



Planned Versus On-Demand Relaparotomy Strategy in Initial Surgery for Non-occlusive Mesenteric Ischemia

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Abstract

Background There has been insufficient evidence regarding a treatment strategy for patients with non-occlusive mesenteric ischemia (NOMI) due to the lack of large-scale studies. We aimed to evaluate the clinical benefit of strategic planned relaparotomy in patients with NOMI using detailed perioperative information.

Methods We conducted a multicenter retrospective cohort study that included NOMI patients who underwent laparotomy. In-hospital mortality, 28-day mortality, incidence of total adverse events, ventilator-free days, and intensive care unit (ICU)-free days were compared between groups experiencing the planned and on-demand relaparotomy strategies. Analyses were performed using a multivariate mixed effects model and a propensity score matching model after adjusting for pre-operative, intra-operative, and hospital-related confounders.

Results A total of 181 patients from 17 hospitals were included, of whom 107 (59.1%) were treated using the planned relaparotomy strategy. The multivariate mixed effects regression model indicated no significant differences for in-hospital mortality (61 patients [57.0%] in the planned relaparotomy group vs. 28 patients [37.8%] in the on-demand relaparotomy group; adjusted odds ratio [95% confidence interval] = 1.94 [0.78–4.80]), as well as in 28-day mortality, adverse events, and ICU-free days. Significant reduction in ventilator-free days was observed in the planned relaparotomy group. Propensity score matching analysis of 61 matched pairs with comparable patient severity did not show superiority of the planned relaparotomy strategy.

Conclusions The planned relaparotomy strategy, compared with on-demand relaparotomy strategy, did not show clinical benefits after the initial surgery of patients with NOMI. Further studies estimating potential subpopulations who may benefit from this strategy are required.

Keywords Acute care surgery · Acute mesenteric ischemia · Open abdominal management · Surgery · Critical care

Introduction

Non-occlusive mesenteric ischemia (NOMI) is generally defined by mesenteric ischemia without occlusion of the mesenteric arteries.¹ It often occurs in critically ill patients with

severe circulatory failure and accounts for the major cause of death in intensive care units (ICUs). Although NOMI was first reported by Ende in 1959,² a large-scale study has not yet been conducted because of the low prevalence of the condition—reported to represent 5–15% of all-cause acute mesenteric ischemia (AMI).³ Therefore, a therapeutic strategy supported by sufficient evidence has not been established, although the mortality rate of NOMI is reported to be up to 70%.⁴

Strategic staged laparotomy was originally proposed for severe trauma cases,⁵ and it has since become common in non-trauma patients as well.⁶ In cases with irreversible ischemic changes in the bowel, resection of the necrotic bowel can be the last treatment option to salvage the patients; however, because of the NOMI-specific characteristics of progressive,

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segmental, and interrupted ischemic lesions,^{7,8} it is often difficult to definitively detect the irreversible ischemic region in order to resect the bowel sufficiently in the appropriate region. In such cases, second-look surgery has been proposed as a strategic option.^{9,10} Actually, in the case of severe neonatal necrotizing enterocolitis, it was reported that ischemic changes of the bowel do not always require surgical resection and can be improved by stabilization of general conditions, and the usefulness of second-look surgery was suggested, although the pathology is not identical.^{11,12}

Accordingly, it could be hypothesized that patients with NOMI represent one of the most suitable candidates to benefit from the planned relaparotomy strategy. This retrospective multicenter observational study aimed to compare two different surgical strategies, the planned relaparotomy strategy and the on-demand relaparotomy strategy, with regard to mortality of patients after the initial surgery for NOMI.

Materials and Methods

Study Design and Settings

This was a multicenter retrospective cohort study analyzing data of patients with NOMI in 17 Japanese hospitals, which compared the treatment strategies, planned relaparotomy strategy or on-demand relaparotomy strategy. All participating hospitals were teaching hospitals, and all except one were government-approved tertiary emergency hospitals. The list of participating facilities is presented in Supplemental Table 1. The study was approved by the institutional ethics committees of each participating hospital.

Study Population

Data of consecutive patients who underwent laparotomy for NOMI in the participating hospitals between January 2010 and December 2016 were analyzed. NOMI was defined as mesenteric ischemia without occlusion of the mesenteric arteries. Mesenteric ischemia was diagnosed by intra-operative findings, and presence or absence of artery occlusion was assessed by radiological and intra-operative findings. Patients younger than 18 years, who were pregnant, who had do-not-resuscitate orders, or who refused to participate by opting-out were excluded at the stage of data collection.

Data Collection and Outcome Measures

We retrospectively collected data from medical, surgical, and anesthesia records, including images of surgical specimens, regarding patient baseline characteristics, perioperative information including treatment strategy (i.e., planned relaparotomy strategy or on-demand relaparotomy strategy),

patient severity, hospital information, and the patient outcomes described below. The indications for the relaparotomy in patients who were treated with on-demand relaparotomy strategy were also collected. Details in collected variables are described in [Supplemental Method](#).

The primary outcome was defined as in-hospital mortality. Secondary outcomes were 28-day mortality, composite of adverse events (in-hospital mortality, pneumonia, acute kidney injury (AKI), thrombosis, hemorrhage, sepsis, anastomotic leakage, ileus, and entero-atmospheric fistulae), ventilator-free days at 28 days, and ICU-free days at 28 days.¹³

Statistical Analysis

Considering the low prevalence of NOMI, the missing values were complemented using the method of multiple imputation by chained equations¹⁴ in order to make maximum use of available data. In all, 15 datasets with 10 iterations were produced. Descriptive statistics displayed after pooling of all the imputed datasets into one dataset. Predictive statistics displayed after integration across the imputed datasets based on Rubin's rule.¹⁵ In univariate analysis, continuous variables were compared using a Student's *t* test, and categorical variables were compared using the χ^2 test.

As the primary analysis, the effect of the planned relaparotomy strategy was evaluated using a mixed effects regression model or a linear-mixed regression model, as appropriate, which could simultaneously adjust for patient-level confounding factors and hospital-level clustering.¹⁶ Based on a clinical perspective, simultaneously considering the issue of multicollinearity and the number of outcomes, the following fixed-effect variables were selected for case mix adjustment: age, sex, Charlson comorbidity index,¹⁷ body mass index, serum lactate value before surgery, Sequential Organ Failure Assessment (SOFA) score before surgery, length of necrotic bowel, and the dose of vasopressors summarized by vasoactive inotropic score (VIS)^{18,19} at the end of initial surgery. The issue of multicollinearity was evaluated by the variance inflation factor, and a value of less than 2 was considered acceptable.

Considering the heterogeneity of the study population, we performed propensity score matching analysis,²⁰ as the sensitivity analysis, to extract a population with a similar likelihood of receiving the planned relaparotomy or the on-demand relaparotomy strategy. The propensity score for predicting the planned relaparotomy strategy was calculated by a logistic regression model with adjustment for APACHE II score before surgery, fluid balance during the initial surgery, and the surgeon experience, in addition to the variables used in the aforementioned mixed-effect regression models. Propensity score matching extracted 1:1 matched pair from the planned relaparotomy group (planned group) and on-demand relaparotomy group (on-demand group). The balance of

matching between the two groups was assessed by the absolute standardized mean difference of all variables, in which values lower than 0.1 were regarded as acceptable. Intergroup comparison of the outcomes with propensity score-matched subjects was performed using a chi-square test.

Furthermore, the primary analysis was also performed for the naïve dataset, not the multiply imputed data, as a validation of multiple imputation method, in which variables mentioned above were used for severity adjustment.

All statistical analyses were performed using R software (version 3.5.1; R Foundation for Statistical Computing, Vienna, Austria). The level of significance was defined as $p < 0.05$.

Results

Study Population

A total of 181 NOMI patients were analyzed. Patient characteristics of the naïve data, including the proportion of missing data in each variable, are summarized in Supplemental Table 2. For approximately 34.8% and 23.8% cases, data on Acute Physiology and Chronic Health Evaluation (APACHE) score and SOFA score, respectively, were lacking due to the absence of data used for calculation of these scores. Data for VIS were missing for 18.8% of cases. The proportions of missing data for other variables were less than approximately 10%. The missing data for these variables were complemented using a multiple imputation method.

Patients' demographic data and their pre-operative status in the multiply imputed cohort are summarized in Table 1. Median age was 77 years, and 110 patients (60.8%) were male. In the initial surgery, 107 patients (59.1%) were treated with the planned relaparotomy strategy. APACHE II scores were higher in patients treated with the planned relaparotomy strategy compared to those treated with the on-demand relaparotomy strategy [25 (20, 32) in the planned group and 21 (17, 29) in the on-demand group], as well as SOFA scores [9 (4, 13) in the planned group and 6 (4, 10) in the on-demand group] and lactate levels [5.4 (2.5, 8.7) in the planned group and 3.1 (1.7, 6.1) in the on-demand group]. Surgical information for the multiply imputed cohort is summarized in Table 2. In the planned group, 99 (92.5%) were treated with OAM; the remaining 8 patients did not undergo OAM, and their abdominal walls were temporally closed. Although the median value of the length of necrotic bowel was similar for both groups, parameters during initial surgery, such as urine volume [40 mL (0, 190) in the planned group and 130 mL (0, 310) in the on-demand group] and the VIS at the end of an initial surgery [17.8 (5.3, 42.9) in the planned group and 7.5 (0.0, 21.4) in the on-demand group], also suggested that more severe cases were likely to be treated with planned relaparotomy

strategy. Shorter operation times were observed in the planned group [98 min (70, 150) in the planned group and 151 min (120, 197) in the on-demand group]. Additional bowel resection, in which the bowel resection in short length for only the purpose of anastomotic procedure was not counted, was performed in 47 patients (43.9%) of the planned group and 3 patients (4.1%) of the on-demand group. Regarding the patients who received additional bowel resection in the on-demand relaparotomy group, the indications for relaparotomy were sustained deteriorated general condition, anastomotic leakage, and remnant abscess.

Primary Analysis

The number of outcomes and the results of univariate analysis are summarized in Table 3. The rates of in-hospital mortality, 28-day mortality, and total adverse events were significantly higher, while the ventilator-free days and ICU-free days were significantly fewer in the planned group. In-hospital mortality was observed in 89 patients (49.2%) among the entire study population: 61 patients (57.0%) in the planned group and 28 patients (37.8%) in the on-demand group. Total adverse events were observed in 123 patients (68.0%) of the entire study population [80 patients (74.8%) in the planned group and 43 patients (58.1%) in the on-demand group]; of those, AKI and sepsis were significantly frequent in the planned group. The ventilator-free days was 0 days (0, 16) in the planned group and 17.5 days (0, 25) in the on-demand group, and the ICU-free days was 0 days (0, 19) in the planned group and 15 days (0, 24) in the on-demand group.

All of the variance inflation factors of the variables that were incorporated into the model were less than 2, which eliminated the issue of multicollinearity in the regression model. The results of the multivariate mixed effects model are summarized in Table 4. After adjusting for potential confounders in the mixed effects regression models, significant differences observed in the univariate comparisons disappeared except for ventilator-free days [adjusted odds ratio (AOR) for in-hospital mortality (95% CI) = 1.94 (0.78–4.81); AOR for 28-day mortality (95% CI) = 1.74 (0.63–4.82); AOR for total adverse events (95% CI) = 1.39 (0.45–4.32); adjusted difference for ventilator-free days (95% CI) = -3.6 (-6.8–0.3); and adjusted difference for ICU-free days (95% CI) = -2.3 (-5.5–0.9)].

Sensitivity Analyses

Through the matching process, 61 propensity score-matched pairs were generated. Patients who had extremely high probability for the implementation of on-demand relaparotomy strategies or planned relaparotomy strategy, respectively, were excluded via the process (Supplemental Figure 1). The standardized mean differences of the variables used in the

Table 1 Demographic and pre-operative status of the study population (multiply imputed cohort)

Variables	Planned relaparotomy	On-demand relaparotomy	<i>P</i> value
Number of subjects, <i>n</i>	107	74	–
Baseline characteristics			
Age, years	78 [67, 84]	76 [64, 84]	0.576
Sex, male	66 (61.7)	44 (59.5)	0.764
Height, cm	160 [150, 165]	156 [150, 165]	0.627
Weight, kg	51.0 [43.0, 59.7]	49.7 [43.0, 58.6]	0.168
Body mass index	20.5 [18.1, 23.5]	20.5 [18.1, 22.8]	0.289
Charlson comorbidity index	2 [1, 4]	3 [2, 4]	0.086
Pre-operative status			
Glasgow coma scale	13 [4, 15]	14 [10, 15]	0.103
Systolic blood pressure, mmHg	91 [72, 115]	97 [77, 116]	0.314
Diastolic blood pressure, mmHg	51 [40, 67]	51 [42, 65]	0.762
Respiratory rate, breath per min	25 [19, 32]	25 [19, 30]	0.529
Heart rate, beat per min	101 [82, 123]	97 [77, 114]	0.051
Body temperature, °C	36.5 [35.6, 37.2]	36.8 [35.8, 37.6]	0.133
PaO ₂ , mmHg	119.7 [88.3, 183.0]	94.9 [76.7, 138.0]	0.042
PaCO ₂ , mmHg	32.6 [26.5, 41.6]	33.8 [29.3, 40.8]	0.673
FiO ₂	0.50 [0.21, 1.00]	0.40 [0.21, 0.60]	0.013
Arterial pH	7.35 [7.25, 7.41]	7.36 [7.30, 7.43]	0.275
Venous HCO ₃ , mmol/L	17.0 [12.9, 22.4]	20.0 [15.9, 23.2]	0.107
White blood cell counts, 10 ³ /μL	9.5 [5.5, 15.2]	10.4 [6.4, 17.1]	0.879
Platelet counts, 10 ⁴ /μL	14.9 [8.2, 21.2]	15.3 [9.8, 20.5]	0.498
Hematocrit, %	34.4 [29.6, 40.5]	33.2 [27.8, 39.3]	0.308
Total bilirubin, mg/dL	0.7 [0.5, 1.2]	0.9 [0.5, 1.4]	0.966
Creatinine, mg/dL	1.9 [1.2, 3.5]	1.7 [1.0, 3.2]	0.532
Na, mEq/L	139 [136, 142]	137 [133, 140]	0.022
K, mEq/L	4.2 [3.7, 5.2]	4.3 [3.9, 4.7]	0.407
Lactate, mmol/L	5.4 [2.5, 8.7]	3.1 [1.7, 6.1]	0.056
Dose of vasopressors			
None	52 (48.6)	48 (64.9)	
Dopamine ≤ 5 μg/kg/min or dobutamine (any dose)	1 (0.9)	5 (6.8)	
Dopamine > 5 μg/kg/min or epinephrine ≤ 0.1 μg/kg/min or norepinephrine ≤ 0.1 μg/kg/min	12 (11.2)	11 (14.9)	
Dopamine > 15 μg/kg/min or epinephrine > 0.1 μg/kg/min or norepinephrine > 0.1 μg/kg/min	42 (39.3)	10 (13.5)	
APACHE II score	25 [20, 32]	21 [17, 29]	0.013
SOFA score	9 [4, 13]	6 [4, 10]	0.052

Continual variables are expressed as median [25th and 75th percentiles]; categorical variables are expressed as number (%). *APACHE* Acute Physiology and Chronic Health Evaluation, *SOFA* Sequential Organ Failure Assessment

propensity score estimation indicated well-balanced matching (Table 5). The results of the propensity score matching analysis are shown in Table 6. The superiority of planned relaparotomy was also not observed in this model.

The results of the mixed-effect regression analysis for the naïve data are summarized in Supplemental Table 3. The results were similar to the primary analysis using multiply imputed data.

Discussion

Although NOMI is a serious disease with a high mortality rate, an evidence-based therapeutic strategy has not yet been established due to the lack of large-scale studies. A randomized controlled trial or a prospective observational study under the strict indication is ideal design to compare two different therapeutic strategies (planned relaparotomy strategy

Table 2 Surgical information of the study population (multiply imputed cohort)

Variables	Planned relaparotomy	On-demand relaparotomy	<i>P</i> value
Information during initial surgery			
Length of ischemic bowel, cm	100 [45, 160]	100 [50, 200]	0.201
Hemorrhage volume, mL	205 [50, 861]	269 [60, 997]	0.277
Urine, mL	40 [0, 190]	130 [0, 310]	0.459
Administered crystalloid, mL	1650 [800, 2700]	1400 [700, 2100]	0.151
Administered colloid, mL	250 [0, 900]	500 [250, 1000]	0.191
Administered transfusion, unit*			
Red blood cells	2 [0, 6]	4 [0, 4]	0.358
Plasma	4 [0, 6]	2 [0, 6]	0.095
Platelets	0 [0, 0]	0 [0, 0]	0.026
Dose of vasopressors at the end of the initial surgery			
Norepinephrine, mg/h	0.48 [0.06, 1.00]	0.10 [0.00, 0.44]	< 0.001
Dopamine, mg/h	0 [0, 0]	0 [0, 9.00]	0.217
Epinephrine, mg/h	0 [0, 0]	0 [0, 0]	0.884
Dobutamine, mg/h	0 [0, 0]	0 [0, 0]	0.864
Vasopressin, unit/h	0 [0, 0]	0 [0, 0]	0.265
Vasoactive inotropic score	17.8 [5.3, 42.9]	7.5 [0.0, 21.4]	< 0.001
Operation time, min	98 [70, 150]	151 [120, 197]	< 0.001
Additional treatments			
Endovascular therapy			0.155
None	102 (95.3)	70 (94.6)	
Pre-surgery	3 (2.8)	0 (0)	
Post-surgery	2 (1.9)	4 (5.4)	
Vasodilator use			0.068
None	97 (90.7)	57 (77.0)	
Pre-surgery	3 (2.8)	6 (8.1)	
During surgery	0 (0)	1 (1.4)	
Post-surgery	7 (6.5)	10 (13.5)	
Heparin use			0.661
None	97 (90.7)	67 (90.5)	
Pre-surgery	4 (3.7)	2 (2.7)	
During surgery	0 (0)	1 (1.4)	
Post-surgery	6 (5.6)	4 (5.4)	
Open abdominal management	99 (92.5)	0 (0)	< 0.001
Additional bowel resection	47 (43.9)	3 (4.1)	< 0.001
Treating hospital-related variables			
Mean number of surgeons per hospital during study period	12 [5, 13]	12 [5, 20]	< 0.001
Mean annual number of surgeries under general anesthesia during study period	230 [150, 371]	371 [371, 850]	< 0.001
Surgeon experience, cases/year	25.3 [14.5, 55.8]	55.0 [15.3, 74.1]	< 0.001

Continual variables are expressed as median [25th and 75th percentiles]; categorical variables are expressed as number (%)

*One unit of transfusion was prepared from 200 mL of whole blood in Japan

and on-demand relaparotomy strategy) in NOMI; however, those would be impractical owing to the rarity of the disease. Therefore, in the present study, we conducted a multicenter retrospective cohort study with adjustment of detailed perioperative variables. The result provided detailed information on baseline characteristics, perioperative conditions, and

strategy of initial surgeries in a larger number of NOMI patients compared with previous literatures. To the best of our knowledge, this is the first well-designed retrospective cohort study that evaluated the efficacy of the planned relaparotomy strategy in patients with NOMI. However, the clinical benefits of the planned relaparotomy strategy were

Table 3 Results of the univariate analysis for the study outcomes

Outcome measurements	Planned relaparotomy (<i>n</i> = 107)	On-demand relaparotomy (<i>n</i> = 74)	<i>P</i> values
Primary outcome			
In-hospital mortality	61 (57.0)	28 (37.8)	0.013
Secondary outcomes			
28-day mortality	47 (43.9)	19 (25.7)	0.014
Total adverse events	80 (74.8)	43 (58.1)	0.020
In-hospital mortality	61 (57.0)	28 (37.8)	0.013
Pneumonia	18 (16.8)	13 (17.6)	0.896
Acute kidney injury	33 (30.8)	10 (13.5)	0.009
Thrombosis	6 (5.6)	4 (5.4)	0.953
Hemorrhage	7 (6.5)	4 (5.4)	0.754
Sepsis	52 (48.6)	20 (27.0)	0.004
Anastomotic leakage	13 (12.1)	3 (4.1)	0.074
Ileus	4 (3.7)	7 (9.5)	0.127
Entero-atmospheric fistulae	4 (3.7)	1 (1.4)	0.357
Ventilator-free days, days	0 [0, 16]	17.5 [0, 25]	< 0.001
ICU-free days, days	0 [0, 19]	15 [0, 24]	0.002

Continual variables are expressed as median [25th and 75th percentiles]; categorical variables are expressed as number (%). *ICU* intensive care unit

not observed. Patients with deteriorated perioperative conditions were likely to be chosen for the strategy of planned relaparotomy rather than on-demand relaparotomy, suggesting that the strategic decision was made according to the patient's condition in some cases. Considering this potential heterogeneity in patients, in this study, we tried to minimize the bias by using propensity score matching analysis to compare patients who had a similar likelihood of undergoing the planned relaparotomy or the on-demand relaparotomy. However, although we made the best effort to control potential biases, completely overcoming the difference was impossible due to the possibility of unmeasured confounding factors, such as operative findings that could not be evaluated quantitatively (e.g., the extent of bowel edema).

Damage control strategy was originally proposed for critically injured trauma patients⁵ and was principally based on the concept of staged surgery.²¹ The use of damage control strategies has spread to emergency general surgery,^{22,23} and recent guidelines recommend that such strategies could be used for patients with AMI, including NOMI,¹⁰ because it is often difficult to sufficiently identify ischemic lesions during initial surgery. Ward et al.²⁴ reported that half of NOMI patients who underwent second-look operations required additional bowel resection. Therefore, planned relaparotomy based on the damage control strategy appears to be a reasonable approach to determine the appropriate region to be resected and to avoid high-risk anastomosis under deteriorated health conditions. On the other hand, it should be noted that several previous

Table 4 Results of multivariate mixed effects regression analysis (primary analysis)

Outcomes	Crude odds ratio [95% CI]	Crude difference [95% CI]	Adjusted odds ratio [95% CI]	Adjusted difference [95% CI]	Adjusted <i>p</i> value
Primary outcome					
In-hospital mortality	2.18 (1.19–3.99)	–	1.94 (0.78–4.80)	–	0.156
Secondary outcomes					
28-day mortality	2.27 (1.19–4.33)	–	1.74 (0.63–4.82)	–	0.291
Total adverse events	2.14 (1.13–4.03)	–	1.39 (0.45–4.32)	–	0.568
Ventilator-free days	–	–6.7 (–9.7–3.6)	–	–3.6 (–6.8–0.3)	0.034
ICU-free days	–	–5.2 (–8.4–2.0)	–	–2.3 (–5.5–0.9)	0.161

CI confidence interval, *ICU* intensive care unit. The level of significance was defined as $p < 0.05$

Table 5 Characteristics of the patients before and after propensity score matching

Variables	Unmatched cohort			Matched cohort		
	Planned relaparotomy	On-demand relaparotomy	ASMD	Planned relaparotomy	On-demand relaparotomy	ASMD
Number of subjects, <i>n</i>	107	74	–	61	61	–
Baseline characteristics						
Age, years	78 [67, 84]	76 [64, 84]	0.08	76 [70, 83]	77 [66, 84]	0.06
Sex, male	66 (61.7)	44 (59.5)	0.05	39 (61.9)	40 (63.5)	0.033
Body mass index	20.5 [18.1, 23.5]	20.5 [18.1, 22.8]	0.18	20.5 [18.8, 23.2]	20.7 [18.1, 22.8]	0.00
Charlson comorbidity index	2 [1, 4]	3 [2, 4]	0.26	3 [2, 4]	3 [2, 4]	0.03
Pre-operative status						
APACHE II score	25 [20, 32]	21 [17, 29]	0.39	24 [18, 33]	22 [19, 30]	0.05
SOFA score	9 [4, 13]	6 [4, 10]	0.30	8 [4, 13]	7 [5, 10]	0.09
Information during initial surgery						
Length of ischemic bowel, cm	100 [45, 160]	100 [50, 200]	0.24	120 [60, 200]	100 [40, 180]	0.00
Fluid balance, mL	2090 [1400, 3552]	1980 [1340, 2955]	0.17	2024 [1200, 3101]	2097 [1480, 3050]	0.05
Vasoactive inotropic score	17.8 [5.3, 42.9]	7.5 [0.0, 21.4]	0.63	10.3 [1.5, 22.4]	11.7 [2.8, 22.8]	0.10
Treating hospital-related variables						
Surgeon’s experience, cases/year	25.3 [14.5, 55.8]	55.0 [15.3, 74.1]	0.51	35.7 [15.3, 74.1]	55.0 [14.5, 74.1]	0.02

Continuous variables are expressed as median [25th and 75th percentiles]; categorical variables are expressed as number (%). *ASMD* absolute standardized mean difference, *APACHE* Acute Physiology and Chronic Health Evaluation, *SOFA* Sequential Organ Failure Assessment

publications have raised concerns regarding the overuse of damage control laparotomy for trauma²⁵ and non-trauma patients.²⁶ The results of the present study could be interpreted as demonstrating that the risks of indiscriminate use of

planned relaparotomy strategy outweigh the benefits in some cases. In fact, approximately 56% of the patients in the planned group did not receive additional bowel resection. This suggests that while some patients may benefit from the

Table 6 Study outcomes in the propensity score-matched population (sensitivity analysis)

Outcome measurements	Planned relaparotomy (<i>n</i> = 61)	On-demand relaparotomy (<i>n</i> = 61)	Odds ratio (95% CI)	Difference (95% CI)	<i>p</i> value
Primary outcome					
In-hospital mortality	32 (52.5)	26 (42.6)	1.49 (0.73–3.03)	–	0.280
Secondary outcomes					
28-day mortality	22 (36.1)	18 (29.5)	1.35 (0.63–2.88)	–	0.443
Total adverse events	40 (65.6)	37 (60.7)	1.24 (0.59–2.58)	–	0.575
In-hospital mortality	32 (52.5)	26 (42.6)	–	–	–
Pneumonia	11 (18.0)	12 (19.7)	–	–	–
Acute kidney injury	15 (24.6)	9 (14.8)	–	–	–
Thrombosis	4 (6.6)	2 (3.3)	–	–	–
Hemorrhage	3 (4.9)	1 (1.6)	–	–	–
Sepsis	26 (42.6)	19 (31.1)	–	–	–
Anastomotic leakage	4 (6.6)	3 (4.9)	–	–	–
Ileus	1 (1.6)	7 (11.5)	–	–	–
Entero-atmospheric fistulae	2 (3.3)	1 (1.6)	–	–	–
Ventilator-free days	0 [0, 19.0]	16 [0, 24]	–	–4.1 (–7.9–0.3)	0.036
ICU-free days	0 [0, 21]	6 [0, 23]	–	–2.3 (–6.3–1.6)	0.253

Continuous variables are expressed as median [25th and 75th percentiles]; categorical variables are expressed as number (%). *CI* confidence interval, *ICU* intensive care unit. The level of significance was defined as *p* < 0.05

planned relaparotomy, it could cause others to incur unnecessary risk, at least from a retrospective view. OAM was said to be one of the risk factors for anastomotic leakage²⁷ and entero-atmospheric fistulae.²⁸ Although these rates of occurrence were relatively greater in the planned group (anastomotic leakage: 12.1% vs. 4.1% and entero-atmospheric fistulae: 3.7% vs. 1.4%, respectively), causal inference for each adverse event could not be evaluated due to the low prevalence.

In this study population, 47 patients (44%) in the planned group received additional bowel resection. These patients might be informative because they could potentially inform the best strategic approaches. In some patients of the planned group, surgeons might have resected only obviously non-viable bowel segment in the initial surgery, leaving the region that was difficult to judge whether or not the ischemic change was irreversible, and the region which was revealed to be irreversible ischemia in the secondary surgery might have been resected additionally. In other patients, surgeons might have performed additional resection of almost all the suspected ischemic bowel segments for only the purpose of safe anastomosis in the secondary surgery regardless of whether the ischemic change of the additionally resected regions was irreversible or not. In the former situation, bowel segment with irreversible ischemia was left in the abdominal cavity in initial surgery; those patients might have been more frequent in the planned group, compared with on-demand group, because surgeons usually do not leave suspected ischemic bowel segment in patients who are intended to close abdomen owing to safety concerns. This could be one of the reasons for the relatively high mortality rate in the planned group. In the latter situation, the concern of unnecessary bowel resection was raised. Although it was not considered to be a reason for relatively worse survival outcome observed in the planned group, it could be one of the explanations why additional resection was more frequent. The ideal treatment for NOMI can be achieved by avoiding unnecessary bowel resection while simultaneously controlling the risk of physiologic deterioration caused by necrotic bowels. Recent improvements in the management of NOMI, including examination modalities and additional treatment options, might affect therapeutic strategy by avoiding the overuse of planned relaparotomy strategy and unnecessary bowel resection. For example, intra-operative use of indocyanine green fluorescence has been reported to precisely detect ischemic lesions.^{29,30} Some patients were reported to be well managed through endovascular therapy.^{31,32} These recent advances in clinical practice might serve to optimize the use of planned relaparotomy strategy.

Several limitations should be considered when interpreting the results of this study. Some of the variables had missing values. Subjective factors concerning surgeons' decision-making process for the choice of surgical strategies (i.e., planned relaparotomy of on-demand relaparotomy) in each case were unclear. Also, a method to assess the viability of

ischemic bowel was not protocolized. Subjective factors, such as visual inspection or palpation of pulse, might have affected the surgeon's decision; collecting these factors was impractical in a retrospective study. Unmeasured variables, such as estimated intra-abdominal pressure at the end of initial surgery, which could influence the outcomes, were not accounted for due to the retrospective nature of the study and limited data availability. Although pre-operative conditions were adjusted using the APACHE II and SOFA scores, the severity of underlying diseases was not evaluated because quantification of these factors is difficult. Limited generalizability would also be a limitation of this study because we analyzed a limited population from 17 Japanese hospitals. Furthermore, the treatment strategy, including technique of temporary abdominal closure (TAC) in the planned group, could not be protocolized; each participating hospital used respective standard operating procedures for TAC such as a self-made vacuum pack closure system or a Bogota bag. However, the main purpose of this study was not to evaluate the effects of different TAC techniques but to compare the two therapeutic strategies in the initial surgery for NOMI. Although this study failed to show any clinical benefit of the planned relaparotomy strategy for NOMI patients, at least in the entire study population, future studies investigating potential subpopulations who benefit from this strategy are required.

Conclusion

The clinical benefit of the planned re-operation strategy was not observed, at least in the entire study population. Further studies estimating potential subpopulations who would benefit from this strategy would be required.

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Conflict of Interest The authors declare that they have no conflicts of interest.

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