Original Article

A strategy for improving the prognosis of non-occlusive mesenteric ischemia (NOMI): a single-center observational study

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Aim: The purpose of this study was to determine the prognostic factors of non-occlusive mesenteric ischemia (NOMI) and to examine treatment strategies that could improve its prognosis.

Methods: We retrospectively identified 30 patients who underwent emergency laparotomy for NOMI in Kansai Medical University Hospital (Hirakata, Japan) from April 2013 to December 2017. We examined prognostic factors related to discharge outcome and also examined the prognostic impact of open abdominal management and second look operation strategy (OSS) by dividing the patients into the non-OSS group and the OSS group.

Results: The primary end-point was a prognostic factor for outcome at discharge of the 30 patients. The outcome at discharge was compared between the survival group and the death group. Multivariate analysis was undertaken on two items from the univariate analysis that showed a significant difference (computed tomography findings of intestinal pneumatosis and acute disseminated intravascular coagulation [DIC] score). As a result, there was a significant difference in the factors of intestinal pneumatosis (odds ratio = 0.054; 95% confidence interval, 0.005–0.607; $P = 0.018$) and DIC score (odds ratio = 1.892; 95% confidence interval, 1.077–3.323; $P = 0.027$). The secondary end-point was the treatment outcome before and after the application of OSS. Operation time was significantly shorter and the amount of bleeding was also significantly less in the OSS group.

Conclusion: Computed tomography findings of intestinal pneumatosis and the acute disseminated intravascular coagulation score were found to be prognostic factors for survival in patients with NOMI. Aggressive laparotomy to determine the definitive diagnosis is needed and OSS could be useful to improve patient prognosis for survival from NOMI.

Key words: Acute DIC score, intestinal pneumatosis, non-occlusive mesenteric ischemia, open abdominal management, second look operation

INTRODUCTION

THE CONCEPT OF non-occlusive mesenteric ischemia (NOMI) was proposed by Ende *et al.*[1] in 1958 and was defined as a disorder that causes ischemia and necrosis of the intestinal tract without organic obstruction in mesenteric blood vessels. In recent years, with the progress made in imaging diagnosis, the number of the reports of NOMI has increased, and its mortality rate is said to exceed 50%.[2–5] The pathophysiology of NOMI is presumably related to prolonged vasospasm of the mesenteric arteries during circulatory shock. Although NOMI is common in dehydrated patients or those in shock, the cause has not been clarified and the treatment strategy has not been decided.[1–3,6,7] Methods to improve the prognosis of patients treated for suspected NOMI are presently unclear.

We examined cases of NOMI in our hospital and reviewed their clinical features and treatment strategies. The purposes of this study were to examine the prognostic factors for NOMI and to examine treatment strategies that could improve patient prognosis.

METHODS

THIS SINGLE -center, observational, case series study was carried out in Kansai Medical University Hospital

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(Hirakata, Japan). This facility is a tertiary emergency medical center to which many patients are transferred from other hospitals for intensive care. The study comprised 30 consecutive patients who underwent emergency surgery for NOMI from April 2013 to December 2017. Non-occlusive mesenteric ischemia was diagnosed by clinical suspicion, operative findings, and pathological ischemic lesion without thrombus in the mesenteric blood vessels.

Until December 2014, our hospital had performed a one-time operation consisting of intestinal resection, creation of a colostomy, and abdominal closure for patients with symptoms of peritonitis who were suspected of having NOMI. From January 2015, we changed the treatment strategy for patients suspected of having NOMI.

For patients suspected of having NOMI on the basis of abdominal physical findings, computed tomography (CT) findings, or laboratory findings, we aggressively performed laparotomy to obtain a definite diagnosis. The primary surgery consisted of resection of the ischemic intestinal tract without anastomosis and open abdominal management to shorten the operation time that allows a systematic search for the progression of intestinal necrosis.[8–10] We carefully treated and observed the patients for 24–48 h in the intensive care unit so as not to miss the progression of necrosis or ischemia of the intestinal tract. Thereafter, a planned second-look operation was carried out, and additional intestinal resection was performed if the progression of ischemia or a necrotic intestinal tract was found during the operation. This treatment strategy of NOMI was called the open abdominal management and second look operation strategy (OSS).

We first divided the 30 patients into two groups, survival at discharge and death at discharge groups, and we compared and examined patient characteristics (age, sex, underlying disease, preoperative condition, CT findings, serum lactate level, acute disseminated intravascular coagulation [DIC] score, and Sepsis-related Organ Failure Assessment [SOFA] score) and perioperative factors of the primary operation (operation time, volume of bleeding, and enforcement of OSS). We also further divided the patients into two groups, the non-OSS group and the OSS group. The non-OSS group included 9 patients from April 2013 to January 2015, and the OSS group included 21 patients from February 2015 to December 2017.

The primary end-point was a prognostic factor for outcome at discharge determined from the 30 patients. The secondary end-point was to examine the efficiency of OSS on outcome in patients with and without OSS.

Informed consent was obtained from the patients or their representatives before surgery. This study was approved by the ethics committee of our institution (approval no. 2017106).

Categorical data are presented as number (%) and were compared by χ^2-test or Fisher's exact test as appropriate. Continuous variables are expressed as median and interquartile range and were compared using the non-parametric Mann–Whitney test. The threshold for significance was a *P*-value <0.05. Logistic regression analysis was used for multivariate analysis. All statistical analyses were undertaken using IBM SPSS version 22 (Armonk, NY, USA).

RESULTS

IN TOTAL, 30 consecutive patients were diagnosed with NOMI from April 2013 to December 2017. There were no particular exclusion criteria. Many patients had other diseases (53.3%) or were taking an antithrombotic drug (56.7%) before the occurrence of NOMI. Sepsis was the most frequent other disease present before the occurrence of NOMI (Tables 1, 2). Abdominal physical findings were present in all patients. Abdominal pain was found in 18 patients and abdominal distention in 12 patients who were intubated or sedated. These patients had abnormal CT findings such as intestinal pneumatosis or absence of bowel wall enhancement, and their serum lactate level was also high (Table 1).

Nine (30%) of the 30 patients died prior to discharge. When comparing patient characteristics related to discharge outcomes between the two groups, the rate of intestinal pneumatosis as a CT finding was significantly higher in the survival group. There were also significant differences in acute DIC score and SOFA score between the two groups. However, there were no significant differences in such factors as dialysis history and use of antithrombotic drugs (Table 2).

In the comparison of perioperative factors of the primary operation in relation to discharge outcome, the amount of bleeding was significantly greater in patients who died. However, there were no significant differences in operation time or OSS between those who survived and those who died (Table 3).

Among four items showing a significant difference in the univariate analysis, intestinal pneumatosis and acute DIC score were selected and a multivariate analysis was carried out. The SOFA score was not used for multivariate analysis because this score shows systemic severity, as does the acute DIC score. The amount of bleeding was also not used because it is an evaluation item related only to the surgical procedure. As a result, significant differences were found for intestinal pneumatosis (odds ratio = 0.054; 95% confidence interval, 0.005–0.607; $P = 0.018$) and acute DIC score (odds ratio = 1.892; 95% confidence interval, 1.077–3.323; $P = 0.027$) (Table 4), which indicated their potential use as prognostic factors for survival in patients with NOMI.

Table 1. Characteristics of 30 patients with non-occlusive mesenteric ischemia (NOMI)

Characteristic	*n* = 30
Age, years	74 (49-90)
Male sex	17 (56.6)
Severe disease before NOMI occurrence	16 (53.3)
Head injury	3 (18.8)
Spinal cord injury	1 (6.3)
Severe trunk injury with hemorrhagic shock	1 (6.3)
Cerebral hemorrhage	2 (12.5)
Sepsis	6 (60.0)
Duodenal ulcer with hemorrhagic shock	1 (37.5)
Severe fever	1 (6.3)
Drug addiction (glyphosate)	1 (6.3)
Taking antithrombotic drug	17 (56.7)
Dialysis history	4 (13.3)
Abdominal findings	30 (100)
Stomach ache	18 (60)
Abdominal distension	12 (40)
Use of preoperative vasopressor	13 (43.3)
CT findings	
Intestinal pneumatosis	23 (76.7)
Hepatic portal venous gas	12 (40)
Absence of bowel wall enhancement	19 (63.3)
Wall thickening†	18 (60)
Bowel dilatation‡	14 (46.7)
Organ ischemia	4 (13.3)
Ascites	25 (83.3)
Free air	4 (13.3)
Acute DIC score§	2.5 (0-8)
SOFA score	8 (0-21)
Serum lactic acid level, mmol/L	4.3 (0.78-12.2)

Categorical data are shown as *n* (%); continuous data are expressed as median (interquartile range).
†Wall thickening >3 mm.
‡Diameter of small bowel >3 cm or diameter of the colon >8 cm.
§Diagnostic criteria for disseminated intravascular coagulation (DIC) established by the Japanese Association for Acute Medicine.
CT, computed tomography; SOFA, Sepsis-related Organ Failure Assessment.

Table 2. Comparison of discharge outcomes in 30 patients with non-occlusive mesenteric ischemia (NOMI)

Characteristic	Survival (*n* = 21)	Death (*n* = 9)	*P*-value
Age, years	70 (47-90)	75 (63-86)	0.441
Male sex	13 (61.9)	4 (44.4)	0.443
Severe disease before NOMI occurrence	10 (47.6)	6 (66.7)	0.440
Taking antithrombotic drug	13 (61.9)	4 (44.4)	0.443
Dialysis history	2 (9.5)	2 (22.2)	0.563
Abdominal findings	21 (100)	9 (100)	1.000
Stomach ache	15 (71.4)	3 (33.3)	0.102
Abdominal distension	6 (28.6)	6 (66.7)	0.102
Use of preoperative vasopressor	7 (33.3)	6 (66.7)	0.123
CT findings			
Intestinal pneumatosis	19 (90.4)	4 (44.4)	0.014
Hepatic portal venous gas	9 (42.9)	3 (33.3)	0.704
Absence of bowel wall enhancement	13 (61.9)	6 (66.7)	1.000
Wall thickening†	14 (66.7)	4 (44.4)	0.418
Bowel dilatation‡	8 (38.1)	6 (66.7)	0.236
Organ ischemia	3 (14.3)	1 (11.1)	1.000
Ascites	18 (85.7)	7 (77.8)	0.622
Free air	3 (14.3)	1 (11.1)	1.000
Acute DIC score§	2 (0-6)	4 (2-8)	0.016
SOFA score	6 (0-13)	11 (1-21)	0.017
Serum lactic acid level, mmol/L	4.2 (0.78-19.9)	5.2 (1.7-12.2)	0.319

Categorical data are shown as *n* (%); continuous data are expressed as median (interquartile range).
†Wall thickening >3 mm.
‡Diameter of small bowel >3 cm or diameter of the colon >8 cm.
§Diagnostic criteria for disseminated intravascular coagulation (DIC) established by the Japanese Association for Acute Medicine.
CT, computed tomography; SOFA, Sepsis-related Organ Failure Assessment.

Patient characteristics were not found to be significantly different between the non-OSS group and OSS group (Table 5). Operation time was significantly shorter and the amount of bleeding was significantly less in the OSS group than in the non-OSS group. In the OSS group, regardless of the patient's preoperative background, seven patients (33.3%) required additional intestinal resection in a repeat operation. There was no significant difference between the two groups in mortality at discharge (Table 6).

DISCUSSION

THE PRESENT STUDY results provided very useful information that can be used in determining methods of treatment of NOMI, which continues to result in high mortality and has no specific treatment strategy.

Table 3. Perioperative factors of the primary operation in 30 patients with non-occlusive mesenteric ischemia, for comparison of discharge outcome

Factor	Survival (n = 21)	Death (n = 9)	P-value
Operation time, min	65 (37-206)	121 (46-245)	0.396
Bleeding, mL	142 (0-2945)	771 (247-4435)	0.004
OSS	15 (71.4)	6 (66.7)	1.000

Categorical data are shown as n (%); continuous data are expressed as median (interquartile range).
OSS, open abdominal management and second look operation strategy.

Table 4. Multivariate analysis of factors related to discharge outcome in 30 patients with non-occlusive mesenteric ischemia

Factor	Odds ratio (95% CI)	P-value
Intestinal pneumatosis	0.054 (0.005-0.607)	0.018
Acute DIC score	1.892 (1.077-3.323)	0.027

CI, confidence interval; DIC, disseminated intravascular coagulation.

Table 5. Characteristics of patients undergoing surgery for non-occlusive mesenteric ischemia (NOMI) in open abdominal management and second look operation strategy (OSS) and non-OSS groups

Characteristic	Non-OSS (n = 9)	OSS (n = 21)	P-value
Age, years	75 (51-90)	74 (47-84)	0.415
Male sex	4 (44.4)	13 (61.9)	0.443
Severe disease before NOMI occurrence	3 (33.3)	13 (61.9)	0.443
Taking antithrombotic drug	4 (44.4)	13 (61.9)	0.443
Dialysis history	1 (11.1)	3 (14.3)	1.000
Abdominal findings	9 (100.0)	21 (100.0)	
Stomach ache	5 (55.6)	13 (61.9)	1.000
Abdominal distension	4 (44.4)	8 (38.1)	1.000
Use of preoperative vasopressor	3 (33.3)	10 (47.6)	0.681
CT findings			
Intestinal pneumatosis	6 (66.7)	17 (81.0)	0.640
Hepatic portal venous gas	3 (33.3)	9 (42.9)	0.704
Absence of bowel wall enhancement	7 (77.8)	12 (57.1)	0.419
Wall thickening[†]	3 (33.3)	15 (71.4)	0.102
Bowel dilatation[‡]	5 (55.6)	9 (42.9)	0.694
Organ ischemia	1 (11.1)	3 (14.3)	1.000
Ascites	8 (88.9)	17 (81.0)	1.000
Free air	3 (33.3)	1 (4.8)	0.069
Acute DIC score[§]	3 (1-5)	2 (0-8)	0.765
SOFA score	5 (1-13)	9 (0-21)	0.329
Serum lactic acid level, mmol/L	6.1 (1.7-19.9)	4.2 (0.78-12.2)	0.154

Categorical data are shown as n (%); continuous data are expressed as median (interquartile range).
[†]Wall thickening >3 mm.
[‡]Diameter of small bowel >3 cm or diameter of the colon >8 cm.
[§]Diagnostic criteria for disseminated intravascular coagulation (DIC) established by the Japanese Association for Acute Medicine.
CT, computed tomography; SOFA, Sepsis-related Organ Failure Assessment.

First, we found that CT findings of intestinal pneumatosis could be a potential prognostic factor for survival outcome in patients with NOMI. The reports to date have indicated that CT findings are important for diagnosing NOMI, but few reports have stated that CT findings are a prognostic factor.[2,11–14] We suggest that intestinal pneumatosis is an early CT finding of irreversible NOMI and we know the general condition of the patient can deteriorate after the time through our cases. Computed tomography findings of NOMI vary with time: intestinal pneumatosis, disappearance of intestinal pneumatosis with thinning of the wall of the intestinal tract, intestinal dilation, absence of bowel wall enhancement, increasing ascites, and perforating peritonitis. So, when you encounter patients with intestinal pneumatosis on CT findings who have suspected NOMI, you should operate early.[14]

Second, the acute DIC score has been cited as a poor prognostic factor. The DIC scoring system was released by the Japanese Association for Acute Medicine and The Japanese Society on Thrombosis and Hemostasis in 2005 for early diagnosis of DIC. Although there are many reports indicating that the acute DIC score is related to the severity of several diseases,[15–17] no report, to our knowledge, notes a relation between the acute DIC score and NOMI. The acute DIC score consists of simple measurable factors and can be calculated before surgery. Because it is thought to reflect the patient's general condition, it is reasonable that the acute DIC score is related to poor prognosis.

Finally, the role of OSS requires some discussion. In this study, there was no significant difference in mortality between

Table 6. Perioperative factors of the primary operation and outcome of patients undergoing surgery for non-occlusive mesenteric ischemia (NOMI) in the open abdominal management and second look operation strategy (OSS) and non-OSS groups

Factor	Non-OSS (n = 9)	OSS (n = 21)	P-value
Operation time (min)	184 (100-245)	66 (37-145)	<0.001
Bleeding (mL)	1240 (64-4180)	219 (0-4435)	0.049
Number of days in ICU	16 (1-40)	8 (1-28)	0.511
Discharge mortality	3 (33.3)	6 (28.6)	1.000

Categorical data are shown as n (%); continuous data are expressed as median (interquartile range).
ICU, intensive care unit.

the non-OSS and OSS groups. However, additional resection was needed for 7 of the 21 patients in the OSS group in planned second-look operations. If we had performed a laparotomy and closed the abdomen at the initial surgery for these seven patients, we might have delayed noticing the progression of necrosis in the intestinal tract, and the patients may have experienced the worst outcome. In addition, because a second-look operation is planned, we can choose not to remove intestine that is not completely necrosed at the initial operation. In this study, we could not examine the length of the resected intestine and thus could not compare this aspect between the two groups. As a result, OSS contributed to shortening the operation time and reducing the amount of bleeding, but it did not reduce mortality. Although the difference was not significant, the rate of patients with shock or dehydration and a higher SOFA score was higher in the OSS than in the non-OSS group. It is possible that OSS could have been applied to more severe cases. Taken together, we suggest that OSS for NOMI is useful when it can be undertaken safely. The mortality from NOMI in our hospital is approximately 30%, which is lower than that in previous reports.[2–5]

We aggressively undertake surgery and early intervention for patients suspected of having NOMI, such as those with CT findings of intestinal pneumatosis, to confirm the diagnosis and resect the necrotic intestinal tract. We will continue to add additional cases and attempt to determine an appropriate treatment strategy for NOMI in the future.

There are several limitations in this study. The number of subjects was small, the study was carried out at a single facility, and many of the patients were transferred from other hospitals. Various phases of NOMI might have been present in the patients, and this may have caused some bias. Since the initiation of OSS, surgical treatment was also carried out in some patients who were critically ill and likely could not have survived surgery, and this might have increased the mortality rate.

CONCLUSION

IN PATIENTS WITH NOMI, the acute DIC score can be an adverse prognostic factor for survival. Although intestinal pneumatosis can be a good prognostic factor, it can also be an early CT finding of irreversible NOMI. When patients are suspected of having NOMI, we suggest aggressively performing laparotomy to determine the definitive diagnosis. At this time, OSS could be useful to improve patient prognosis for survival from NOMI.

DISCLOSURE

Approval of the research protocol: This study was approved by the institutional review board of Kansai Medical University (approval no. 2017106).
Informed consent: Informed consent was obtained from the patients or their representatives before surgery.
Registry and registration no. of the study/trial: N/A.
Animal studies: N/A.
Conflict of interest: None.

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