ORIGINAL ARTICLE

Associated factors with delayed ambulation after abdominal surgery

Jun Asada[1,2] · Mitsuru Ida[2] · Mariko Sato[2] · Naoko Okamoto[2] · Masahiko Kawaguchi[2]

Abstract

Purpose After abdominal surgery, ambulatory status is an important indicator of postoperative recovery. This study investigated the inability to ambulate on postoperative day 1 and identified associated predictive factors in patients undergoing abdominal surgery, focusing on preoperative hematologic markers such as the neutrophil-to-lymphocyte ratio (NLR) and prognostic nutritional index.

Methods Adult patients undergoing abdominal surgery from May 2018 to October 2018 were investigated consecutively. Only patients with duration of surgery ≥ 3 h were included for observation. Data on patient characteristics were collected from medical charts and laboratory results. Univariate analysis and multivariate logistic regression were used to determine associations with inability to ambulate without human assistance on postoperative day 1 and postoperative length of stay.

Results Of 416 eligible patients, 217 patients were included in the analysis. Sixty-nine patients (31.7%) were not able to ambulate on postoperative day 1. The NLR (odds ratio, 1.11; 95% confidence interval, 1.01–1.23), duration of surgery (odds ratio per 1 h, 1.27; 95% confidence interval, 1.06–1.43), and American Society of Anesthesiologists physical status of 3 (odds ratio, 4.99; 95% confidence interval, 1.15–21.5) were independently associated with the inability to ambulate without assistance on postoperative day 1, which was also associated with longer hospital stays (13 [11, 22] vs 21 [15, 39] days, $P < 0.001$).

Conclusions The NLR, surgical duration, and American Society of Anesthesiologists physical status were significantly associated with the inability to ambulate without human assistance on postoperative day 1 and prolonged hospitalization.

Keywords Abdomen · Biomarkers · Early ambulation · Operative time

Introduction

After abdominal surgery, even in the absence of comorbidity, there is often a 20–40% reduction in physiologic and functional capacity [1]. Prolonged bed rest is associated with muscle loss and weakness, which leads to further reduction of mental and physical function [2]. Therefore, the achievement of early postoperative mobilization is one of the important components for early recovery and it is also essential to focus on postoperative ambulatory status to improve recovery.

It has been widely accepted that safe and effective postoperative pain management, including prevention of side effects such as nausea and vomiting, plays an important role in early recovery after surgery [3, 4]. In recent years, preoperative hematologic markers such as neutrophil-to-lymphocyte ratio (NLR) and prognostic nutritional index (PNI) have been paid attention to as modifiable indicators for postoperative severe complications and long-term prognosis [5–7]. Furthermore, preoperative high systemic inflammation and poor nutritional status might exert an adverse effect on postoperative patient recovery, although it remains unclear how these factors related with postoperative ambulation status.

Thus, this study aimed to evaluate the incidence of the inability to walk without assistance at postoperative day (POD) 1 and to explore that NLR and PNI are associated with the incidence of ambulation on POD1. Secondly, we analyzed the relation to length of hospital stay.

✉ Mitsuru Ida
  nwnh0131@yahoo.co.jp

1   Department of Central Operating Room, Yamatotakada
    Municipal Hospital, 1-1 Isono-cho kita-machi,
    Yamatotakada, Nara 635-8501, Japan

2   Department of Anesthesiology, Nara Medical University, 840
    Shijo-cho, Kashihara, Nara 634-8522, Japan

Materials and methods

Ethics approval

This retrospective cohort study was approved by the Institutional Review Board of Nara Medical University (Kashihara, Nara, Japan; Chairperson Prof. M. Yoshizumi, Approval No. 2078, December 18, 2018).

Study population

The inclusion criteria were as follows: patients aged ≥ 20 years who could walk without human assistance preoperatively, patients who underwent upper or lower abdominal surgery under general anesthesia that lasted 3 or more hours at Nara Medical University between May 2018 and October 2018, and patients who received epidural analgesia or intravenous patient-controlled analgesia for postoperative pain management. Patients were excluded if surgery was done within or equal to 3 h, because it was thought that shorter duration surgery does not have a big influence on patients' recovery including postoperative ambulation status. Patients with missing data were also excluded from statistical analysis. The beginning of patient enrollment coincided with a new postoperative care system at the study site (refer to "Postoperative data and care").

Data collection

Data on patient characteristics, including gender, age, body mass index, and the American Society of Anesthesiologists physical status (ASA-PS), were collected using medical charts. In addition, laboratory data, including serum albumin, hemoglobin, serum creatinine, total neutrophil, and total lymphocyte counts, were collected. The NLR was calculated as the neutrophil count divided by the lymphocyte count [8]. The PNI was calculated using the following formula: $10 \times$ serum albumin value (g/dL) $+ 0.005 \times$ total lymphocyte count in the peripheral blood (per mm^3) [9]. Intraoperative data were recorded by the anesthesiologist. These included circumstances of surgery (elective or emergency), types of surgery (upper or lower abdominal), types of maneuver (open or laparoscopic), presence or absence of intraoperative antiemetic drug, the type of anesthetic used (inhalation or propofol), postoperative pain management (epidural analgesia or intravenous patient-controlled analgesia), amount of intravenous fentanyl and remifentanil during anesthesia, net fluid balance, blood loss volume, and duration of surgery.

Postoperative data and care

All patients who received epidural analgesia or intravenous patient-controlled analgesia were assessed by anesthesiologists as part of the institution's postoperative care service. During the study period, the postoperative care protocol changed (May 2018) and both an anesthesiologist and a nurse in clinical training specializing in anesthesia provided postoperative care at least 2 days after surgery. Postoperative data were collected between 8:30 am and 10:00 am and included the presence or absence of nausea and vomiting, pain at rest, and pain with cough, which were assessed using a numerical rating scale. In addition, ambulation status and other concerns were recorded. After our assessment on POD 1, the attending nurse in the surgical ward engaged patients to be out of bed along the following flow. At first, the attending nurse encouraged to achieve sitting position after stabilization of patient's vital signs. Next, the attending nurse confirmed that patients did not complain of nausea, vomiting and dizziness and helped patients to stand and to walk with assistance. Then, patients were allowed to walk without assistance.

Outcomes

The primary outcome measure of interest was the inability to ambulate without human assistance on POD 1. The secondary outcome was postoperative length of stay. Postoperative data were assessed using nursing and postoperative care records.

Statistical analyses

Continuous data are presented as medians with 25th and 75th percentile values and categorical variables as numbers. Univariate analysis and multivariate logistic regression analysis were used to identify variables associated with the primary outcome. Univariate analysis was performed using Fisher's exact test or the Mann–Whitney U test as appropriate. The explanatory factors with P value less than or equal to 0.1 were used as explanatory variables for multivariate analysis with stepwise selection. Discrimination of the final model was assessed with the likelihood ratio test. Calibration of the model was tested using the Hosmer–Lemeshow test. The area under the receiver-operating characteristic curve was computed as a descriptive tool for measuring model bias. Furthermore, the postoperative length of stay was compared between patients based on their ability to ambulate without human assistance on POD 1 using the Mann–Whitney U test. All

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416 eligible patients
      40 who underwent cholecystectomy
      143 who underwent surgery within 3 hours
233 patients included
      14 who did not have the data about ambulation
       1 who did not have the data about height and weight
       1 who did not have the data about white blood cell fraction
217 patients included
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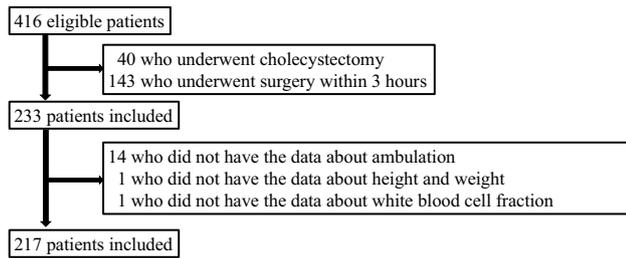
Fig. 1 Patient flowchart for study inclusion and exclusion

data were analyzed with SPSS version 22.0 (IBM Inc, Armonk, NY, USA) where $P < 0.05$ was considered statistically significant.

Results

Of 416 eligible patients, 217 were included in the analysis (Fig. 1). Patient demographics and perioperative data are shown in Table 1. In all, 69 patients (31.8%) were not able to ambulate on POD 1 and the reasons were follows: fever ($n = 1$), hypotension ($n = 30$), inadequate management of postoperative nausea and vomiting ($n = 8$), inability to recognize time, place and person ($n = 5$), lower extremity weakness ($n = 3$), inadequate management of postoperative pain control ($n = 12$), tachycardia ($n = 1$), and no description about reason unable to ambulate ($n = 9$).

The occurrence of 31.8% allowed inclusion of seven explanatory variables in multiple logistic model. Thus,

Table 1 Patient demographics and perioperative data

	Total ($n = 217$)	Ambulation (+) ($n = 148$)	Ambulation (−) ($n = 69$)	P value
Age (year)	70.0[60.0, 75.0]	68.50 [59.00, 75.00]	71.0 [66.0, 76.0]	0.11
Male/female	138/80	98/50	39/30	0.17
Body mass index (kg/m^2)	22.3[20.0, 24.6]	22.3 [20.0, 24.8]	22.2 [20., 24.3]	0.67
ASA physical status classification				0.02
1	21	18	3	
2	168	116	52	
3	28	14	14	
Serum albumin (g/dL)	4.1 [3.8, 4.4]	4.2 [3.9, 4.4]	3.9 [3.6, 4.3]	0.009
Hemoglobin (g/dL)	12.6 [11.0, 13.8]	12.8 [11.3, 14.0]	12.0 [10.5, 13.2]	0.003
Serum creatinine (mg/dL)	0.77 [0.63, 0.92]	0.76 [0.64, 0.89]	0.81 [0.62, 0.94]	0.45
Neutrophil-to-lymphocyte ratio	2.29 [1.65, 3.59]	2.23 [1.62, 3.29]	2.62 [1.73, 4.12]	0.04
Prognostic nutritional index	49.0 [44.8, 52.5]	49.5 [45.0, 52.7]	48.5 [44.0, 51.0]	0.03
Elective/Emergency	198/19	138/10	60/9	0.19
Types of surgery				1
Upper abdominal	127	87	40	
Lower abdominal	90	61	29	
Types of maneuver				0.047
Open	76	45	31	
Laparoscopy	141	103	38	
Types of anesthesia				
Inhalation/intravenous	198/19	136/12	62/7	0.61
Antiemetic drug	49	36	13	0.39
Postoperative pain management				
Epidural anesthesia/IVPCA	133/84	90/58	43/26	0.88
Dose of fentanyl (mcg/kg/h)	0.93 [0.58, 1.49]	0.92 [0.62, 1.47]	0.98 [0.55, 1.60]	0.68
Dose of remifentanil (mcg/kg/min)	0.04 [0.01, 0.15]	0.04 [0.01, 0.16]	0.06 [0.02, 0.14]	0.48
Net fluid balance (mL/kg/h)	6.07 [4.37, 7.87]	5.98 [4.35, 7.52]	6.59 [4.86, 8.91]	0.19
Blood loss volume (mL)	95 [26, 268]	66 [20, 181]	130 [58, 360]	0.001
Duration of surgery (min)	289 [240, 385]	287 [240, 352]	296[239, 485]	0.05
Postoperative nausea and vomiting	29	17	12	0.28
Pain at rest on POD 1	2.0 [0.0, 3.0]	2.0 [0.0, 3.0]	1.0 [0.0, 3.0]	0.72
Pain with cough on POD 1	4.0 [2.0, 6.0]	4.0 [2.0, 6.0]	5.0 [1.0, 6.0]	0.87

All values reported are median [25th percentile, 75th percentile] or number

ASA America Society of Anesthesiology, *IVPCA* intra-venous patient-controlled analgesia, *POD* postoperative day

ASA-PS was adopted as a representative indicator to reflect preoperative patient status, excluding serum albumin and hemoglobin as explanatory variables in the multiple logistic model. Finally, ASA-PS (2 and 3), NLR, PNI, types of maneuver, duration of surgery, and blood loss volume were included in the multiple logistic regression model. Results from multiple regression analysis showed that ASA-PS 3, NLR, and the duration of surgery were independent factors for inability to ambulate on POD 1 (Table 2). Furthermore, patients with the inability to ambulate without human assistance on POD 1 were associated with a longer length of hospital stay (13 [11, 22] vs 21 [15, 39] days, $P < 0.001$).

Discussion

This retrospective analysis showed that 31.8% patients were not able to ambulate on POD 1 and ASA-PS, preoperative NLR, and surgical duration were significantly associated with delayed ambulation after upper and lower abdominal surgery. Furthermore, delayed ambulation in patients was associated with longer hospital stays.

Previous studies reported that early mobilization was associated with postoperative outcomes such as shorter hospital stay and return of bowel function [10–13]. However, the incidence of delayed mobilization and its related factors have not been fully evaluated. One recent randomized control trial evaluated the inability to walk without human assistance at POD 5 or upon hospital discharge in patients undergoing major abdominal cancer surgery and 27.8% of all enrolled patients met the outcome [14]. In our cohort, 31% patients had inability to walk without human assistance

Table 2 Multivariate logistic regression model for inability to ambulate at least once on postoperative day 1

	Odds Ratio*	95% Confidential Interval	P value
ASA physical status classification			
1	1	–	–
2	2.06	0.56–7.52	0.27
3	4.99	1.15–21.5	0.03
Neutrophil-to-lymphocyte ratio	1.11	1.01–1.23	0.03
Duration of surgery (h)	1.27	1.06–1.43	0.002

ASA America Society of Anesthesiology

*Discrimination of the final model assessed by the likelihood ratio test was significant ($P < 0.001$). The Hosmer–Lemeshow test did not reject a logistic regression model fit ($P = 0.097$). The explanatory model based on these variables had an area under the receiver-operating characteristic curve of 0.68 (95% CI 0.60-0.76). No value exceeded the expected value by $3 \pm$ standard deviation

on POD1. Considering that in our study and a recent randomized controlled trial, the evaluation dates were different for POD1 and POD5/upon hospital discharge, respectively, the incidence rate of inability to walk without human assistance was comparable in two studies.

Regarding preoperative factors, ASA-PS, which is a fixed factor, has been identified as one of the predictors for delay in postoperative recovery as shown in previous studies [15–17]. Among the hematologic markers included in this study, only higher NLR was associated with the inability to ambulate after abdominal surgery on POD 1. However, the exact reason, which is beyond the scope of this study, why preoperative higher NLR is associated with poor postoperative outcomes is poorly understood. It is possible that patients with preoperative high inflammatory status are vulnerable to surgical stress and continue to have high inflammation after surgery, resulting in delay of postoperative recovery. On the other hand, in our cohort, the median PNI was 49.0 [44.8, 52.5], which is higher than the cutoff value (41–48) considered in previous studies and may thus reflect a good nutritional status [6, 18, 19]. Consequently, pre-operative PNI might not be identified as a significant indicator of the inability to ambulate on POD 1.

Longer duration of surgery was found to be associated with the inability to ambulate among intraoperative factors and it may reflect the effects of more surgical stress that lead to delayed postoperative recovery.

In univariate analysis, serum albumin and hemoglobin were statistically significant covariates, although these factors were not included in multiple logistic regression analysis to avoid overfitting the regression model. Since PNI is calculated with serum albumin and total lymph count PNI was considered a suitable factor to consider in the model. Preoperative anemia is associated with poor outcomes after surgery and defined as a hemoglobin concentration of less than each cutoff value in female 12.0 g/dL and in male, 13.0 g/dL, respectively, according to World Health Organization criteria [20, 21].

In our cohort, preoperative hemoglobin level was statistically significant, although the median preoperative hemoglobin was more than each cutoff value in both male [13.0 (11.6, 14.3)] and female [12.1 (10.5, 13.1)] groups.

Our study had several limitations. First, the retrospective study design may have omitted consideration of factors associated with our primary outcome, such as preoperative physical condition. This could be included in future studies with additional staff and time to measure preoperative physical function using a validated assessment tool. However, it is easy to calculate NLR based on routine preoperative laboratory examination. Second, since the findings are a result of a single-center trial, results cannot be generalized and the different ambulation protocols may lead to different results. Finally, surgical field, rather than surgical procedure,

was used as one of the covariates since the cohort did not include enough patients to be evaluated by surgical procedure. The small sample size limited the functionality of the multiple regression model and therefore, future studies need to include large patient populations.

In conclusion, this retrospective study showed that 31.8% of patients were unable to ambulate without assistance on POD 1 after abdominal surgery and higher ASA-PS, higher preoperative NLR and longer surgical duration were associated factors. Furthermore, these patients prolonged hospitalization. In the future, approaches to optimize preoperative patient status need to be investigated.

Compliance with ethical standards

Conflict of interest The author declares that they have no competing interest.

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