)	3 (27%)	21 (35%)
CT scan	48 (68%)	6 (55%)	42 (70%)
▪ Effusion	21 (44%)	2 (18%)	19 (32%)
▪ Enhancing defect	8 (17%)	0 (0%)	8 (13%)
▪ Perforation	1 (2%)	0 (0%)	1 (2%)
Surgery	29 (41%)	3 (27%)	26 (44%)
Death	24 (34%)	2 (18%)	(37%)

¹ $P < 0.05$ in univariate analysis.

² Missing data from patients who arrived confused/unconscious.

surgery and endoscopic grade 3 (n = 11), seven patients (65 %) died.

CT scan data

Forty-eight patients (68 %) had a CT scan, with 42 (88 %) of them having abnormal findings, including colonic wall thickening in 34 (71 %), defect of colonic enhancement at contrast injection in eight (17 %), intraperitoneal fluid collection in 21 (44 %), and perforation in one patient. Overall, 22 patients (46 %) had at least one severity sign on CT scan (fluid collection and/or deficit of enhancement and/or perforation). Among patients who were hemodynamically unstable and had a CT scan (N = 12), seven (58 %) had severity signs on CT scan. Among patients with a defect of colonic enhancement in injection (n = 8), five (63 %) underwent surgery and four (50 %) finally died.

The location of colonic ischemia suspected on CT scan was always well correlated with the resected specimen in operated patients.

Endoscopy features

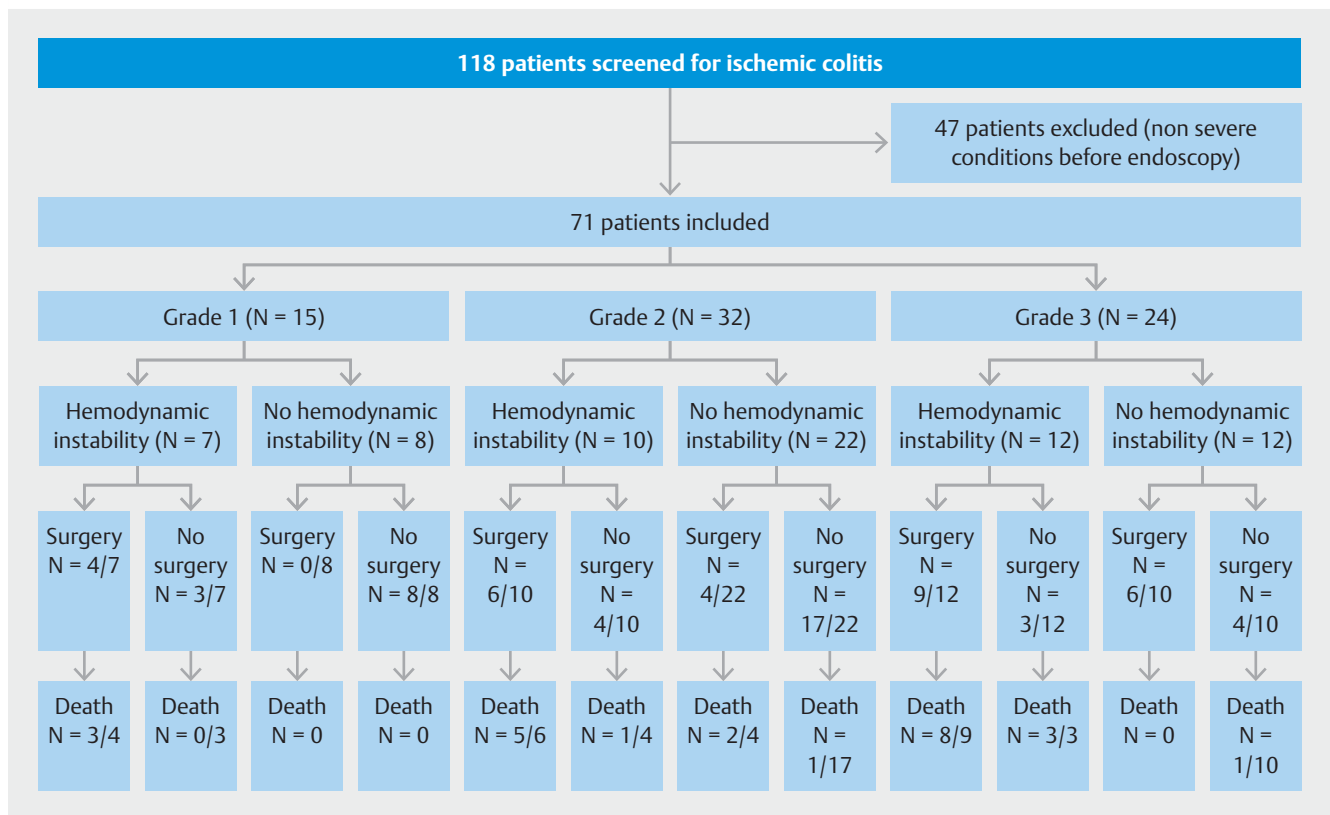
All patients underwent lower gastrointestinal endoscopy: 23 (32 %) within 6 hours from suspected diagnosis, 17 (24 %) within 6 to 24 hours and 31 (44 %) after 24 hours. The endoscopy was performed in the ICU in 32 patients, in the Emergency Room in 30, in the Operating Room in two, and in the endoscopy unit in seven. Among them, 23 patients (32 %) had an emergency endoscopy during shift hours. No complications occurred during endoscopies.

The endoscopic stages were Favier 1 in 15 patients (21 %), Favier 2 in 32 patients (45 %), and Favier 3 in 24 patients (34 %). Focusing on patient with endoscopic stage 3 (n = 24), eight patients (33 %) had undergone endoscopy within 6 hours, 10 (42 %) within 6 to 24 hours and six (25 %) after 24 hours. A delay in endoscopy of more than 24 hours was not associated with stage 3 results on endoscopy.

Outcomes related to endoscopic stages

Regarding the severity of IC in patients depending on the Favier stage, in the patients with endoscopic stage 1 (n = 15), seven (47 %) had hemodynamic instability, two (13 %) had severity signs on CT scan, four (27 %) had colectomy, and three patient (20 %) died (► Fig. 2, ► Table 2). In the patients with endoscopic stage 2 IC (n = 32), 10 (31 %) had hemodynamic instability, nine (28 %) had severity signs on CT scan, 10 (31 %) had colectomy and nine patients (28 %) died. In the patients with endoscopic stage 3 IC (n = 24), 12 (50 %) had hemodynamic instability, 14 (58 %) had severity signs on CT scan, 15 (63 %) had a colectomy, and 12 patients (50 %) died.

A mismatch between endoscopic mucosal and surgical serious findings was seen in 18 % of patients (n = 13): 13 % (n = 2) of patients with a stage 1 of Favier, 12 % (n = 4) with grade 2, and 29 % of patients (n = 7) with grade 3.



► **Fig. 2** Outcomes depending on endoscopic stages and hemodynamic stability.

► **Table 2** Hemodynamic instability, results of CT scan, colectomy, and death depending on the endoscopic grade.

Endoscopic grades (N = 71)	Grade 1 (N = 15)	Grade 2 (N = 32)	Grade 3 (N = 24)	P
Etiology: aortic surgery (N = 26)	6 (40%)	9 (29%)	11 (46%)	0.38
Hemodynamic instability (N = 29)	7 (46%)	10 (32%)	12 (55%)	0.32
Severity signs at CT scan (N = 25)	2 (13%)	9 (29%)	14 (58%)	0.0009
Surgery/colectomy (N = 29)	4 (27%)	10 (32%)	15 (68%)	0.028
Death (N = 24)	3 (20%)	9 (29%)	12 (55%)	0.10
Time of endoscopy < 24 h (N = 40)	8 (53%)	14 (44%)	18 (75%)	0.06

CT, computed tomography.

Factors associated with the presence of a Favier 3 endoscopic stage

In univariate analysis, factors associated with a Favier endoscopic stage 3 were: diarrhea ($P=0.012$), defect of colonic enhancement on injection during CT scan ($P=0.023$), surgery ($P=0.028$), and death ($P=0.039$). In multivariate analysis, the only factor associated with Favier stage 3 on endoscopy was a defect in colonic enhancement (OR=10.7; 95%CI [1.7–67.1]; $P=0.011$).

Surgical data and decision for surgery

Twenty-nine (41%) patients underwent surgery. The surgical decision was made based on hemodynamic status in 62% of cases ($n=18$), CT scan data in 14% ($n=4$), endoscopic grade in 10% ($n=3$), and other in 14% of cases ($n=4$: cholecystitis and IC with hemodynamic instability, duodenal fistula and IC with hemodynamic instability, perforation before endoscopy, recurrence of ischemic colitis).

All three patients of the patients for whom the surgical decision was made because of endoscopy had endoscopic grade 3 IC. Only one had a CT scan and had a left colitis with little fluid collection, two had a mismatch between endoscopic mucosal (necrosis) and surgical serous (normal), all had colonic resec-

► **Table 3** Association between ischemic colitis and mortality in univariate and multivariate analysis.

	Death (N = 24)	P (univariate)	OR [IC95%] (univariate)	P (multivariate)	OR [IC95%] (multivariate)
Hemodynamic instability (N = 29)	20	<0.0001	26.7 [6.5–109]	0.001	142 [12–19507]
Endoscopic grade 3 (N = 24)	12	0.039	2.9 [1.0–8.2]	0.97	NS
Aortic aneurysm surgery before IC (N = 26)	13	0.033	3.0 [1.1–8.4]	0.14	NS
Short delay (<6h) between suspicion of ischemic colitis and endoscopy (N = 23)	14	0.002	5.7 [1.7–20.2]	0.59	NS
Surgery (N = 29)	18	<0.0001	9.8 [3.1–30.8]	0.006	20.9 [2.2–199]
Charlson score >5 (N = 23)	16	<0.017	3.6 [1.2–10.3]	0.005	56 [3.1–1000]

OR, odds ratio.

► **Table 4** Association between ischemic colitis and colectomy in univariate and multivariate analysis.

	Surgery (N = 29)	P (univariate)	OR [IC95%] (univariate)	P (multivariate)
Hemodynamic instability (N = 26)	18	0.001	5.5 [1.9–15.7]	0.31
Endoscopic grade 3 (N = 24)	15	0.008	3.9 [1.4–11.1]	0.34
Aortic aneurysm surgery (N = 26)	16	0.009	3.8 [1.4–10.6]	0.8
No colic enhancement in CT scan (N = 8)	5	0.037	5.0 [1.0–24.8]	0.14

OR, odds ratio; CT, computed tomography.

tion, and none died. Of the 18 patients for whom the surgical decision was made based on hemodynamic status, 10 had grade 3 IC on endoscopy, six patients had a mismatch between mucosal and serous aspect, 15 underwent colonic resection, and 15 patients died. Four patients underwent surgery because of arterial lesions on CT scan.

All patients with endoscopic stage 1 who underwent surgery had hemodynamic instability (N=4). Ten patients with endoscopic stage 2 IC underwent surgery: 6 for hemodynamic instability and four for signs of severity on CT scan.

Twenty-two of 29 patients who underwent surgery had a colonic resection. Of them, 14 (64%) died. The seven remaining patients did not have resection; of them, four (57%) died. In contrast, among the 42 patients who did not undergo surgery, the death rate was 14% (n = 6). Three patients had an additional resection of the small bowel.

A mismatch between endoscopic mucosal (necrosis) and surgical serous (normal) aspect was noted in 13 patients (45%). Of them, six had a colonic resection (4 deaths among these patients) and seven had no resection (4 deaths among these patients).

Risk factors for surgery and mortality

Mortality

In univariate analysis, the identified risk factors for mortality were hemodynamic instability ($P < 0.0001$), endoscopic stage 3 ($P = 0.039$), aortic aneurysm surgery before IC ($P = 0.033$), surgery ($P < 0.0001$), a short delay (<6 hours) between suspicion

of IC and endoscopy ($P = 0.002$), and Charlson score >5 ($P = 0.017$) (► **Table 3**). In multivariate analysis, hemodynamic instability (OR = 26.7; 95%CI [6.5–109]; $P = 0.001$), surgery (OR = 9.8; 95%CI [3.1–30.8]; $P = 0.006$) and a Charlson comorbidity score >5 (OR = 3.6; 95%CI [1.2–10.3]; $P = 0.005$) were independently associated with a higher mortality rate.

Risk factors for surgery

In univariate analysis, the identified risk factors for surgery were hemodynamic instability ($P = 0.001$), endoscopic stage 3 ($P = 0.008$), aortic aneurysm surgery before IC ($P = 0.009$), and colic enhancement defect on CT scan ($P = 0.037$) (► **Table 4**). In multivariate analysis, hemodynamic instability, endoscopic stage 3, aortic aneurysm surgery before IC, and colic enhancement defect on CT scan were not associated with surgery.

Discussion

The diagnostic and therapeutic management was heterogeneous in our patients with severe IC, as already suggested in other published studies [1, 4, 13, 14, 16, 19–24]. However, the impact of endoscopy, except to confirm the diagnosis, has never been clearly assessed in relation to therapeutic decision making [1]. For these reasons, we attempted, in this study, to assess the role of endoscopy in the therapeutic management of such patients.

However, our study has some limitations. This study was retrospective with some missing data (biological and clinical). The management of IC is quite heterogeneous and this monocen-

tric study reflects the practices of our center over the period studied. This study was not designed to compare our patients with patients with IC who had not undergone colonoscopy (contraindication for endoscopy, endoscopy unnecessary after CT scan, or patients underwent surgery without waiting for endoscopy).

The severity of the endoscopic involvement (Favier stage 3) is an identified risk factor for IC mortality in our study, which is consistent with the literature [16,19]. However, several patients died despite having Favier grade 1 IC, which calls into question the sensibility of endoscopy for assessing the severity and indicating a surgical resection. Other studies have suggested the value of colonoscopy to evaluate the length of mucosal involvement, and thus, to guide surgical resection [1,20,21]. Actually, the rate of total colonoscopy was low in our series, especially because of the risk of perforation and the absence of bowel preparation due to the emergency.

Moreover, the mismatch between endoscopic and surgical findings is a real issue and could lead to a wrong therapeutic decision. Indeed, in our series, half the patients who underwent surgery had a mismatch between the mucosa (necrotic) and serous (normal). Furthermore, half the patients with a mismatch had a digestive resection but the mortality rate was the same as for patients who had not undergone. In addition, the risk of mismatch appeared higher (30%) in the patients with Favier stage 3 IC, which is the stage linked to the decision to operate on a patient. Other studies have found the same results without any standard rationale for surgery [6]. In another hand, it is well established that CT scan is accurate for evaluation of the extent of colic lesions and to identify severity signs, such as a defect in colonic enhancement, as also confirmed by our results [1,25,26].

Regarding the rate of colectomy, it depended on the studies and ranged between 19% and 58% with a mortality rate varying from 33 to 50% [19,22,27–29], if patients required surgical resection [19,23,27–30]. In case of transparietal necrosis, surgery with resection of all thickened colon is the only curative treatment, despite the high rate of mortality [1]. The consensus in the United States is for colectomy in the presence of IC in patients who have hypotension, tachycardia, and abdominal pain without rectal bleeding; for isolated right IC and pan-colonic IC; and in the presence of gangrene [1]. In our study, no factor was associated with colectomy in multivariate analysis. Also, surgeons follow a therapeutic strategy based on hemodynamic instability, and very rarely based on endoscopic findings.

The management of patients with IC is very heterogeneous, but it seems that those who have signs of transparietal colonic necrosis should undergo surgery and that the extension of the resection should not be guided by the appearance of the serosa, but rather, by the extent of mucous necrotic lesions [1,24].

Finally, in our series, the death rate related to IC was 34%, which is consistent with the literature [1,24]. Factors associated with death were hemodynamic instability, Favier grade 3, aortic aneurysm surgery before IC, colectomy, and Charlson comorbidity score index >5. After aortic surgery, 15% of patients developed IC [20,31]. Among them, the rate of mortality was around 50% [31]. The literature shows that early colectomy of

patients, when it is necessary (prior to the installation of shock related to transparietal necrosis of the colon), would reduce postoperative mortality. In our series, all the patients who died (except one) were hemodynamically unstable at the time of colonoscopy, which suggests that when patients become unstable, it may be too late.

Conclusions

In conclusion, this study suggested that endoscopy impacted the decision to proceed with surgery in patients with IC in only 10% of cases, with a high rate of mismatch (50%) between mucosa and serous aspect. Hemodynamic instability was the first indication of colectomy in patients with IC, and hemodynamic instability, colectomy, and a Charlson score >5 were risks factors for death in this study. CT scan as well as lactatemia seem also to adequately predict the need for surgery.

There is a critical need for a prospective, multicenter study of the impact of clinical, radiological, and endoscopic evaluation of patients with suspected IC to establish their respective place in management of these cases.

Acknowledgements

This study was approved by the appropriate institution (Commission Nationale Informatique et Liberté).

Competing interests

The authors declare that they have no conflict of interest.

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