



Received: February 3, 2023

Revised: April 21, 2023 (1st); May 9, 2023 (2nd)

Accepted: May 9, 2023

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## Quality of recovery in hospital and disability-free survival at three months after major abdominal surgery

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**Background:** The Quality of Recovery-15 (QoR-15) and 12-item World Health Organization Disability Assessment Schedule 2.0 scales are post-surgery patient-reported outcome measures. We aimed to evaluate the association between immediate in-hospital postoperative recovery and mid-term disability-free survival (DFS) after discharge.

**Methods:** We conducted a prospective observational study at a university hospital and enrolled 260 patients aged  $\geq 65$  years with cancer who were undergoing elective major abdominal surgery. The association between poor postoperative recovery, defined as a QoR-15 score  $< 90$  on postoperative day (POD) 2, and the DFS three months later was assessed using Fisher's exact test. The odds ratio of poor recovery on POD 2 to DFS was calculated using multiple logistic regression analysis adjusted for prominent factors (age, preoperative frailty, preoperative DFS, surgical duration, and intraoperative blood loss volume).

**Results:** A total of 230 patients completed the 3-month follow-up. On POD 2, 27.3% of the patients (63/230) had poor recovery. A greater number of patients without poor recovery on POD 2 had DFS at three months after surgery (79.6%) than those with poor recovery (65.1%) ( $P = 0.026$ ). The adjusted odds ratio of poor recovery on POD 2 to DFS at three months was 0.481 (95% CI [0.233, 0.994]).

**Conclusions:** Patients with poor recovery on POD 2 were less likely to have DFS three months after abdominal surgery. These findings may allow for early and effective interventions to be initiated based on each patient's condition after abdominal surgery.

**Keywords:** Aged; General surgery; Neoplasms; Operative surgical procedures; Patient outcome assessment; Postoperative complications.

### Introduction

Although traditional postsurgical outcomes, such as postoperative complications and length of hospital stay, remain important, advances in surgical and anesthetic techniques have improved these outcomes to the degree that patient-reported outcome measures arising directly from the patient have gained more attention [1-3].

Quality of recovery is a subjective measurement that covers the physical (pain, nausea, and vomiting), mental (anxiety and depression), and social (return to work and support from medical staff) domains. Although several measures of immediate postoperative recovery have been developed since 2000, the Quality of Recovery-15 (QoR-15) has become the most widely reported measure of recovery in hospitals following surgery [4-6]. Furthermore, disability-free survival (DFS), assessed using the 12-item World Health Organization Disability Assessment Schedule (WHODAS) 2.0, has played an important role



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as a mid-term patient-reported outcome measurement for surgical interventions [3,5–8]. Although the influence of anesthetic, surgical, and patient factors on postoperative recovery and their clinical and prognostic importance have previously been investigated [6,9,10], limited research on the association between immediate postoperative recovery in hospital and mid-term DFS after discharge currently exists.

Based on the hypothesis that poor immediate postoperative recovery decreases DFS at three months after abdominal cancer surgery, we aimed to evaluate the following: (1) the association between poor postoperative recovery and DFS, (2) the odds ratio (OR) of poor recovery to DFS, (3) the QoR-15 scores after surgery for patients with and without poor recovery on postoperative day (POD) 2, (4) the effects of poor recovery on postoperative complications, postoperative length of hospital stay, and the postoperative 12-item WHODAS 2.0 scores, and (5) differences in the mean value for each item of the QoR-15 on POD 2 between patients with and without DFS at three months after surgery.

## Materials and Methods

### Ethical approval

This prospective observational study was approved by the Institutional Review Board at Nara Medical University (Approval number: 2975; April 28, 2021), and written informed consent was obtained from all included patients before enrollment. This study was registered in the University Hospital Medical Information Network (UMIN000044062) and conducted in accordance with the Declaration of Helsinki, 2013.

### Inclusion and exclusion criteria

A total of 260 patients aged  $\geq 65$  years undergoing elective major abdominal surgery (general, urologic, and gynecologic surgery) with a cancer diagnosis associated with a reduced likelihood of DFS were included. Patients were excluded if they had dementia, psychiatric disease requiring treatment, or poor comprehension of Japanese; were undergoing emergent or palliative surgery; or had a planned postoperative hospital stay  $< 3$  days. The research staff recruited patients before surgery at the preoperative anesthesia clinic of our hospital between June 1, 2021 and April 6, 2022.

### Data collection

Before surgery, each patient's age, sex, height, weight, American

Society of Anesthesiologists physical status score, comorbidities, respiratory function, medication ( $\beta$ -blockers, steroids, and statins), laboratory data (serum albumin and creatinine levels), frailty, handgrip strength, and nutritional status were routinely assessed. Handgrip strength of the dominant hand was measured three times using a digital Jamar hand dynamometer (MG-4800 MORITOH, Japan), and the maximum value was recorded. Preoperative frailty was assessed using the Fried Frailty Phenotype Questionnaire, which includes five domains (fatigue, resistance, ambulation, inactivity, and weight loss). The total score ranges from 0 to 5 points, and frailty is defined as follows: non-frail (robust) = 0 or 1 point; pre-frail = 2 points; and frail = 3–5 points [11]. Nutritional status was assessed using the Mini Nutritional Assessment-Short Form, with a total score ranging from 0 to 14 points. We also collected intraoperative data on the anesthetic agents used (inhalation and intravenous agents), surgical field (general, urologic, and gynecologic), postoperative analgesia (none, patient-controlled epidural analgesia, and intravenous patient-controlled analgesia), surgical duration, and blood loss volume. Postoperative chemotherapy and radiotherapy were assessed as postoperative covariates.

### Postoperative quality of recovery

The QoR-15, which was developed to rapidly evaluate the quality of recovery after surgery and anesthesia in clinical settings, was translated into Japanese in 2021 [12,13]. This assessment tool consists of 15 items, including breathing, rest, well-being, pain, nausea, and mental health, with a total score ranging from 0 to 150 points [12]. According to the QoR-15 score, the quality of recovery after surgery is classified as excellent (QoR-15  $> 135$ ), good ( $122 \leq \text{QoR-15} \leq 135$ ), moderate ( $90 \leq \text{QoR-15} \leq 121$ ), and poor (QoR-15  $< 90$ ) [10,14]. In this study, the QoR-15 was assessed four times: on the day before surgery and on PODs 2, 4, and 7. In the case of discharge within 4 days of surgery, a telephone assessment was conducted to complete the questionnaire on PODs 4 and 7. We determined POD 2 as the first evaluation day after surgery because the dropout rate on POD 1 had been high in our previous study [13].

### Disability-free survival

The 12-item WHODAS 2.0, developed to measure disability, has a total score ranging from 0 to 48 points [15]. In clinical settings, this total score is converted to a percentage (0% = no disability and 100% = complete disability) and for this study, DFS was defined as survival with a WHODAS score  $< 16\%$  [16]. In-

dividuals who died after surgery were assigned the maximum WHODAS score of 100%. In this study, the 12-item WHODAS 2.0 was assessed on the day before and three months after the surgery.

## Outcomes

The primary outcome of this study was the association between poor recovery on POD 2 and DFS at three months after surgery. Secondary outcomes included the QoR-15 score, severe postoperative complications with a Clavien-Dindo classification of IIIa–V [17], length of postoperative hospital stay, and postoperative 12-item WHODAS 2.0 score.

## Statistical analysis

The QoR-15 scores had a normal distribution in this study and are presented as mean  $\pm$  SDs [12,13]. The other continuous data are presented as medians (Q1, Q3), and categorical variables are presented as numbers (%). The univariate analysis was performed to compare the groups (poor recovery vs. non-poor recovery and DFS vs. non-DFS) using an unpaired t-test (QoR-15 score), Mann-Whitney *U* test, or Fisher's exact test, as appropriate. The primary outcome of this study was evaluated using the Fisher's exact test. The ORs of poor recovery on POD 2 to DFS were calculated using multiple logistic regression analyses with and without adjusting for prominent factors, such as age, preoperative frailty, preoperative DFS, surgical duration, and intraoperative blood loss volume. The ORs of poor recovery to DFS on PODs 4 and 7 were also calculated using multiple logistic regression analysis after adjusting for the same prominent factors. The trajectory of the QoR-15 scores after surgery between patients with and without poor recovery on POD 2 was assessed using a linear mixed model with a random intercept. The effects of poor recovery on POD 2 on postoperative complications, length of postoperative hospital stay, and the postoperative 12-item WHODAS 2.0 scores were compared using univariate analysis. Differences in the mean values for each item of the QoR-15 on POD 2 between patients with and without DFS were also compared using an unpaired t-test.

We estimated that 65% and 85% of patients with and without poor recovery, respectively, would have DFS at three months after surgery. Assuming a ratio of 1 : 3 for each patient group and a dropout rate of 20%, the minimum number of cases required was 260 in this study, with a power of 0.8 and an alpha error of 0.05. All data were analyzed using SPSS version 25.0 (IBM Inc., USA), and statistical significance was set at  $P < 0.05$ .

## Results

During the study period, 260 patients provided informed consent and completed the questionnaires (QoR-15 and 12-item WHODAS 2.0) before surgery. None of the surgeries were postponed or cancelled. Of the 260 patients, 240 completed the questionnaire on POD 2 and 230 completed the follow-up at three months (Fig. 1). Among the 230 patients included in the analysis, the median age was 73.0 years and 70% were male (Table 1).

The mean QoR-15 score on POD 2 was 106.7 (Table 2). According to the QoR-15 score on POD 2, 13.9% (32/230) of patients had excellent recovery, 19.1% (44/230) had good recovery, 39.5% (91/230) had moderate recovery, and 27.3% (63/230) had poor recovery. No statistically significant differences in preoperative and intraoperative characteristics were found between the patients with and without poor recovery on POD 2 (Table 1).

The perioperative mean  $\pm$  SDs of the QoR-15 scores are shown in Table 2. The patients with poor recovery on POD 2 had lower QoR-15 scores than those without poor recovery on POD 2 at all time points. Fig. 2 shows the postoperative mean QoR-15 scores and 95% CIs for the three time points (POD 2,  $n = 230$ ; POD 4,  $n = 226$ ; and POD 7,  $n = 229$ ). The linear mixed model with repeated measures revealed that the QoR-15 scores increased over time ( $P < 0.001$ ); however, patients with poor recovery on POD 2

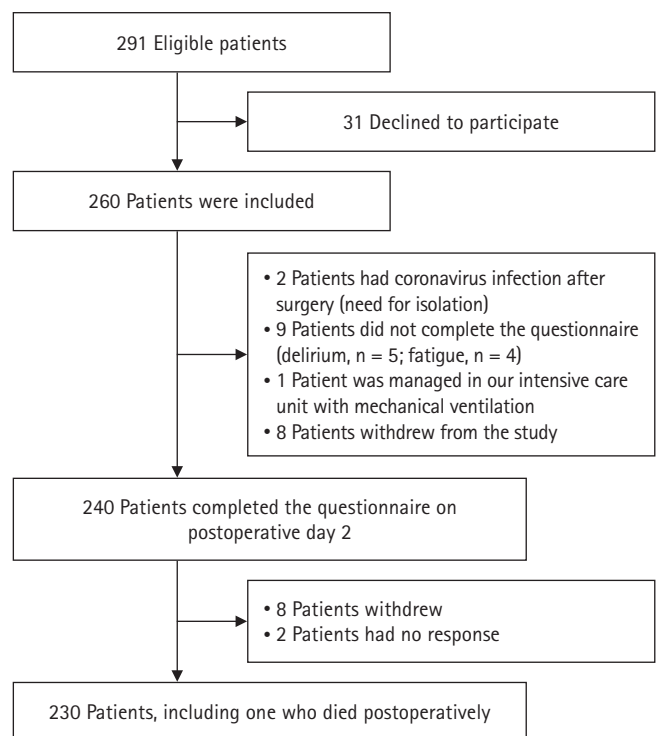


Fig. 1. Flowchart of patient selection.

**Table 1.** Preoperative and Intraoperative Characteristics

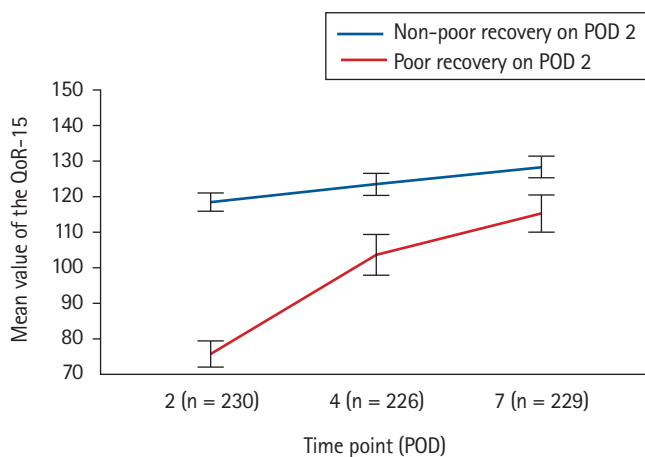
	Total (n = 230)	Non-poor recovery on POD 2 (n = 167)	Poor recovery on POD 2 (n = 63)	P value
Age (yr)	73.0 (69.0, 77.0)	74.0 (69.0, 77.0)	72.0 (69.0, 77.0)	0.250
Sex (Male)	161 (70.0)	120 (71.9)	41 (65.1)	0.336
Height (cm)	163.0 (156.0, 167.0)	162.0 (156.0, 167.0)	163.0 (153.0, 168.0)	0.946
Weight (kg)	60.80 (53.1, 67.3)	60.80 (53.2, 67.4)	60.80 (52.7, 67.0)	0.870
ASA-PS				
1	9 (3.9)	7 (4.2)	2 (3.2)	0.853
2	178 (77.4)	127 (76.0)	51 (81.0)	
3	42 (18.3)	32 (19.2)	10 (15.9)	
4	1 (0.4)	1 (0.6)	0 (0.0)	
Comorbidity				
Symptomatic cerebral vascular disease	12 (5.2)	9 (5.4)	3 (4.8)	0.999
Hypertension	130 (56.5)	95 (56.9)	35 (55.6)	0.882
Ischemic heart disease	18 (7.8)	12 (7.2)	6 (9.5)	0.585
Atrial fibrillation	18 (7.8)	15 (9.0)	3 (4.8)	0.411
Peripheral arterial disease	1 (0.4)	0 (0.0)	1 (1.6)	0.274
Pacemaker or defibrillator	4 (1.7)	3 (1.8)	1 (1.6)	0.999
Asthma	8 (3.5)	4 (2.4)	4 (6.3)	0.219
Diabetes	60 (26.1)	44 (26.3)	16 (25.4)	0.999
Respiratory function				0.789
Normal	145 (63.0)	106 (63.5)	39 (61.9)	
Obstructive lung disease	73 (33.1)	51 (30.5)	22 (34.9)	
Restrictive lung disease	18 (7.8)	14 (8.3)	4 (6.3)	
Medication				
$\beta$ -blocker	13 (5.7)	8 (4.8)	5 (7.9)	0.351
Steroid	4 (1.7)	3 (1.8)	1 (1.6)	0.999
Statin	63 (27.4)	42 (25.1)	21 (33.3)	0.247
Laboratory data				
Serum albumin (g/dl)	4.20 (4.00, 4.40)	4.20 (4.00, 4.50)	4.20 (4.00, 4.40)	0.993
Serum creatinine (mg/dl)	0.80 (0.68, 0.97)	0.81 (0.69, 0.98)	0.78 (0.68, 0.92)	0.540
Preoperative frailty				0.585
Non-frail	129 (56.0)	97 (58.0)	32 (50.7)	
Prefrail	50 (21.7)	34 (20.3)	16 (25.3)	
Frail	51 (22.1)	36 (21.5)	15 (23.8)	
Preoperative grip-hand strength (kg)	30.80 (23.10, 38.40)	30.80 (24.70, 39.30)	30.80 (21.00, 36.90)	0.260
Mini Nutritional Assessment-short form	13.0 (11.0, 14.0)	13.0 (11.0, 14.0)	12.0 (10.0, 14.0)	0.117
Intraoperative covariate				
Anesthetics agents				0.194
Inhalation agents	223 (97.0)	160 (95.8)	63 (100.0)	
Intravenous agents	7 (3.0)	7 (4.2)	0 (0.0)	
Surgical field				0.119
General	167 (72.6)	116 (69.4)	51 (80.9)	
Urologic	57 (24.7)	45 (26.9)	12 (19.0)	
Gynecologic	6 (2.6)	6 (3.5)	0 (0.0)	
Postoperative analgesia				0.511
None	4 (1.7)	4 (2.3)	0 (0.0)	
PCEA	101 (43.9)	74 (44.3)	27 (42.9)	
IV-PCA	125 (54.3)	89 (53.3)	36 (57.1)	
Surgical duration (min)	290.0 (217.0, 374.0)	276.0 (215.0, 367.0)	330.0 (231.0, 391.0)	0.072
Intraoperative blood loss volume (ml)	66.0 (16.0, 261.0)	60.0 (15.0, 246.0)	100.0 (23.0, 302.0)	0.271

Values are presented as median (Q1, Q3) or number (%). POD: postoperative day, ASA-PS: American Society of Anesthesiologists physical status, PCEA: patient-controlled epidural analgesia, IV-PCA: intravenous patient-controlled analgesia.

**Table 2.** Outcome Data of Patients with and without Poor Recovery on POD 2

	Total (n = 230)	Non-poor recovery on POD 2 (n = 167)	Poor recovery on POD 2 (n = 63)	P value
Mean QoR-15 score				
Preoperative	139.7 ± 12.6	141.4 ± 11.7	135.3 ± 13.9	0.001
POD 2	106.7 ± 24.9	118.4 ± 16.6	75.8 ± 14.5	< 0.001
POD 4	118.2 ± 22.5	123.6 ± 20.0	103.6 ± 22.3	< 0.001
POD 7	124.8 ± 21.4	128.4 ± 20.6	115.3 ± 20.6	< 0.001
Number of patients with postoperative complications (Clavien-Dindo classification ≥ IIIa)	16 (6.9)	11 (6.5)	5 (7.9)	0.773
Median length of postoperative hospital stay (days)	9.0 (8.0, 12)	9.0 (7.5, 11.0)	10.0 (8.0, 13.0)	0.165
Median disability score (12-item WHODAS 2.0)				
Preoperative	2.0 (0.0, 8.3)	2.0 (0.0, 8.3)	4.1 (0.0, 12.5)	0.063
3 months postoperative	4.1 (0.0, 14.5)	4.1 (0.0, 12.5)	6.2 (0.0, 29.1)	0.046
Number of patients with disability-free survival				
Preoperative	197 (85.6)	145 (86.8)	52 (82.5)	0.408
3 months postoperative	174 (75.7)	133 (79.6)	41 (65.1)	0.026

Values are presented as mean ± SD, number (%) or median (Q1, Q3). POD: postoperative day, QoR-15: Quality of Recovery-15, WHODAS: World Health Organization Disability Assessment Schedule.



**Fig. 2.** Comparison of the mean score of the Quality of Recovery-15 (QoR-15) between patients with and without poor recovery on postoperative days (POD) 2, 4 (n = 226), and 7 (n = 229). The linear mixed model includes time points as categorical data with random intercepts and shows that the mean score of the QoR-15 increased over time (POD 4,  $P < 0.001$ ; POD 7,  $P < 0.001$ ); however, patients with poor recovery on POD 2 had lower mean scores on the QoR-15 on PODs 4 ( $P < 0.001$ ) and 7 ( $P < 0.001$ ) than patients without poor recovery on POD 2.

had lower scores than those without poor recovery at all time points ( $P < 0.001$ ).

No statistically significant differences in severe postoperative complications ( $P = 0.773$ ) or the length of postoperative hospital stay ( $P = 0.165$ ) were found between the two groups (Table 2). Additionally, no statistically significant differences in the propor-

tion of patients who received postoperative chemotherapy (poor recovery group: 28.5% [18/63] vs. non-poor recovery group: 34.1% [57/167],  $P = 0.442$ ) or postoperative radiotherapy (poor recovery group: 1.5% [1/63] vs. non-poor recovery group: 0.6% [1/167],  $P = 0.471$ ) were found between the two groups.

The 12-item WHODAS 2.0 scores and number of patients with DFS did not differ significantly between the two groups preoperatively. In contrast, patients with poor recovery on POD 2 had a significantly higher median WHODAS score at three months after surgery compared to patients without poor recovery on POD 2 (6.2 [0.0, 29.1] vs. 4.1 [0.0, 12.5];  $P = 0.046$ ) (Table 2). A greater number of patients without poor recovery on POD 2 (79.6%) than those with poor recovery on POD 2 (65.1%) had DFS at three months after surgery ( $P = 0.026$ ) (Table 2). The OR of poor recovery on POD 2 to DFS at three months after surgery was 0.481 (95% CI [0.233, 0.994]), even after adjusting for relevant factors (Table 3). Two of the patients who underwent postoperative radiotherapy also received chemotherapy; thus, only postoperative chemotherapy was included as a postoperative covariate for multiple analysis.

Additionally, poor recovery on PODs 4 and 7 was not associated with DFS at three months after surgery (Supplementary Table 1).

Among the QoR-15 items on POD 2, breathing ( $P = 0.001$ ), rest ( $P = 0.016$ ), well-being ( $P = 0.022$ ), moderate pain ( $P = 0.010$ ), severe pain ( $P < 0.001$ ), and depression ( $P = 0.004$ ) were significantly different between patients with and without DFS three months after surgery (Supplementary Table 2).



**Table 3.** Odds Ratio for the Association between Poor Recovery on POD 2 and DFS at Three Months after Surgery

	Unadjusted estimated		Adjusted estimated	
	Odds ratio (95% CI)	P value	Odds ratio (95% CI)	P value
Poor recovery on POD 2	0.476 (0.251, 0.904)	0.023	0.481 (0.233, 0.994)	0.048

The adjusted model was adjusted for age, preoperative frailty, preoperative DFS, surgical duration, intraoperative blood loss volume, and postoperative chemotherapy. The area under the curve was 0.763 (95% CI: 0.684, 0.841; Hosmer-Lemeshow,  $P = 0.867$ ). POD: postoperative day, DFS: disability-free survival.

## Discussion

This study showed that, according to QoR-15 scores, patients with poor recovery on POD 2 had a decreased likelihood of DFS at three months after surgery compared to patients without poor recovery, with an OR of 0.483 after adjusting for baseline risk and surgical factors. Furthermore, although patients with poor recovery on POD 2 had lower perioperative QoR-15 scores, poor recovery was not significantly associated with postoperative complications or length of postoperative hospital stay.

Although surgery contributes to life support and functional recovery, not all patients benefit from surgery. In this study, the incidence of DFS at three months after surgery was 75.7% (174/230), a decrease from the estimated rate preoperatively (85.6% [197/230]). Although this incidence was not compared to previous studies using different definitions (WHODAS scores < 25%), the high prevalence of patients without DFS is a considerable social concern that would need to be addressed after discharge. Although preoperative frailty is a well-known factor associated with postoperative functional disability, it is not necessarily optimized preoperatively. Thus, early postoperative detection of factors affecting mid-term functional disability is essential. The only immediate postoperative factor associated with DFS that has been reported to date is anemia [9,18,19]; thus, this study provides new evidence that poor immediate postoperative recovery is a predictor of DFS.

Patients with poor recovery on POD 2 had lower QoR-15 scores on PODs 4 and 7 than those without poor recovery on POD 2; however, poor recovery on PODs 4 and 7 were not associated with DFS at three months after surgery. This may be explained by the limited number of patients with poor recovery on POD 4 ( $n = 28$ ) and POD 7 ( $n = 12$ ). Regardless, accurately identifying patients who are likely to have poor outcomes after hospital discharge is essential. Although we also evaluated QoR-15 scores preoperatively in this study, the QoR-15 was developed for postoperative assessment and the preoperative score does not necessarily reflect the patient's baseline score; thus, we did not include the preoperative QoR-15 scores in this analysis [3,14]. Six of the QoR-15 items (breathing, rest, well-being, moderate pain, severe

pain, and depression) showed differences between the patients with and without DFS at three months after surgery. Previous studies have shown that well-controlled pain after abdominal surgery leads to better postoperative recovery [20–22]; therefore, providing strategies to control postoperative pain and optimize mental status can contribute to an increase in DFS.

Two previous studies found an association between the severity of postoperative recovery classified according to the QoR-15 score and postoperative complications, which is not consistent with the findings of this study [10,14]. This could be explained by the following: (1) these studies included relatively minor complications (e.g., additional opioids for pain control), while our study only included severe complications (Clavien-Dindo classification IIIa–V) and (2) our sample size may not have been large enough to detect this association.

This study had some limitations. First, we could not demonstrate a causal relationship between poor postoperative recovery and DFS three months after surgery owing to the observational nature of the study. Second, although factors after hospital discharge may affect DFS, detecting patients at risk of not achieving DFS early allows for the initiation of timely and appropriate interventions. Finally, because this was a single-center study involving only patients who underwent major abdominal surgery, the generalizability of our findings may be limited.

In conclusion, we found that patients with poor recovery on POD 2, as defined using the QoR-15, were more likely to not have DFS at three months after abdominal surgery. These findings may allow for early and effective interventions to be initiated based on each patient's condition after abdominal surgery.

## Funding

None.

## Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

## Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## Author Contributions

Yuki Kinugasa (Conceptualization; Data curation; Investigation; Writing – original draft)

Mitsuru Ida (Conceptualization; Formal analysis; Methodology; Visualization; Writing – original draft)

Shohei Nakatani (Investigation; Writing – review & editing)

Kayo Uyama (Investigation; Writing – review & editing)

Masahiko Kawaguchi (Conceptualization; Supervision; Writing – review & editing)

## Supplementary Materials

Supplementary Table 1. Odds ratio for the association between poor recovery on PODs 4 and 7 and DFS at 3 months.

Supplementary Table 2. Mean QoR-15 scores on POD 2 between patients with and without DFS at 3 months after surgery.

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