Original Article

The preoperative SOFA score and remnant small intestine length are postoperative risk factors for mortality in patients with non-occlusive mesenteric ischemia: a case–control study

Kazufumi Umemoto,[1,2] Kentaro Kato,[1] Takumi Yamabuki,[1] Minoru Takada,[1] Yoshiyasu Ambo,[1] Fumitaka Nakamura,[1] and Satoshi Hirano[2]

[1]Department of Surgery, Teine Keijinkai Hospital, Sapporo, Japan, and [2]Division of Surgery, Department of Gastroenterological Surgery II, Hokkaido University Faculty of Medicine, Sapporo, Japan

Aim: Non-occlusive mesenteric ischemia (NOMI) is a fatal condition with a low survival rate in most cases. The risk factors for perioperative mortality in NOMI cases are unclear. The purpose of this study was to define the risk factors for mortality in patients with NOMI undergoing surgery.

Methods: Thirty-eight consecutive patients who underwent surgery for NOMI at Teine Keijinkai Hospital between 2012 and 2020 were included in the study. Patient information, including age, sex, physical findings, comorbidities, laboratory data, and computed tomography and surgical findings were retrospectively analyzed.

Results: Of the 38 patients, 18 (47%) died before discharge. Significant univariate predictors of mortality were a high Sequential Organ Failure Assessment (SOFA) score, high lactate level, low blood pH, and short intestinal length after surgery. In the multivariate analysis, a high SOFA score (odds ratio 1.33, $P = 0.036$) and short intestine length after surgery (odds ratio 34.7, $P = 0.003$) were identified as independent risk factors for perioperative mortality.

Conclusion: The preoperative SOFA score and postoperative residual intestinal length may be predictors of death in NOMI surgical patients, not age and the content of comorbidities.

Key words: Acute mesenteric ischemia, intestinal length, non-occlusive mesenteric ischemia, perioperative mortality, SOFA score

INTRODUCTION

NON-OCCLUSIVE MESENTERIC ISCHEMIA (NOMI) is a condition that causes ischemic changes in a blood flow–controlled area, even though there is no organic obstruction in the mesenteric blood vessels. The first report of NOMI was by Ende in 1958.[1] Ischemic changes in the intestinal tract occur due to either spasms or diffuse narrowing of peripheral arteries, which eventually leads to necrosis. NOMI is associated with a poor prognosis resulting in widespread intestinal ischemia and necrosis due to decreased circulating plasma volume, organ perfusion, and cardiac output. It can occur secondary to major invasive procedures, such as cardiac and gastrointestinal surgeries, and the mortality rate in patients with NOMI is reported to be over 50%.[2–5]

Treatment of NOMI involves the necrotic intestinal tract in addition to improving hemodynamics. Treatment may be surgical, involving resection of the necrotic bowel or non-surgical, involving medications using interventional radiology, such as vasodilators.[6,7] However, mortality is relatively high even though they have been treated; furthermore, even patients who survive frequently experience a significant deterioration in their quality of life (QOL).[8]

It is unclear how the prognosis of NOMI is predicted, therefore this study aimed to search for factors that predict the prognosis of patients with NOMI who underwent surgery from perioperative parameters.

Corresponding: Kazufumi Umemoto, MD, Department of Surgery, Teine Keijinkai Hospital, Maeda 1-12-1-40, Teine Ward, Sapporo, Japan. E-mail: umemoto-ka@keijinkai.or.jp.
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MATERIALS AND METHODS

A SINGLE-CENTER, RETROSPECTIVE, observational study of patients with NOMI who underwent

surgical treatment at the Teine Keijinkai Hospital between 2012 and 2020 was conducted. The study population included 38 consecutive patients with NOMI who underwent surgery during the 9-year period. Research was conducted with the approval of the Teine Keijinkai Hospital Ethics Committee (approval number 2-019139-00).

All patients were clinically diagnosed with NOMI and underwent surgical treatment involving necrotic intestinal resection. In this study, NOMI was defined as a condition in which ischemia of the intestinal tract was suspected based on physical examination and imaging findings, without obstruction of the intestinal mesenteric vessels, and was used as inclusion criteria because the diagnosis of NOMI remains controversial. Surgery was performed to preserve the intestinal tract that had not yet reached complete ischemia, and resection was performed only for the intestinal tract that was irreversibly necrotic. The intestinal transection line was determined using intestinal coloration and indocyanine green (ICG) fluorescence techniques.[9] If the ischemia was judged to be progressive during surgery, a second-look surgery was planned. In some cases, bowel reconstruction, ileostomy, or jejunostomy was chosen as a one-stage procedure at the surgeon's discretion. A planned second-look surgery was usually performed 48–72 h after the initial surgery, with additional ischemic bowel resection performed as needed. The resected intestinal tract was examined by a pathologist and pathologically diagnosed as intestinal ischemic necrosis without embolization.

Patient information, including age, sex, physical findings, comorbidities, laboratory data, computed tomography (CT) findings, length of intensive care unit (ICU) stays, use of vasopressors, and surgical findings were retrospectively reviewed from medical records. The Sequential Organ Failure Assessment (SOFA) score[10] was used as an indicator of the preoperative general condition. The SOFA score is an index that quantifies the degree of impairment of vital organs, and is an index that evaluates six items: respiratory, coagulation, liver, cardiovascular, central nervous system, and renal function. The SOFA score immediately before surgery were used in the analysis. The Charlson Comorbidity Index[11] was used to asses comorbidity. Survival status at discharge was the primary outcome rather than 30-day postoperative survival because NOMI often requires a long in-hospital treatment and patients have relatively high mortality even postoperatively. Patients were divided into two groups: survival or nonsurvival, and prognostic factors were identified.

The Mann—Whitney *U* test was used for nonparametric analyses and a logistic regression model was used for multivariate analyses to calculate odds ratios. JMP Pro 16 software (SAS Institute Inc., Cary, NC, USA) was used for all statistical analyses, and $P < 0.05$ was set as the significance level.

RESULTS

THIRTY-EIGHT PATIENTS UNDERWENT surgery for the treatment of NOMI during the study period. The median age was 76.5 years (interquartile range, 70–82) years and 26 of the 38 participants were male (68%); 18 patients (47%) died before discharge. The procedure was necrosis small bowel resection in 28 cases, and colon resection was added to small bowel resection in 10 cases. A second-look operation was performed in 25 cases (66%). The patient demographic and medical characteristics are presented in Table 1.

Some patients underwent surgery without preoperative CT, depending on their condition. Preoperative CT was performed in 36 patients (95%). Contrast-enhanced CT (CECT) was not performed in 11 patients due to preoperative renal dysfunction. CT was used to evaluate intestinal emphysema, portal vein emphysema, thinning of the intestinal wall, poor intestinal angiography, presence of ascites, intestinal dilation (small intestine >3 cm, colon >8 cm), and presence of free gas in the abdominal cavity. All patients who underwent CT had one or more findings indicative of intestinal abnormalities. Intestinal emphysema was noted in 23 (63.9%), portal emphysema in 22 (61.1%), thinning of the intestinal wall in 27 (75%), poor bowel contrast in 15 (60%), ascites in 27 (75%), intestinal dilatation in 21 (58.3%), and free gas in the abdominal cavity in 3 (8.3%) patients (Table 2).

Prognostic factors were identified by dividing the patients into two groups: survival and nonsurvival. As the CECT was not conducted in some cases, they were excluded from the multivariate analysis. Univariate analyses were used to compare the following variables between the survival and nonsurvival groups: age, sex, SOFA score, arterial blood pH, lactate level, Charlson Comorbidity Index score, operation time, operative blood loss, the length of the remaining small intestine after intestinal resection due to necrosis, and the presence or absence of a second-look operation. Overall, patients in the nonsurvival group displayed higher SOFA scores ($P = 0.0062$), higher lactate levels ($P = 0.0086$), lower arterial pH level ($P = 0.0327$), and shorter residual small intestinal lengths ($P = 0.0005$) than patients in the survival group (Table 3). The four items identified as significant prognostic factors in the univariate analysis (higher SOFA score, higher lactate level, lower arterial pH level, and shorter residual small intestine length) were analyzed in the multivariate analysis. Multivariate analyses showed that for every one-unit increase in the SOFA score, there was a 1.33-fold increase in odds of perioperative mortality ($P = 0.036$).

Table 1. Patients' demographic and medical characteristics

Characteristics	Values (n = 38)
Age, years	76.5 (70–82)
Male sex	26 (68.4)
Comorbidity	
Chronic kidney disease requiring hemodialysis	12 (31.5)
History of cerebral infarction	10 (26.3)
Diabetes mellitus	12 (31.5)
Active malignancies	6 (15.8)
Sepsis	3 (7.9)
Ischemic heart disease	13 (34.3)
History of cardiovascular surgery within 30 days	6 (15.8)
History of gastrointestinal operation within 30 days	4 (10.5)
Charlson Comorbidity Index	3 (1–5)
Preoperative use of vasopressors, yes	15 (39.5)
Preoperative laboratory data	
White blood cell count (10^3/μL)	10.2 (5.86–16.9)
Hemoglobin (g/dL)	11.2 (9.6–12.9)
Platelet (10^4/μL)	19.6 (9.9–26.4)
Albumin (g/dL)	2.5 (2.2–3.0)
Serum creatinine (mg/dL)	2.62 (1.49–3.61)
C-reactive protein (mg/dL)	12.8 (4.2–27.9)
Total bilirubin (mg/dL)	0.5 (0.4–1.1)
Body mass index (kg/m^2)	21.2 (18.5–23.3)
ASA physical status (3E/4E)	26/12
Postoperative hospital stay, days	30.5 (13.75–79)
ICU stay, days	7 (4–15.75)

Categorical variables are given as frequencies (percentages). Continuous variables are expressed as medians (interquartile range).
ASA, American Society of Anesthesiologists; ICU, intensive care unit.

Table 2. Computed tomography findings in 36 patients with non-occlusive mesenteric ischemia

Computed tomography findings	Values (n = 36)
Intestinal emphysema	23 (63.9)
Hepatic portal emphysema	22 (61.1)
Bowel wall thickening[†]	27 (75.0)
Absence of bowel wall enhancement	15 (60.0)[‡]
Bowel dilation[§]	21 (58.3)
Ascites	27 (75.0)
Free air	3 (8.3)

Values are presented as frequencies (percentages).
[†]Bowel wall thickening <3 mm.
[‡]n = 25, because only 25 patients were able to undergo contrast-enhanced computed tomography preoperatively.
[§]Diameter of small intestine >3 cm or diameter of colon >8 cm.

Patients with a residual small intestine length of <100 cm had a 34.70-fold greater odds of perioperative mortality than those with a residual small intestine length of >200 cm (P = 0.0030; Table 4).

DISCUSSION

NOMI IS A condition characterized by necrotic lesions of the intestinal tract secondary to any kind of circulatory failure, and necrotic intestinal resection alone is not considered radical treatment. The main pathological condition that is causing the collapse of hemodynamics must be treated and circulation should recover. Therefore, NOMI should be considered separately from other intestinal ischemia.

The results of this study suggest that the SOFA score as a preoperative factor and the residual small bowel length as a surgical factor are predictors of postoperative prognosis in patients with NOMI. A high preoperative SOFA score, which reflects the respiration, blood coagulation, liver, circulation, central nervous system, and renal function, was identified as a predictor of poor prognosis. Our results suggest that a patient's general condition immediately before surgery reflects the severity of NOMI more accurately than the patient's comorbidity type and number.

In this study, among findings suggestive of bowel necrosis, only the absence of bowel wall enhancement was identified as a factor associated with mortality in patients with NOMI. CECT is often not feasible for patients with NOMI who have renal dysfunction, but when available, it can be a useful prognostic imaging finding. In addition, Nakamura *et al*.[7] reported that acute disseminated intravascular coagulation (DIC) scores have been associated with the prognosis of NOMI cases. In this study, although the DIC score was not statistically significant as a prognostic factor for NOMI, high DIC scores tended to be associated with a poor prognosis (P = 0.053; Table 3). Both SOFA and DIC scores are quantitative indicators of general condition, but the SOFA score was extracted as the more reliable factor in this study. This is likely because the SOFA score also includes other organ conditions in the score, including coagulopathy. In addition, it is easy to use because it provides a simple way to score the comprehensive condition of patients with NOMI, even those who develop the disease from a complex course.

Table 3. Comparison of demographic, medical, imaging, and laboratory characteristics between surviving and non-surviving patients with non-occlusive mesenteric ischemia using univariate analyses

Characteristics	Survivor, $n = 20$	Nonsurvivor, $n = 18$	*P*-value
Age, years	77 (68.5–82.75)	74.5 (70.75–80.25)	0.598
Male sex	16 (80.0)	10 (55.6)	0.106
Comorbidity			
Chronic kidney disease requiring hemodialysis	4 (20.0)	8 (44.4)	0.106
History of cerebral infarction	7 (35.0)	3 (16.7)	0.200
Diabetes mellitus	4 (20.0)	8 (44.4)	0.106
Active malignancies	3 (15.0)	3 (16.7)	0.888
Sepsis	1 (5.0)	2 (11.1)	0.486
Ischemic heart disease	7 (35.0)	6 (33.3)	0.914
Cardiovascular surgery within last 30 days	3 (15.0)	3 (16.67)	0.889
Gastrointestinal operation within last 30 days	3 (15.0)	1 (5.6)	0.344
Charlson Comorbidity Index	2.5 (1–4)	3 (2–5.25)	0.183
Preoperative use of vasopressors, yes	5 (25.0)	10 (55.6)	0.054
Preoperative laboratory data			
White blood cell count ($10^3/\mu L$)	8.6 (5.0–16.8)	12.2 (8.11–17.3)	0.526
Hemoglobin (g/dL)	11.0 (9.5–12.9)	11.3 (9.9–12.8)	0.941
Platelet ($10^4/\mu L$)	20.4 (10.7–25.9)	18.3 (9.7–30.7)	0.900
Albumin (g/dL)	2.6 (2.1–3.4)	2.5 (2.3–2.9)	0.335
Serum creatinine (mg/dL)	2.23 (1.79–3.21)	3.18 (1.07–4.10)	0.583
C-reactive protein (mg/dL)	10.6 (4.05–24.1)	14.7 (4.35–28.7)	0.262
Total bilirubin (mg/dL)	0.5 (0.4–1.1)	0.5 (0.3–1.2)	0.361
CT findings			
Intestinal emphysema	11 (55.0)	12 (75.0)	0.214
Hepatic portal emphysema	12 (60.0)	10 (62.5)	0.876
Bowel wall thickening	13 (65.0)	14 (87.5)	0.121
Absence of bowel wall enhancement	6 (37.5)	10 (100)	<0.01
Bowel dilation	10 (50.0)	11 (68.8)	0.257
Ascites	16 (80.0)	11 (68.8)	0.439
Free air	2 (10.0)	1 (6.25)	0.686
SOFA score	5 (2–6.75)	9 (5.75–13.25)	<0.01
DIC score	2 (1–4)	4 (2–5)	0.053
Blood pH	7.35 (7.19–7.48)	7.25 (7.13–7.35)	<0.05
Serum lactate level (mg/dL)	28 (12.75–88.75)	88.5 (39.25–120.25)	<0.01
Preserved intestinal length			<0.001
<100 cm	1 (5.0)	10 (55.6)	
100–200 cm	4 (20.0)	5 (27.8)	
200 cm<	15 (75.0)	3 (16.7)	
Second-look operation	12 (60.0)	13 (72.2)	0.428
Operation time, min	78 (45–127)	85 (69–146)	0.417
Operative blood loss, g	5 (5–105)	20 (5–93.75)	0.281
ICU stay, days	6.5 (4–12.5)	9 (3–18)	0.965

Categorical variables are given as frequencies (percentages). Continuous variables are expressed as medians (interquartile range).
CT, computed tomography; DIC, disseminated intravascular coagulation; ICU, intensive care unit; SOFA, Sequential Organ Failure Assessment.

Furthermore, the SOFA score is superior to CECT in terms of predicting prognosis because CECT cannot always be performed in situations suggestive of intestinal ischemia. Yu *et al.*[12] reported that a SOFA score of 8 or higher at ICU admission was a poor prognostic factor in a prognostic study of patients with NOMI, including non-operative cases. The

Table 4. Risk of death in patients with non-occlusive mesenteric ischemia according to physiological and morphological characteristics calculated as odds ratios using multivariate analyses

Characteristics	*P*-value	Odds ratio	95% CI
SOFA score	0.036	1.33	1.02–1.95
Blood pH	0.597	0.18	7.46e-6–629.80
Serum lactate (mg/dL)	0.832	1.00	0.963–1.03
Preserved intestinal length			
<100 cm	0.003	34.70	3.02–1117.2
100–200 cm	0.067	12.18	0.87–440.0
200 cm<		Control	

CI, confidence interval; SOFA, Sequential Organ Failure Assessment.

present study, which included only surgical patients, showed similar results, suggesting that the SOFA score may be a tool to reflect the prognosis of patients with NOMI.

The intestinal length preserved after surgery was identified as a strong surgical prognostic factor. It is inevitable to resect necrotic intestine to save one's life. Therefore, this result suggests that the longer the necrotic intestine, the more severe the NOMI itself.[2] Moreover, postoperative short bowel syndrome causes long-term deterioration of intestinal functions, such as nutrition, metabolism, and immune function, resulting in a significant decrease in QOL. In surgery, it is difficult to determine the exact extent of necrotic bowel resection because NOMI itself is a progressive, discontinuous ischemic lesion.[2] To determine the exact extent of resection, Irie *et al*.[9] reported the usefulness of ICG fluorescence, and Ward *et al*.[13] reported additional bowel resection in a second-look operation, but nothing established exists at this time. To improve the prognosis of patients with NOMI, it is important to wean them from circulatory failure as quickly as possible, in addition to promptly resecting the intestinal tract that has led to irreversible necrosis as conservatively as possible.

This study has several limitations. This was a single-center retrospective study with a small number of patients, and the long-term prognosis after discharge could not be determined. In addition, the study targeted only patients who had undergone surgery for NOMI and did not include patients who had undergone nonsurgical therapy. It would be more useful if a larger-number analysis was needed and if the risk of death could be stratified based on the SOFA score and residual intestinal length.

CONCLUSION

A PATIENT'S PREOPERATIVE SOFA score and postoperative residual intestinal length may be useful factors for predicting the patient's prognostic mortality risk in NOMI surgical cases. Future studies should aim to identify QOL after surgery, and prognosis after discharge.

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DISCLOSURE

APPROVAL OF THE Research Protocol with Approval No. and Committee Name: The protocol for this research project has been approved by a suitably constituted Ethics Committee of the institution and it conforms to the provisions of the Declaration of Helsinki. The research was conducted with the approval of the Teine Keijinkai Hospital Ethics Committee (approval number 2-019139-00).

Informed Consent: All informed consent was obtained from the patients and/or guardians.

Registry and the Registration No. of the Study/Trial: N/A.

Animal Studies: N/A.

Conflict of Interest: K Umemoto and other co-authors have no conflict of interest.

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