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RESEARCH

Preoperative risk factors for 90-day postoperative mortality outcome in patients with non-occlusive mesenteric ischemia

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Abstract

Purpose The mortality rate for non-occlusive mesenteric ischemia remains high even after patients survive the acute postoperative period with tremendous treatment efforts, including emergency surgery, which is challenging. The aim of this study was to explore the preoperative risk factors for 90-day postoperative mortality in patients with non-occlusive mesenteric ischemia.

Methods This single-center, retrospective cohort study included patients diagnosed with non-occlusive mesenteric ischemia who underwent emergency surgery between August 2014 and January 2023. All patients were divided into survival-to-discharge and mortality outcome groups at the 90-day postoperative follow-up. Preoperative factors, including comorbidities, preoperative status of vital signs and consciousness, blood gas analysis, blood test results, and computed tomography, were compared between the two groups.

Results Twenty patients were eligible, and 90-day mortality was observed in 10 patients (50%). The mortality outcome group had significantly lower HCO3- (20.9 vs. 14.6, $p=0.006$) and higher lactate (4.4 vs. 9.4, $p=0.023$) levels than did the survival outcome group. The median postoperative time to death was 19 [2–69] days, and five patients (50%) died after postoperative day 30, mainly because hemodialysis was discontinued because of hemodynamic instability in patients requiring hemodialysis.

Conclusion Low preoperative HCO3- and high lactate levels may be preoperative risk factors for 90-day postoperative mortality in patients with non-occlusive mesenteric ischemia. However, patients on hemodialysis die from discontinuing hemodialysis even after surviving the acute postoperative phase. Therefore, indications for emergency surgery in patients with risk factors for postoperative mortality should be carefully determined.

Keywords Mesenteric ischemia · Risk factors · Renal dialysis · Lactates

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Introduction

Non-occlusive mesenteric ischemia (NOMI) was first described by Ende in 1958 as necrosis of the small intestine in patients with heart failure [1]. According to Heer et al., NOMI is defined as the absence of obstruction in the mesenteric arteriovenous system in the area of intestinal necrosis, discontinuity of necrotic and ischemic changes in the intestinal tract, and histopathological findings of bleeding and necrotic changes; however, there is a lack of fibrin thrombus in the small veins [2]. The incidence of this disease is high in older patients with cardiovascular disease, cerebrovascular disease, diabetes, and other underlying diseases, as well as patients with burns and those undergoing hemodialysis (HD) [3, 4]; however, the cause of NOMI remains unclear.

The mortality rate of patients with NOMI is extremely high, ranging from 56 to 79%, and the prognosis is poor [5, 6]. With surgical intervention, the life-saving rate is approximately 53% [7]. Although there have been several reports on the risk factors for postoperative mortality in patients with NOMI, there is no consensus, and no clear risk factors have been identified to date. Furthermore, most previous reports have focused only on early postoperative mortality [8], with only a few reports on mid- to long-term follow-up after survival through the acute postoperative phase.

Knowledge of the possibility of mortality not only during the perioperative period but also after survival through the acute postoperative phase is important for making subsequent treatment decisions for both healthcare providers and patients. Therefore, the aim of this study was to conduct a medium-term review of patients with NOMI who underwent surgery, with comparisons between those who were discharged alive and those with mortality outcomes. We also explored the risk factors for 90-day postoperative mortality in patients with NOMI.

Materials and methods

Study design

This single-center retrospective cohort study used a prospectively collected clinical database. Informed consent was obtained from all participants by providing them with an opt-out option following the Good Clinical Practice Guidelines of the Ministry of Health and Welfare of Japan [9]. The study protocol was approved by the ethics committee of the University of Tsukuba Hospital, Ibaraki, Japan (registration number: R04-206). The study conformed to the provisions of the Declaration of Helsinki of 1964 (revised in Brazil in 2013).

Patient selection

Patients diagnosed with NOMI based on preoperative computed tomography (CT) who underwent emergency surgery between August 2014 and January 2023 were included in the study. The CT findings used for diagnosis were segmental ischemia or necrosis in the absence of obvious major vessel occlusion, according to the definition reported by Suzuki et al. [7]. The study involved a medium-term follow-up period, with patients followed for 90 days after the perioperative management period, even if they were transferred from the department of surgery to other departments. All eligible patients were divided into the survival-to-discharge and mortality outcome groups. The survival-to-discharge group included patients with home or nursing facility discharge or transfer from the hospital (excluding death within 90 days after surgery at the transfer site). In contrast, the mortality outcome group included patients who died during hospitalization and those who died within 90 days after surgery at the transfer site.

Data collection

The following clinical information was collected from medical records as prognostic factors for the risk of postoperative mortality.

- Patient information: sex, age, body mass index (BMI), and co-morbidities.
- Preoperative status: mean blood pressure (BP), body temperature, heart rate (HR), respiratory rate (RR), syncope status, and consciousness level.
- Blood gas analysis data: pH, $PaCO_2$, PaO_2, HCO3-, lactate, alveolar arterial oxygen difference (AaDo2), and base excess.
- Blood test data: white blood cell, hematocrit, platelets, creatine kinase, and C-reactive protein (CRP).
- CT findings: portal vein gas and distribution of necrotic bowel.

In this study, the mean BP was calculated at the time of preoperative NOMI diagnosis using the following formula:

$$Mean\ BP = \frac{(2 \times diastolic\ BP) + systolic\ BP}{3}$$

Data were analyzed for each group to compare preoperative factors related to the outcome at discharge. A flowchart of patient enrollment is displayed in Fig. 1.

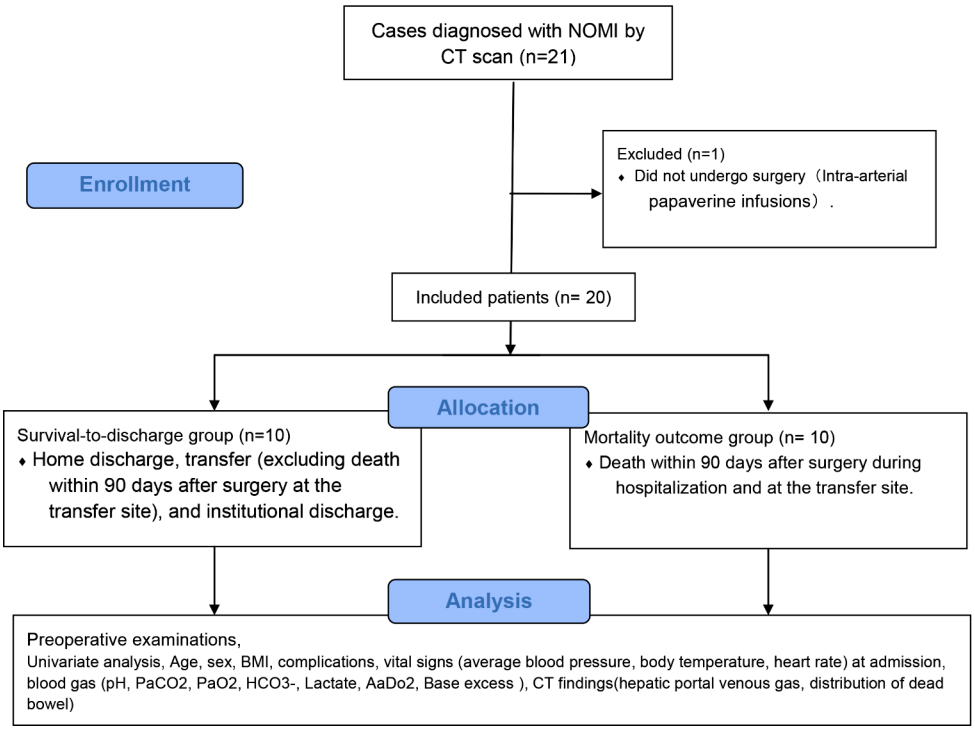

Fig. 1 Flowchart of patient enrollment. *NOMI* non-occlusive mesenteric ischemia, *CT* computed tomography, *BT* body temperature, *BP* blood pressure, *HR* heart rate, *RR* respiration rate, *BGA* blood gas analysis, *AaDo2* alveolar arterial oxygen difference, *CRP* c-reactive protein

Statistical analyses

Numerical data are described as median (range) and were compared using the Mann–Whitney *U* test. Categorical data are presented as number (percentage) and were compared using Fisher's exact test. All *P*-values were two-sided, and the level of significance was set at $P < 0.05$. All statistical analyses were performed using EZR [10], a graphical user interface for the R, version 4.2.1 (The R Foundation for Statistical Computing, Vienna, Austria).

Results

The patient characteristics in each group are presented in Table 1. Twenty patients were eligible for this study, and each of the survival, discharge, and mortality outcome groups included 10 patients. In the entire cohort, preoperative comorbidities included cardiovascular disease, pulmonary disease, liver failure, renal failure, diabetes mellitus, and cancer in 11, three, one, seven, six, and five patients, respectively. Ten patients were in shock preoperatively, 13 had a preoperative consciousness disorder, seven were on HD, and four used steroids. There were more HD patients in the mortality outcome group than in the survival-to-discharge group (60% vs. 10%).

Table 2 indicates the findings of the physical examination, blood gas analysis, blood tests, and CT in each group. CT findings included portal gas and distribution of the necrotic intestinal tract before surgery. The mortality outcome group had significantly lower HCO3- (20.9 vs. 14.6, $p = 0.006$) and higher lactate (4.4 vs. 9.4, $p = 0.023$) than did the patients within the survival-to-discharge group.

The causes of mortality, listed in supplementary Table, included multiorgan failure due to septic shock in six patients and inability to continue HD due to hemodynamic instability in four patients. The median time to death was 19 [2–69] days. Five patients survived the acute postoperative phase but had a fatal outcome > 30 days after surgery.

Discussion

This study summarized the short- and mid-term outcomes of 20 patients with NOMI who underwent emergency surgery; we found that 50% patients did not survive. Low HCO3- and high lactate levels may be preoperative risk factors for mortality. Six of these patients died in the early postoperative period within 30 days after surgery because of septic shock; however, the remaining four patients died because of septic shock or were unable to continue HD despite surviving the acute postoperative period. These results suggest that patients on HD, even if they avoid early postoperative death, have a high risk of postoperative mortality because they are unable to continue HD. The indications for surgery in patients with these risk factors should be carefully evaluated.

Table 1 Patient characteristics

	Survival-to-discharge group ($N=10$)	Mortality outcome group ($N=10$)	*P*-value
Age (years)	81 [43–87]*	68 [52–85]*	0.079
Sex			
Male	3	5	0.650
Female	7	5	0.650
BMI (kg/m²)	21.9 [18.3–31.9]*	22.1 [18.0–38.9]*	0.935
Comorbidities			
Cardiovascular disease	5 (50%)	6 (60%)	1.000
Pulmonary disease	1 (10%)	2 (20%)	1.000
Liver failure	0	1 (10%)	1.000
Renal failure	2 (20%)	6 (60%)	0.170
Diabetes mellitus	3 (30%)	3 (30%)	1.000
Cancer	0	5 (50%)	0.033
Total	6 (60%)	8 (80%)	
Pre-operative status			
Shock	3 (30%)	7 (70%)	0.179
Consciousness disorder	7 (70%)	6 (60%)	1.000
Hemodialysis	1 (10%)	6 (60%)	0.057
Steroid use	3 (30%)	1 (10%)	0.582

*Median [range]

BMI body mass index

The concept of NOMI includes acute mesenteric ischemia, occlusive mesenteric arterial ischemia, and mesenteric venous thrombosis. NOMI was found to occur in 20–30% cases of acute mesenteric ischemia cases in previous reports

Table 2 Clinical findings at diagnosis

	Survival-to-discharge group ($N=10$)	Mortality outcome group ($N=10$)	*P*-value
Preoperative status			
BT (°C)	37.2 [35.1–38.0]	36.95 [35.4–40]	*0.677*
Mean BP (mmHg)	75.5 [38–128]	61.0 [45–108]	*0.111*
HR (/min)	107.5 [58–144]	97.0 [70–128)	*0.791*
RR (/min)	22.0 [15–36]	24.5 [16–32)	*0.403*
BGA			
pH	7.410 [7.226–7.506]	7.325 [6.963–7.449]	*0.079*
PaCO2 (mmHg)	32.85 [11.0–43.7]	36.1 [15.5–44.0]	*0.400*
PaO2 (mmHg)	83.3 [64.3–247.0]	133.0 [52.0–303.4]	*0.387*
HCO3- (mmHg)	20.9 [14.9–22.4]	14.6 [8.4–20.7]	*0.006*
Na (mEq/L)	141.5 [131–157]	137.5 [128–142]	*0.225*
K (mEq/L)	4.585 [3.5–5.5]	4.11 [2.4–7.0]	*0.185*
Lactate (mmol/L)	4.35 [1.4–10.4]	9.4 [2.5–14.9]	*0.023*
Base excess	−4.75 [(−15.8)–(−0.4)]	−9.90 [(−21.8)–(−3.5)]	*0.079*
AaDo2	80.9 [45.7–398.6]	85.8 [−2.6–478]	*0.470*
Blood tests			
White blood cell (/μL)	13,200 [6900–37,400]	11,750 [6000–23,300]	*0.850*
Hematocrit (%)	30.7 [23.1–44.1]	30.9 [16.9–45.8]	*0.739*
Platelets (10^4/μL)	21.2 [9.9–33.9]	14.4 [7.6–25.5]	*0.064*
Creatine kinase (IU/L)	87 [23–20,348]	169 [8–3673]	*0.780*
CRP (mg/dL)	4.31 [0.03–42.9]	18.9 [6.64–19.2]	*0.052*
CT findings			
Portal gas	5 (50%)	1 (10%)	*0.141*
Small bowel necrosis	7 (70%)	8 (80%)	*1.000*

Median [range]

BT body temperature, *BP* blood pressure, *HR* heart rate, *RR* respiration rate, *BGA* blood gas analysis, *AaDo2* alveolar arterial oxygen difference, *CT* computed tomography, *CRP* C-reactive protein

[11, 12]. According to previous reports, physiological findings of NOMI include elevations in aspartate aminotransferase, alanine aminotransferase, creatine phosphorus kinase, and lactate dehydrogenase, as well as lactic acidosis and metabolic acidosis without an elevated inflammatory response [11, 13]; however, these indicate a generalized poor general condition of the patient and lack of specific clinical physiological findings. Although the pathogenic mechanism of NOMI has not been elucidated, it is believed to be caused by endogenous vasopressin and angiotensin secreted to maintain the blood supply to vital organs when systemic perfusion is reduced due to heart failure, shock, or dehydration, resulting in decreased intestinal blood flow [11].

Several prognostic factors for NOMI have been reported. Kvarstein et al. reported a base excess decrease with increasing lactate and H^+ in arterial blood gas analysis and discovered an increase in arteriovenous lactate in a major area of the gut and a decrease in arteriovenous lactate in skeletal muscle due to supply dependency [14]. In the present study, we observed a similar increase in lactate, reflecting intestinal ischemia, and a decrease in HCO3- due to associated metabolic acidosis. The mortality rate increased with the lactate level; this reflects extensive or irreversible ischemia of the intestinal tract and systemic ischemia involving other organs, which may be a high-risk factor for postoperative mortality. Recently, Suzuki et al. stated that the mean BP (<68.2 mmHg) and base excess (<-4.95 mmol/dL) were poor prognostic factors [7]. In this study, a low mean BP was not found to be a significant risk factor for postoperative mortality because of the small sample size; however, a trend was observed.

NOMI is a fatal complication in patients on dialysis, and the increased incidence of NOMI in these patients may be related to overly aggressive recombinant human erythropoietin therapy and the unsuspected presence of mesenteric arterial medial calcifications [15]. In the present study, we could not confirm the dose of recombinant human erythropoietin therapy, and there was no between-group difference in the calcification of arteries, which is also considered a risk.

CT for patients with NOMI shows signs of vascular stenosis in the branches of the superior mesenteric artery, in addition to portal gas and distribution of the necrotic intestinal tract, before surgery [16]. However, no significant between-group differences were observed in this study. The same was true for Sequential Organ Failure Assessment scores, which were not significantly different in this study [17].

Furthermore, we noted that patients with HD had postoperative mortality outcomes, especially after the acute postoperative phase. We divided the HD and non-HD patients ($n=7$ and $n=13$, respectively) and examined mortality based on whether the necrotic intestine was confined to the colon or colonized in the small bowel in HD patients and lactate levels in non-HD patients. All five patients on HD who showed necrosis of the small intestine with or without the colon, rather than necrosis of the colon alone, had a fatal outcome, suggesting that the distribution of the necrotic intestine (i.e., when the necrosis extends into the small intestine) is a prognostic factor in patients on HD. In non-HD patients, when 6.5 mmol/L was used as the cut-off for lactate, four and nine patients showed lactate levels of >6.5 mmol/L and <6.5 mmol/L, respectively. All patients with lactate >6.5 mmol/L had a mortality outcome, while all those with lactate <6.5 mmol/L were discharged alive.

Patients with a high risk of postoperative mortality benefit by avoiding the invasiveness and prolonged duration of surgery and having more time to choose and initiate other treatment options. With regard to patients with a high risk of death, a less invasive bedside laparoscopic examination is also recommended [18].

This study has several limitations. First, it was a single-center retrospective study with a small number of patients. Therefore, a few biases and confounding factors could not be eliminated, and the statistical power was insufficient. Second, only surgical cases were collected; thus, cases where surgery was not performed after diagnosis were not included, resulting in underestimation of mortality. Third, patients treated with drugs such as intravenous papaverine hydrochloride without any surgery were not analyzed.

Conclusions

In summary, 50% patients with NOMI died despite undergoing emergent surgery. Low preoperative HCO3- and high lactate levels may be used as preoperative predictors of mortality in these patients. Moreover, patients on HD showed a trend toward mortality outcomes in the mid-to-long term. Therefore, patients with suggested preoperative risk factors for postoperative mortality should be carefully evaluated for emergent surgery.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00423-024-03391-z.

Author contributions All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by [MU] and [DK]. The first draft of the manuscript was written by [MU] and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Data availability The datasets used and/or analyzed in the present study are available from the corresponding author on reasonable request. The corresponding author had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Declarations

Ethical approval This retrospective chart review study involving human participants was in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study protocol was approved by the Ethics Committee of the University of Tsukuba Hospital, Ibaraki, Japan (registration number: R04-206).

Consent to participate Informed consent was obtained from all participants by providing them with an opt-out option following the Good Clinical Practice Guidelines of the Ministry of Health and Welfare of Japan.

Consent to publish Not applicable.

Conflict of interest The authors declare that they have no conflict of interest.

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