Still time to perform intestinal revascularization in patients with acute mesenteric ischemia with peritonitis: An analysis of bowel viability in resections

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Abstract

Objective: Acute mesenteric ischemia is often fatal, and many survivors develop short bowel syndrome. To avoid massive bowel resection, revascularization is recommended for acute mesenteric ischemia patients. However, whether acute mesenteric ischemia patients with clinical peritonitis can be revascularized remains uncertain. Therefore, this study aimed to evaluate the histopathological potential reversibility of resected bowel in acute mesenteric ischemia patients with peritonitis.

Methods: We retrospectively reviewed the medical records of acute mesenteric ischemia patients treated at the Kameda Medical Center between January 2001 and March 2015. Pathological evaluation regarding bowel resection was performed. Patients with and without peritonitis were compared. The primary outcome was the proportion of patients with reversible or irreversible ischemia. Patients with reversible and irreversible ischemia were characterized.

Results: Of 41 patients, 17 underwent laparotomy, 6 endovascular surgery, and 18 palliative care. Among 23 patients receiving curative treatment, 7 had peritonitis and 13 did not. Seven patients of each group received bowel resection, but 85.7% of those with peritonitis had reversible ischemia. We categorized patients with ischemia into reversible and irreversible groups. The median time between symptom onset and diagnosis in the reversible group was >27h. Systemic inflammatory response syndrome was found in 72.2% and 66.7% of the reversible and irreversible groups, respectively.

Conclusion: Acute mesenteric ischemia patients with clinical peritoneal signs may have potentially reversible ischemia. As a result, revascularization should be considered, even in the case of peritonitis.

Introduction

Although acute mesenteric ischemia (AMI) is uncommon, it often leads to bowel necrosis, which has a mortality rate as high as 60%–80%.[1] Subsequently, AMI patients may experience short bowel syndrome (SBS) and a poor quality of life (QOL). Therefore, this condition requires rapid and efficient treatment.

Until recently, the traditional treatment strategy for AMI was laparotomy; however, recent advances have made endovascular surgery (EVS) a promising method for revascularization with favorable results in terms of life expectancy and bowel salvage in AMI.[1,2] Several retrospective studies compared EVS and laparotomy, but they could not show conclusive results.[3–8] Moreover, patients indicated for EVS in previous studies may have a relatively less severe condition without signs of peritoneal irritation,[3,4,9–11] and the possibilities of performing reperfusion for AMI patients with peritonitis remain unclear. Therefore, this study aimed to evaluate the histopathological potential reversibility of resected bowel in AMI patients with peritonitis.

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Methods

Patients

Between January 2001 and March 2015, a total of 41 consecutive AMI patients were treated at Kameda Medical Center. Those with arterial thrombotic or arterial embolic superior mesenteric artery (SMA) etiologies for AMI were included in our study; those presenting etiologies secondary to mesenteric venous thrombosis, non-occlusive mesenteric ischemia, and aortic dissections complicated by visceral ischemia were excluded. AMI was diagnosed and classified based on its etiology using contrast-enhanced computed tomography (CT), abdominal ultrasonography, or angiography.

Study design and observational methods

Medical records were retrospectively reviewed; patient-specific demographics, including age, sex, preoperative risk factors, perioperative variables, clinical presentations and outcome, and technical details, were collated. The clinical presentation comprised physical, laboratory, and radiographic findings, including surgical approach and treatment outcome. SBS was defined as a resection with a remaining length of the small bowel shorter than 150 cm.

Treatment strategy

Patients were categorized according to the treatment administered: laparotomy, EVS, or palliative care. The treatment was determined by the surgeon's interpretation of each patient's clinical status, along with physical, laboratory, and radiographic findings. Laparotomy was performed by gastroenterological surgeons, while EVS was performed by an interventional radiologist.

Following physical examination, laparotomy was indicated in patients with signs of peritoneal irritation, such as muscular defense or rebound tenderness, or patients clinically suspected with bowel necrosis, such as those with poor contrast enhancement, pneumatosis intestinalis, or mesenteric venous air on CT scans.

Laparotomy included the exploration of bowel viability and the resection of non-viable bowel segments. Bowel viability was clinically assessed based on the color of the bowel wall and the pulsation of the mesenteric arteries, and determination of the presence or absence of peristalsis. Laparotomy was performed by a board-certified gastrointestinal surgeon as an attending doctor who decided whether the bowel should be resected or not. However, during the study period, no revascularization under laparotomy was performed because of its low success rate in our hospital. In addition, transferring patients to another hospital is difficult because our hospital is a tertiary hospital in a rural medical region. Therefore, when we found pulsation without any signs of poor perfusion, we completed the operation after exploration alone without revascularization. In addition, we completed an operation with exploration under special situations only (when a patient with obvious massive necrotic bowels refused to undergo massive bowel resection).

EVS was indicated in patients without evidence of bowel necrosis. EVS included both mechanical thrombectomy and thrombolysis. Mechanical thrombectomy was used to achieve initial reperfusion of the viscera followed by initiating thrombolysis based on residual arterial occlusions. After initiating thrombolysis, the decision to continue the procedure was determined by the patient's overall condition and his or her response. Angiography was repeated several times, every 1 or 2 days, or until conversion to laparotomy upon discovering any signs of bowel necrosis or when thrombolysis was terminated due to successful bowel reperfusion.

Palliative care was indicated when the patient, or his or her family members, decided against laparotomy or EVS considering the perioperative risks: extremely advanced age, poor performance of activities of daily living (ADL), or a low chance of maintaining a good QOL after surgery, particularly when significant bowel resection may occur, which inevitably leads to SBS.

In this study, we compared patients who had peritonitis with those who did not; the primary outcome was the proportion of cases with reversible or irreversible ischemia. We characterized those patients with reversible or irreversible ischemia according to the assumption that patients who survived without bowel resection and those whose resected bowel pathologically revealed mucosal necrosis may be categorized as the reversible group. In contrast, the irreversible group comprised patients whose resected bowel pathologically revealed transmural necrosis.

The pathological evaluation was performed in cases with resected bowel, focusing particularly on the severity of ischemic necrosis, such as transmural or mucosal necrosis. Pathological diagnosis was determined by considering the most severe ischemic site.

Statistical methods

Data were analyzed by univariate analyses. Differences between the two groups were determined using Student's t-test for parametric data and the Mann–Whitney U test for nonparametric data. We used the Kolmogorov–Smirnov test to test raw data for normality. Fisher's exact test was used to compare nominal data. A p-value of < 0.05 was considered statistically significant.

Ethical regulations

The study protocol complied with the Declaration of Helsinki and was approved by the Kameda Medical Center Ethical Committee. The requirement for written informed consent was waived because of the retrospective observational nature of this study. The study outline, including the ethical statement, was published on the hospital website.

Table 1. Details of all patients.

No.	Peritonitis	Procedure	Revascularization	Bowel resection	Short bowel syndrome[a]	Pathology	Reversible or irreversible[b]	Outcome
1	Yes	Laparotomy	No	Yes	Yes	Mucosal	Reversible	Alive
2	Yes	Laparotomy	No	Yes	Yes	Mucosal	Reversible	Alive
3	Yes	Laparotomy	No	Yes	Yes	Mucosal	Reversible	Alive
4	Yes	Laparotomy	No	Yes	Yes	Mucosal	Reversible	Alive
5	Yes	Laparotomy	No	Yes	Yes	Mucosal	Reversible	Dead
6	Yes	Laparotomy	No	Yes	Yes	Transmural	Irreversible	Alive
7	Yes	Laparotomy	No	Yes	No	Mucosal	Reversible	Alive
8	No	EVS	Yes	No	No		Reversible	Alive
9	No	EVS	Yes	No	No		Reversible	Alive
10	No	EVS	Yes	No	No		Reversible	Alive
11	No	EVS	Yes	No	No		Reversible	Alive
12	No	EVS	No	Yes	Yes	Mucosal	Reversible	Alive
13	No	Laparotomy	No	Yes	Yes	Mucosal	Reversible	Alive
14	No	Laparotomy	No	Yes	Yes	Mucosal	Reversible	Dead
15	No	Laparotomy	No	Yes	Yes	Unknown	Unknown	Dead
16	No	Laparotomy	No	Yes	No	Mucosal	Reversible	Alive
17	No	Laparotomy	No	Yes	No	Mucosal	Reversible	Alive
18	No	Laparotomy	No	Yes	No	Transmural	Irreversible	Alive
19	No	Laparotomy	No	No	No		Reversible	Alive
20	No	Laparotomy	No	No	No		Unknown	Dead
21	Unknown	EVS	Yes	Yes	Yes	Unknown	Unknown	Alive
22	Unknown	Laparotomy	No	Yes	Yes	Mucosal	Reversible	Alive
23	Unknown	Laparotomy	No	Yes	Yes	Transmural	Irreversible	Alive

Mucosal: mucosal necrosis; Transmural: transmural necrosis; EVS: endovascular surgery.
[a]Short bowel syndrome was defined as a resection with a remaining length of small bowel shorter than 150 cm.
[b]Reversible: Those who survived without bowel resection and those whose resected bowel were pathologically revealed as mucosal necrosis. Irreversible: Those whose resected bowel was pathologically revealed as transmural necrosis.

Results

Patient characteristics and the proportion of cases with peritonitis

Of the 41 patients, 18 patients received palliative care. The remaining 23 patients who received treatments for mesenteric ischemia were included in our analysis (Table 1). Among the 23 patients, 21 patients were diagnosed by contrast-enhanced CT and 2 patients were diagnosed by non-contrast-enhanced CT. One of the two patients was followed up by angiography and the other underwent laparotomy. Seven of these patients had signs of peritoneal irritation, while 13 patients did not. These data were not available for the remaining three patients. We compared data of patients with and without peritonitis (Table 2) and found no significant difference in patient demographics, including the duration between symptom onset to diagnosis of AMI in the emergency department, or the proportion of patients with systemic inflammatory response syndrome (SIRS). However, there were a significantly greater number of patients with hypertension in the non-peritonitis group (p < 0.05).

With regard to the primary outcome, 6 patients (85.7%) in the peritonitis group and 10 patients (90.9%) in the non-peritonitis group had reversible ischemia (p = 1.00) (Table 3). One patient (20th patient in Table 1) who received laparotomy but refused to undergo massive bowel resection due to the risk of SBS was judged as a case of unknown reversibility because we could not obtain pathological results from this patient. In each group, seven patients had bowel resection; pathological data were missing in one of these patients. Among patients who underwent bowel resection, 6 (85.7%) in the peritonitis group and 5 (71.4%) in the non-peritonitis group had mucosal necrosis.

Characteristics of reversible and irreversible ischemia

We assessed the characteristics of patients with reversible or irreversible ischemia (Table 4). Of the 23 patients who received curative treatment for SMA occlusion, ischemic characteristics of the three patients were unknown — two patients were not examined pathologically (one patient was treated by EVS and the other by laparotomy) and one patient in the laparotomy group refused massive bowel resection. Three of the remaining 20 patients were found to have transmural irreversible ischemia and 17 had mucosal reversible

Table 2. Patient characteristics.

Variable	Missing	Peritonitis (n = 7)[a]	Non-peritonitis (n = 13)[a]	P value
Age, mean ± SD, year	0	80.7 ± 5.0	78.1 ± 10.3	0.53
Male (%)	0	1 (14.3)	9 (69.2)	0.06
Comorbidity (%)	0			
Hypertension		3 (42.9)	12 (92.3)	<0.05[b]
Diabetes mellitus		1 (14.3)	5 (38.5)	0.35
Hyperlipidemia		1 (14.3)	3 (23.1)	1.00
Ischemic heart disease		2 (28.6)	4 (30.8)	1.00
Atrial fibrillation		4 (57.1)	6 (46.2)	1.00
Cerebral stroke		2 (28.6)	7 (53.8)	0.37
Chronic kidney disease		1 (14.3)	1 (7.7)	1.00
Anticoagulant drugs (%)	0	1 (14.3)	0 (0.0)	0.35
Antiplatelet drugs (%)	0	4 (57.1)	4 (30.8)	0.36
Details of peritoneal irritation sign (%)	0			
Rebound tenderness (%)		3 (42.9)	0 (0.0)	
Muscular guarding (%)		7 (100.0)	0 (0.0)	
Duration of symptoms onset to diagnosis, median (range), h[c]	0	28 (8, 96)	27 (1, 74)	0.84
Systemic inflammatory response syndrome	0	6 (85.7)	8 (61.5)	0.34

Parametric continuous variables were analyzed using Student's t-test and are reported as mean ± standard deviation (SD). Nonparametric variables were analyzed using the Mann–Whitney U test and are reported as median and range.
Proportions were analyzed using Fisher's exact test and are expressed as percentages.
[a]We missed three cases regarding peritoneal irritation signs.
[b]Statistically significant.
[c]Duration between symptom onset and the diagnosis of acute mesenteric ischemia (AMI).

Table 3. Proportions of patients with reversible or irreversible necrosis.

Variable	Missing	Peritonitis (n = 7)[a]	Non-peritonitis (n = 13)[a]	P value
Reversible or Irreversible bowel ischemia[b]	2			1.00
Reversible (%)		6 (85.7)	10 (90.9)	
Irreversible (%)		1 (14.3)	1 (9.1)	
Bowel resection	0			
EVS without bowel resection (%)		0 (0.0)	4 (30.8)	
Laparotomy without bowel resection (%)		0 (0.0)	2 (15.4)[c]	
EVS with bowel resection (%)		0 (0.0)	1 (7.7)	
Laparotomy with bowel resection (%)		7 (100.0)	6 (46.2)	
Pathology of resected bowels	1			
Mucosal necrosis (%)		6 (85.7)	5 (71.4)	
Transmural necrosis (%)		1 (14.3)	1 (14.3)	
Etiology (%)	0			0.52
Embolism		7 (100.0)	10 (76.9)	
Thrombosis		0 (0.0)	3 (23.1)	

EVS: endovascular surgery.
[a]Data regarding peritoneal irritation signs were not available for three patients.
[b]Cases without bowel resection and cases with pathologically mucosal necrosis were counted as reversible. Pathologically transmural necrosis cases were counted as irreversible.
[c]Laparotomy was performed in one patient in whom no necrotic signs were found and this patient survived conservatively. Another patient had massive necrotic signs but refused to undergo any resection of massive bowels and finally died.

ischemia or survived without bowel resection. Seven patients (43.8%) in the reversible group had bloody stools (p = 0.26). The median duration between symptom onset and diagnosis was 27 h (range: 1–96 h) in the reversible group and 39 h (range: 18–40 h) in the irreversible group (p = 0.49). Twelve patients (70.6%) in the reversible group had SIRS compared to 2 (66.7%) in the irreversible group (p = 1.00).

According to our imaging study, 6 patients (38.9%) with reversible ischemia and 1 (33.3%) with irreversible ischemia had occlusion within the proximal SMA to the middle colic

artery (p = 1.00). Eight patients (44.4%) with reversible ischemia and 2 (66.7%) with irreversible ischemia showed enhancement of the SMA distal to the embolus (p = 1.00).

Pathological review of patients with peritonitis

Figure 1 shows an example of mucosal necrosis with signs of peritoneal irritation. Figure 2 presents the pathological features. Patients diagnosed with SMA occlusion and receiving laparotomy due to signs of peritoneal irritation inevitably developed SBS following massive bowel resection (Figure 2). Despite signs of peritoneal irritation, the pathological analysis revealed mucosal necrosis of the resected bowel. The patient shown in Figures 1 and 2 could have been treated with EVS, and bowel resection may have been avoided, despite the presence of signs of peritoneal irritation.

Discussion

Determination of reversible and irreversible ischemia

In this study, we evaluated the feasibility of revascularization to rescue the ischemic bowels of AMI patients with peritonitis. In this study, 85.7% of the AMI patients with peritonitis had reversible ischemia. Among the 23 patients who received curative treatment for AMI, the analysis of the pathological tests revealed only three patients with irreversible ischemia. According to our summary of the characteristics of patients with reversible ischemia, the median time elapsed between symptom onset and diagnosis in reversible cases was more than 27 h. Twelve patients (70.6%) in the reversible group and two patients (66.7%) in the irreversible group had SIRS. Imaging studies revealed that the level of occlusion, distal enhancement of SMA, or other signs may not suggest reversible or irreversible ischemia. These results may suggest that many AMI patients with peritonitis can be saved by reperfusion.

Possibility of revascularization in patients with peritonitis

According to the published literature and existing guidelines, patients with peritonitis are not eligible for revascularization by EVS.[2–4,9–11] This may be attributed to the peritoneal signs indicating the possibility of bowel infarction. However, our study showed that 85.7% of patients with peritonitis had reversible ischemia during operation. When peritonitis is detected based on peritoneal irritation signs, it may not necessarily indicate irreversible bowel ischemia.

Acute bowel ischemia is believed to comprise three stages, namely, reversible, mucosal necrosis; submucosal and muscular necrosis (which causes fibrotic strictures); and irreversible, transmural necrosis.[12–14] In this study, peritoneal irritation might have been observed with mucosal necrosis as a clinical symptom of peritonitis.

The sensitivity and specificity of muscular guarding were reported to be 13%–90% and 40%–97%, respectively, while those of rebound tenderness are reported to be 37%–95% and 13%–91%, respectively.[15] Therefore, obtaining a preoperative diagnosis of whether patients have peritonitis or reversible ischemia is difficult. Considering our results and the difficulty in diagnosing peritonitis preoperatively, peritoneal irritation signs may not preclude the possibility of revascularization.

In our study, 18 elderly patients chose palliative care in case they survive with severe complications, including SBS, following a late diagnosis. However, our results indicate that few of the elderly and frail patients with peritonitis can be treated by revascularization. Although few of them were poor surgical candidates, attempts for revascularization could be carried out through EVS because EVS is less invasive than laparotomy and may be more suitable for elderly patients.[16] In addition, in patients with peritonitis, EVS was not recommended, but it is not prohibited as well.[17] We hope that our results may provide such frail patients with peritonitis with wider clinical options and increased chances of survival.

Characteristics of patients with reversible or irreversible ischemia

We attempted to identify a factor that could distinguish cases of reversible ischemia from those with reversible ischemia, but we failed. Interestingly, Nuzzo et al.[18] also reported that peritoneal irritation signs were not significant predictive factors of intestinal irreversible necrosis in AMI patients.

Previous reports claimed that the reperfusion time and, consequently, the prevention of necrosis depend on the level of occlusion.[19,20] However, according to our pathological evaluation, some patients were able to survive a much longer time until diagnosis than previously thought possible. Furthermore, the level of occlusion did not correlate with reversible ischemia. To avoid necrosis, the reperfusion time depends on the level of atherosclerosis, dehydration, and other comorbidities. Therefore, the level of occlusion, or time to diagnosis, may not be a simple predictor of indicating time for reperfusion to avoid necrosis. Early diagnosis does not necessarily improve the chances of survival.[21] We agree with a previous report,[8] which states that revascularization may still be considered a treatment option in cases with a significant delay to surgery.

With regard to radiological tests, CT findings have a sensitivity of 58%–88% and a specificity of 76%–90% for the diagnosis of partial mucosal or transmural bowel ischemia.[22] Several reports show that bowel dilatation is a predictive factor of bowel necrosis.[18] However, Wiesner and Mortele[23] highlighted the difficulty in diagnosing mucosal or transmural necrosis using radiological testing. They found that bowel

Table 4. Characteristics of reversible and irreversible ischemia based on the histopathology or successful intestinal revascularization.

Variable	Missing	Reversible (n = 17)[a]	Irreversible (n = 3)[a]	P value
Age, mean ± SD, year	0	80.1 ± 8.3	75.3 ± 5.0	0.36
Male (%)	0	8 (47.1)	2 (66.7)	1.00
Symptoms (%)	1			
Abdominal pain		15 (93.8)	3 (100.0)	1.00
Nausea		10 (62.5)	3 (100.0)	0.52
Vomiting		9 (56.2)	2 (66.7)	1.00
Diarrhea		9 (56.2)	1 (33.3)	0.58
Bloody stools		7 (43.8)	0 (0.0)	0.26
Constipation		3 (18.8)	0 (0.0)	1.00
Hypotension		0 (0.0)	0 (0.0)	1.00
Fever		3 (18.8)	1 (33.3)	0.53
Duration of symptoms onset to diagnosis, median (range), h[b]	0	27 (1, 96)	39 (18, 40)	0.49
Peritoneal irritation sign (%)	2	6 (37.5)	1 (50.0)	1.00
Rebound tenderness		3 (18.8)	0 (0.0)	1.00
Muscular guarding		6 (37.5)	1 (50.0)	1.00
Systemic inflammatory response syndrome (%)	0	12 (70.6)	2 (66.7)	1.00
Imaging study (%)	0			
Etiology (%)				
Embolism		16 (94.1)	2 (66.7)	0.28
Thrombosis		1 (5.9)	1 (33.3)	
Level of occlusion of SMA main trunk (%)				
Proximal to 1st JA, proximal to MCA		3 (17.6)	1 (33.3)	1.00
Distal to 1st JA, proximal to MCA		3 (17.6)	0 (0.0)	
Distal to 1st JA, distal to MCA		11 (64.7)	2 (66.7)	
Enhancement of SMA distal to the embolus on CT	2[c]	8 (47.1)	2 (66.7)	1.00
Occlusion of IMA on CT	2[c]	1 (6.2)	0 (0.0)	1.00
Smaller SMV sign		5 (29.4)	1 (33.3)	1.00

SMA: superior mesenteric artery; 1st JA: first jejunal artery; MCA: middle colic artery; CT: computed tomography; IMA: inferior mesenteric artery; SMV: superior mesenteric vein.
Parametric continuous variables were analyzed using Student's t-test and are reported as mean ± standard deviation (SD). Nonparametric variables were analyzed using the Mann–Whitney U test and reported as median and range. Proportions were analyzed using Fisher's exact t-test and expressed as percentages.
[a]Pathological results were not available for three cases.
[b]Time period between symptoms onset and the diagnosis of acute mesenteric ischemia (AMI) in the emergency department.
[c]Two cases did not undergo contrast-enhanced computed tomography; both were in the reversible group.

wall thickness, peritoneal stranding, peritoneal fluids, or bowel wall enhancement cannot differentiate mucosal ischemia from transmural infarction.

Limitations

This study had several limitations. First, this was a retrospective study with a small sample size. Therefore, there might be a type 2 statistical error due to the limited sample size. The generalizability of our data needs verification by further studies, and pathological evaluation from other hospitals is awaited. In addition, there may be a selection bias for the patients undergoing EVS. Because EVS is indicated for patients with less severe disease having no peritonitis, these patients might have better outcomes. This is also mentioned in a previous study.[10] Second, we may have performed excessive bowel resection because revascularization cannot be

done under laparotomy. There might be questionable bowels that would respond to revascularization, but we could not perform revascularization under laparotomy or hybrid open and endovascular treatment. However, due to the low revascularization rates, we were able to evaluate reversibility via pathological results during the operation and proved the reversibility of ischemic bowels in patients with peritonitis. We believe these are valuable data that are difficult to obtain under common practice with more increased revascularization. Third, the clinicians might have overinterpreted the patients' peritoneal signs. Most doctors who evaluated the peritoneal irritation signs were general surgeons, but few were emergency medicine specialists. In addition, whether peritoneal irritation signs were local or generalized was unknown. Finally, we used SIRS score to evaluate severity, instead of a sequential organ failure assessment (SOFA) or quick SOFA which is present in published sepsis guidelines,
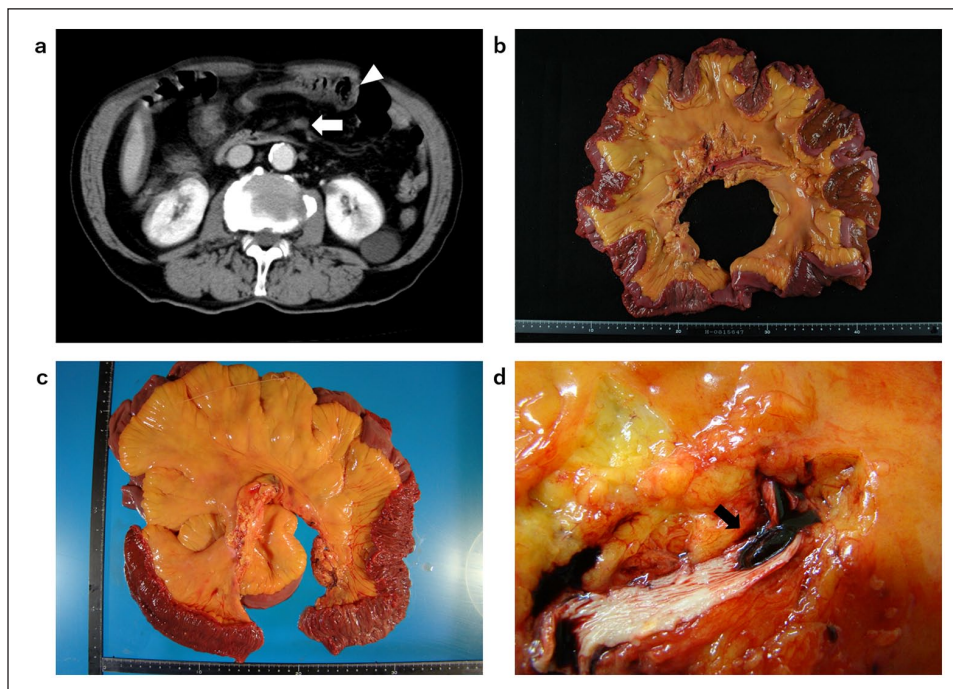
Figure 1. An example of a resected bowel specimen from a patient with mural necrosis who had signs of peritoneal irritation upon physical examination. (a) Computed tomography revealed contrast defects in the superior mesenteric artery (SMA; arrow) and the small intestines (arrowhead). There was no dilatation in the intestines or free air. (b) Macroscopic image of the resected specimen. (c) Macroscopic image of the mucosa. (d) The lumen of the SMA was filled with clots (arrow).
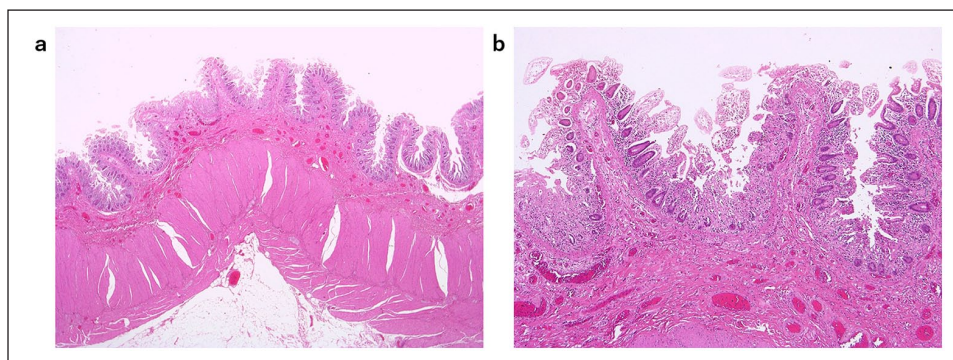

Figure 2. Pathological findings. (a) The muscular layer was intact. (b) Diffuse mural necrosis and congestion in the submucosa.

because these options have only recently been adopted[24] and we could not access medical records related to changes in the mental status of many of our patients. In addition, organ failure or serum lactate levels were suspected to be a predictive factor of intestinal necrosis, but we could gather these data from only a few patients.

Conclusion

Our clinicopathological review of resected bowel specimens indicates the possibility that AMI patients with clinical peritoneal signs may have potentially reversible ischemia. Since differentiating between reversible and irreversible ischemia can be challenging, revascularization should be considered, even in the case of peritonitis.

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