Factors Predicting Prolonged Postoperative Ileus in Patients Undergoing Major Gastrointestinal Surgery

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ABSTRACT

Objective: This study aimed to investigate the rate of prolonged postoperative ileus (PPOI) and its predictive factors focusing on age, body mass index, smoking status, postoperative mobilization, and preoperative anxiety and depression among patients undergoing major gastrointestinal surgery.

Materials and Methods: This prospective observational study included patients who underwent elective major gastrointestinal surgery in a super tertiary hospital in Thailand. The data were collected using a uniform case record form including the Hospital Anxiety and Depression Scale and Fagerstrom Test for Nicotine Dependence. PPOI was defined using criteria of Vather et al. (2013). Predictive factors for PPOI were determined by multivariate analysis.

Results: A total of 123 patients were enrolled, with an average age of 59.8 ± 12.7 years. The most common indication for surgery was gastrointestinal malignancy (96 patients, 78%), followed by an open approach (75 patients, 61%) and a combined general and epidural anesthesia (58 patients, 47%). Approximately 30% of patients had a history of smoking. Preoperative anxiety and depression were equally found in nine patients (7%). Twenty-seven patients (22%) experienced PPOI. The significant predictive factors of PPOI were having preoperative anxiety (OR = 6.26, 95% CI = 1.22–44.41, $p = 0.046$) and being unable to ambulate on postoperative day 1 (OR = 3.26, 95% CI = 1.25–8.50, $p = 0.015$).

Conclusion: Preoperative anxiety and delayed postoperative ambulation were two predictors for PPOI in this study. Some interventions to reduce preoperative anxiety and encourage early postoperative ambulation should be considered in patients undergoing major elective gastrointestinal surgery.

Keywords: Prolonged postoperative ileus; PPOI; major gastrointestinal surgery (Siriraj Med J 2022; 74: 537-547)

INTRODUCTION

Postoperative ileus (POI), or the temporary dysfunction of bowel motility, is one the most common complications following surgeries involving the gastrointestinal tract. It seems to be an inevitable event since the development of POI is induced in response to the surgery.[1,2] Normally, POI is expected to resolve 2-3 days after surgery as a mechanism of bowel recovery.[3] Therefore, POI that lasts longer than this period is usually considered to be a pathological abnormality, or prolonged POI (PPOI). A wide variety of cutoff times and criteria have been used by studies to determine PPOI; however, 8-32% of patients suffer from PPOI following surgery.[4–13]

PPOI is known to burden both patients and the health care system. Numerous studies have reported that patients with PPOI are prone to develop postoperative

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complications[4,9,13] that can lead to negative outcomes such as a prolonged length of stay[9–11], increased reoperation rate and readmission rate[6,9,11,14], and increased mortality rate.[15] In terms of the health care system, PPOI increases the use of medical resources as well as the economic burden of the treatment.[13]

The literature has shown that several methods can reduce the incidence of PPOI such as laparoscopic surgery,[7,9] chewing gum,[16,17] coffee consumption,[18] postoperative administration of mosapride[19], and early enteral feeding.[20,21] However, some interventions are not applicable in the clinical setting due to several limitations such as patients' condition and health care providers' competency. Moreover, although interventions are applied, the incidence of PPOI remains.

Several factors are associated with the development of PPOI such as age,[6,7] body mass index (BMI),[5,6,22] smoking status,[4,6] time to first ambulation,[12] previous abdominal surgery,[5] and operative time.[6] These factors have been shown to predict PPOI, mostly in retrospective studies of colorectal surgery patients, but conflicting results have been found. Therefore, the factors predicting PPOI in major gastrointestinal surgery remain unclear. In this study, the investigators selected factors based on their potential effect on gastrointestinal motility reported in the literature, including age, BMI, smoking status, preoperative anxiety and depression, and time to first ambulation.

In the literature, advanced age is known to increase the risk, severity, and duration of PPOI due to an imbalance between proinflammatory processes and pro- and anti-inflammatory mechanisms in older adults.[23] In obese patients, it is more difficult to manipulate the fatty tissue surrounding the internal organs, thus resulting in more tissue inflammation and a higher rate of PPOI.[24] Smoking might cause delayed bowel motility as a consequence of nicotine consumption.[25] Anxiety and depression can release catecholamine, which affects the sympathetic innervation of the gastrointestinal tract, thus inhibiting bowel motility.[26,27] Lastly, delayed ambulation might cause a lack of stretch stimulation to the gastrointestinal tract, which is a key factor to enhance intestinal smooth muscle motility and a lack of stimulation to parasympathetic innervation activity, thus decreasing intestinal smooth muscle motility.[28]

Therefore, the purpose of the study was to prospectively determine whether age, BMI, smoking status, time to first ambulation, and preoperative anxiety and depression predict PPOI in major gastrointestinal surgery in Thailand. In particular, the knowledge of such risk factors is crucial, as they could be used to screen patients with a high probability of PPOI, monitor them closely, and manage them suitably to prevent the development of PPOI.

MATERIALS AND METHODS

The sample size was calculated based on a previous study of intraabdominal surgery in which the rate of PPOI was 32.4%.[13] With a power of test of 80% and a significance level of 5% (two-sided test), a sufficient sample size was 123 patients.

Population and samples

The study was conducted in adult patients (aged ≥ 18 years) scheduled for major gastrointestinal surgery in the Faculty of Medicine at Siriraj Hospital, Thailand from February to September 2020. The inclusion criteria were 1) having elective major gastrointestinal surgery; 2) having good consciousness (Glasgow Coma Score ≥ 13); 3) having a Mini-cog score ≥ 3 (patients aged ≥ 60 years); 4) having the ability to walk (with or without assistance); and 5) having the ability to communicate in the Thai language. Patients were excluded from the study if they underwent major gastrointestinal surgery due to trauma or laparoscopic cholecystectomy and appendectomy. Moreover, they were withdrawn from the study if they needed a postoperative ventilator or were discharged before postoperative day 4 and were unable to be contacted by phone.

Instruments

1. Patient record form: The data were collected by interviewing patients and from patients' files. They were divided into three parts. Part 1 (demographic and preoperative data) included sex, age, height, weight, BMI, diagnosis, comorbidity, history of previous abdominal surgery, history of smoking, and method of bowel preparation. Part 2 (intra-operative data) included surgical approach, procedure, anesthetic technique, operative time, and estimated blood loss. Part 3 (postoperative data) included opioid used, time to first enteral feeding, time to first flatus and stool, time to first ambulation, nasogastric tube insertion, complications, reoperation, and length of postoperative stay.

2. Hospital Anxiety and Depression scale (HADS) Thai version.[29] The questionnaire was a self-reported survey comprising 14 items (seven items on the anxiety subscale and seven items on the depression subscale). It was interpreted from its scoring system (0–21 points) as non-case (0–7), doubtful case (8–10), and confirmed case (11–21). The questionnaire was translated into the Thai language and tested with patients with cancer.[29] Both subscales presented good internal consistency, with

Cronbach's alpha coefficients of 0.8551 for the anxiety subscale and 0.8259 for the depression subscale. The questionnaire was used to identify preoperative anxiety and depression in patients undergoing gastrointestinal surgery.[30] Before the study, the questionnaire was tested with 30 patients undergoing major gastrointestinal surgery; the Cronbach's alpha coefficient was 0.82 (unpublished data).

3. The Fagerstrom Test for Nicotine Dependence (FTND) Thai version.[31] The FTND was a self-reported questionnaire comprising six items. The total possible score ranged from 0 to 10. A score of 0–4 was considered as very low to low nicotine dependence, 5 as moderate nicotine dependence, and 6–10 as high to very high nicotine dependence. The intraclass correlation coefficient of the Thai version of the FTND was 0.83 and the Cronbach's alpha was 0.52.[31]

4. Prolonged postoperative ileus: The development of PPOI was determined based on the definition of PPOI by Vather et al.,[32] which included five criteria; 1) nausea or vomiting, 2) the lack of tolerance to an oral diet within 24 hours, 3) the absence of flatus in 24 hours, 4) abdominal distension, and 5) radiologic results of ileus. PPOI was determined if at least two of the criteria were met on the fourth day after surgery. Radiologic evidence of ileus was assessed using the hospital database and the result was confirmed by a physician.

Data collection

Patients who met the inclusion criteria were approached preoperatively on an individual basis and informed about the details of the study together with the right to withdraw at any time. They were ensured that participation in this study would not affect the care and treatment they received. Once patients agreed to participate in the study, they were asked to provide written consent. The data were obtained through questionnaires, interviews, and patients' files. On the first day of admission, patients were asked to complete the HADS questionnaire (15-20 minutes). Patients who had a history of smoking were also asked to complete the FTND questionnaire (5-10 minutes).

The investigators revisited patients on postoperative day 4 between 9 and 10 a.m. to assess whether they had experienced PPOI. However, during the data collection period, if patients needed a ventilator, they were withdrawn from the study. If patients were discharged before postoperative day 4, the investigators called them on postoperative day 4 to assess the development of PPOI.

This prospective observational study was approved by the institutional ethics committee, Faculty of Medicine Siriraj Hospital, Mahidol University (Si 838/2019).

Statistical analysis

The data were analyzed by SPSS version 25 and descriptive statistics were generated. The relationships among the variables were analyzed using a Chi-square test. The powers of the predictive factors were analyzed using binary logistic regression. A p-value of 0.05 was considered to be statistically significant.

RESULTS

During the study period, 132 patients initially met the inclusion criteria. However, nine patients were later excluded from the study: four because their operation was canceled, three because a prolonged postoperative ventilator was used, and two were lost in follow-up. As a result, 123 patients were enrolled, with an average age of 59.8 ± 12.7 years and 52% men. The most common indication for surgery was gastrointestinal malignancy (96 patients, 78%), followed by an open approach (75 patients, 61%) and a combined general and epidural anesthesia (58 patients, 47%). Nearly half (46%) had a history of previous abdominal surgery. The details of patients' demographics and operative characteristics are shown in Table 1.

Approximately 30% of patients had a history of smoking and one-third of them had high to very high nicotine dependence (FTND score 6–10) (Table 2). The same proportion of patients had anxiety and depression preoperatively (7.3% and 7.3%, respectively) (Table 3).

After the operation, around 50% of patients had their first oral feeding on postoperative day 1, first flatus on postoperative day 1, and first stool on postoperative day 2. Up to one-third got out of bed on postoperative day 2. Complications except PPOI were found in 9.8% of patients. Only 1.6% of patients required reoperation. The median postoperative length of stay was five days (IQR 5-7).

As detailed in Table 4, PPOI was observed in 22% of patients undergoing elective major gastrointestinal surgery. In the PPOI group, most patients could not tolerate an oral diet within the first 24 hours (77.8%), had abdominal distension (70.4%), and had nausea/vomiting (66.7%). Only a few patients had an absence of flatus/stool over 24 hours on postoperative day 4 (26%). In particular, PPOI was confirmed by X-ray in 63% of patients with PPOI.

Univariate analysis revealed that having preoperative anxiety (p = 0.025) and starting ambulation on or after postoperative day 2 (p = 0.004) were significantly associated with PPOI (Figs 1 & 2). According to the multivariate analysis, the significant predictive factors of PPOI were having preoperative anxiety (OR = 6.26,

TABLE 1. Patient characteristics and the development of prolonged postoperative ileus (PPOI) (n = 123).

Characteristics	Overall n (%)	PPOI	
		No (n = 96)	Yes (n = 27)
Sex			
Male	64 (52%)	52 (81.3%)	12 (18.7%)
Female	59 (48%)	44 (74.6%)	15 (23.4%)
Age (years)			
Early adulthood (22-40)	14 (11.4%)	11 (78.6%)	3 (21.4%)
Middle adulthood (41-60)	44 (35.8%)	32 (72.7%)	12 (27.3%)
Old age (> 60)	65 (52.8%)	53 (81.5%)	12 (18.5%)
Mean ± SD (years)	59.8±12.7	60.1±12.1	58.9±14.7
BMI (kg/m^2)			
< 18.5	13 (10.6%)	10 (76.9%)	3 (23.1%)
18.5–22.9	53 (43.1%)	38 (71.7%)	15 (28.3%)
23–27.5	35 (28.5%)	30 (85.7%)	5 (14.3%)
> 27.5	22 (17.9%)	18 (81.8%)	4 (18.2%)
Mean ± SD (kg/m^2)	24.34±6.90	24.62±6.82	23.40±7.04
Diagnosis			
Diseases of the liver	25 (20.3%)	24 (96%)	1 (4%)
Diseases of the pancreas	13 (10.6%)	5 (38.5%)	8 (61.5%)
Diseases of the biliary tract and gall bladder	21 (17.1%)	14 (66.7%)	7 (33.3%)
Diseases of the stomach and small intestine	7 (5.7%)	4 (57.1%)	3 (42.9%)
Diseases of the large intestine	46 (37.4%)	40 (87%)	6 (13%)
Morbid obesity	9 (7.3%)	8 (88.9%)	1 (11.1%)
Other	2 (1.6%)	1 (50%)	1 (50%)
Pathology			
Non-cancer	27 (22%)	22 (81.5%)	5 (18.5%)
Cancer	96 (78%)	74 (77.1%)	22 (22.9%)
Comorbidity			
No	33 (26.8%)	22 (66.7%)	11 (33.3%)
Yes	90 (73.2%)	74 (82.2%)	16 (17.8%)
Type of comorbidity (n = 90)			
Diabetes mellitus	27 (30%)	26 (96.3%)	1 (3.7%)
Hypertension	55 (61%)	42 (76.4%)	13 (23.6%)
Dyslipidemia	39 (43.3%)	30 (76.9%)	9 (23.1%)
Coronary artery disease	8 (8.9%)	8 (100%)	0 (0%)
Kidney disease	6 (6.7%)	5 (83.3%)	1 (16.7%)
COPD	2 (2.2%)	2 (100%)	0 (0%)
Other	34 (37.8%)	26 (76.5%)	8 (23.5%)
Previous abdominal surgery			
No	66 (53.7%)	54 (81.8%)	12 (18.2%)
Yes	57 (46.3%)	42 (73.7%)	15 (26.3%)
Smoking status			
Never	84 (68.3%)	65 (77.4%)	19 (22.6%)
Current smoker	12 (9.8%)	11 (91.7%)	1 (8.3%)
Ex-smoker	27 (22%)	20 (74.1%)	7 (25.9%)

TABLE 1. Patient characteristics and the development of prolonged postoperative ileus (PPOI) (n = 123). (Continue)

Characteristics	Overall n (%)	PPOI	
		No (n = 96)	Yes (n = 27)
Bowel preparation			
No	77 (62.6%)	58 (75.3%)	19 (24.7%)
Yes	46 (37.4%)	38 (82.6%)	8 (17.4%)
Type of bowel preparation (n = 46)			
Osmotic agent	37 (80.4%)	30 (81.1%)	7 (18.9%)
Combination of osmotic agent and stimulant laxative	9 (19.6%)	8 (88.9%)	1 (11.1%)
Surgical approach			
Open	75 (61%)	57 (76%)	18 (24%)
Laparoscopy	32 (26%)	31 (96.9%)	1 (3.1%)
Robot-assisted	16 (13%)	8 (50%)	8 (50%)
Procedure			
HPB surgery	45 (36.6%)	38 (84.5%)	7 (15.5%)
Upper GI surgery	15 (12.2%)	12 (80%)	3 (20%)
Colorectal surgery	48 (39%)	42 (87.5%)	6 (12.5%)
Whipple's operation	15 (12.2%)	4 (26.7%)	11 (73.3%)
Anesthesia			
General anesthesia	65 (52.8%)	54 (83.1%)	11 (16.9%)
General anesthesia with epidural anesthesia	58 (47.2%)	42 (72.4%)	16 (27.6%)
Operative time (minutes)			
60-120	2 (1.6%)	2 (100%)	0 (0%)
121-180	14 (11.4%)	13 (92.9%)	1 (7.1%)
181-240	32 (26%)	31 (96.9%)	1 (3.1%)
241-300	27 (22%)	24 (88.9%)	3 (11.1%)
> 300	48 (39%)	26 (54.2%)	22 (45.8%)
Mean±SD (minutes)	317±148	274±113	467±159
Estimated blood loss (ml)			
≤ 500	85 (69.1%)	74 (87.1%)	11 (12.9%)
> 500	38 (30.9%)	22 (57.9%)	16 (42.1%)
Median (IQR)	300 (50–650)	200 (31–500)	550 (300–890)
Postoperative opioid used			
No	9 (7.3%)	9 (100%)	0 (0%)
Yes	114 (92.7%)	87 (76.3%)	27 (23.7%)
Time to the first oral feeding			
Day 0	46 (37.4%)	40 (87%)	6 (13%)
Day 1	67 (54.5%)	50 (74.6%)	17 (25.4%)
Day 2	6 (4.9%)	5 (83.3%)	1 (16.7%)
Day 3	0 (0%)	0 (0%)	0 (0%)
≥ Day 4	4 (3.3%)	1 (25%)	3 (75%)
Time to the first flatus			
Day 1	43 (35%)	39 (90.7%)	4 (9.3%)
Day 2	60 (48.8%)	49 (81.7%)	11 (18.3%)
Day 3	16 (13%)	8 (50%)	8 (50%)
≥ Day 4	4 (33%)	0 (0%)	4 (100%)

TABLE 1. Patient characteristics and the development of prolonged postoperative ileus (PPOI) (n = 123). (Continue)

Characteristics	Overall n (%)	PPOI	
		No (n = 96)	Yes (n = 27)
Time to the first stool			
Day 1	17 (13.8%)	15 (88.2%)	2 (11.8%)
Day 2	44 (35.8%)	38 (86.4%)	6 (13.6%)
Day 3	34 (27.6%)	27 (79.4%)	7 (20.6%)
≥ Day 4	28 (22.8%)	16 (57.1%)	12 (42.9%)
Time to the first ambulation			
Day 1	84 (69.3%)	72 (85.7%)	12 (14.3%)
≥ Day 2	39 (31.7%)	24 (61.5%)	15 (38.5%)
Mean±SD (days)	1.5±0.9	1.3±0.5	2.1±1.4
Nasogastric tube (NGT) insertion			
No NGT insertion	95 (77.2%)	80 (84.3%)	15 (15.8%)
NGT removed by protocol	17 (13.8%)	11 (64.7%)	6 (35.3%)
Delayed NGT removal	9 (7.3%)	4 (44.5%)	5 (55.5%)
NGT reinsertion	2 (1.6%)	1 (50%)	1 (50%)
Complications			
No	111 (90.2%)	94 (84.7%)	17 (15.3%)
Yes	12 (9.8%)	2 (16.7%)	10 (83.3%)
Type of complication (n = 12)			
Intraabdominal collection	4 (33.3%)	3 (75%)	1 (25%)
Surgical site infection	4 (33.3%)	4 (100%)	0 (0%)
Pancreatic fistula	2 (16.7%)	1 (50%)	1 (50%)
Anastomosis leakage	2 (16.7%)	2 (100%)	0 (0%)
Cholangitis	1 (8.3%)	1 (100%)	0 (0%)
Chyle leak	1 (8.3%)	1 (100%)	0 (0%)
Incisional hernia	1 (8.3%)	0 (0%)	1 (100%)
Efferent loop syndrome	1 (8.3%)	0 (0%)	1 (100%)
Septic shock	1 (8.3%)	0 (0%)	1 (100%)
Hospital acquired pneumonia	1 (8.3%)	0 (0%)	1 (100%)
Reoperation			
No	121 (98.4%)	96 (79.3%)	25 (20.7%)
Yes	2 (1.6%)	0 (0%)	2 (100%)
Postoperative length of stay (days)			
2	2 (1.6%)	2 (100%)	0 (0%)
3	20 (16.3%)	20 (100%)	0 (0%)
4	39 (31.7%)	37 (94.9%)	2 (5.1%)
5	21 (17.1%)	21 (100%)	0 (0%)
≥ 6	41 (33.3%)	16 (39%)	25 (61%)
Median (IQR)	5 (4–7)	4 (4–5)	11 (7–22)
Mean ± SD (days)	6.5±5.9	4.5±1.6	13.6±9.5

TABLE 2. Fagerstrom Test for Nicotine Dependence (FTND) and development of prolonged postoperative ileus (PPOI) (n = 39).

FTND score	n (%)	PPOI	
		No (n = 31)	Yes (n = 8)
Very low to low nicotine dependence (0–4)	25 (64.1%)	20 (80%)	5 (20%)
Moderate nicotine dependence (5)	2 (5.1%)	2 (100%)	0 (0%)
High to very high nicotine dependence (6–10)	12 (30.8%)	9 (75%)	3 (25%)
Mean ± SD	1.24±2.27	1.32±2.31	0.93±2.13

TABLE 3. Hospital Anxiety and Depression Scale (HADS) and development of prolonged postoperative ileus (PPOI) (n = 123).

HADS score	n (%)	PPOI	
		No (n = 96)	Yes (n = 27)
Anxiety score			
0-7 (Non-case)	91 (74%)	75 (82.4%)	16 (17.6%)
8-10 (Doubtful case)	23 (18.7%)	17 (73.9%)	6 (26.1%)
11-21 (Confirmed case)	9 (7.3%)	4 (44.4%)	5 (55.6%)
Mean ± SD	5.83±2.94	5.67±2.84	6.41±3.27
Depression score			
0-7 (Non-case)	90 (73.2%)	71 (78.9%)	19 (21.1%)
8-10 (Doubtful case)	24 (19.5%)	18 (75%)	6 (25%)
11-21 (Confirmed case)	9 (7.3%)	7 (77.8%)	2 (22.2%)
Mean ± SD	6.16±2.49	6.16±2.50	6.19±2.50

TABLE 4. Development of prolonged postoperative ileus (PPOI) (n = 123).

Development of PPOI	n	(%)
Development of PPOI		
No (0-1)	96	78
Yes (2-5)	27	22
Diagnosis criteria for PPOI* (n = 27)		
Nausea/vomiting	18	66.7
Lack of tolerance to an oral diet over 24 h	21	77.8
Absence of flatus/stool over 24 h	7	26
Abdominal distension	19	70.4
Radiologic results	17	63

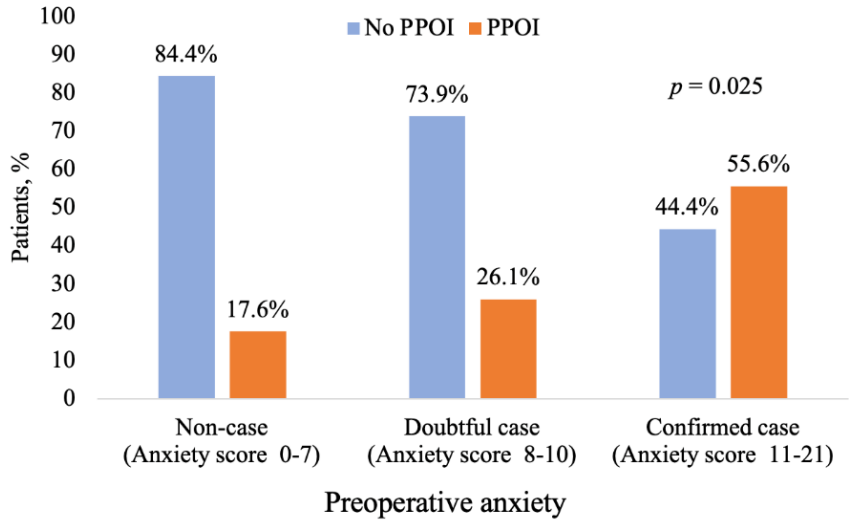

Fig 1. Association between preoperative anxiety and prolonged postoperative ileus.

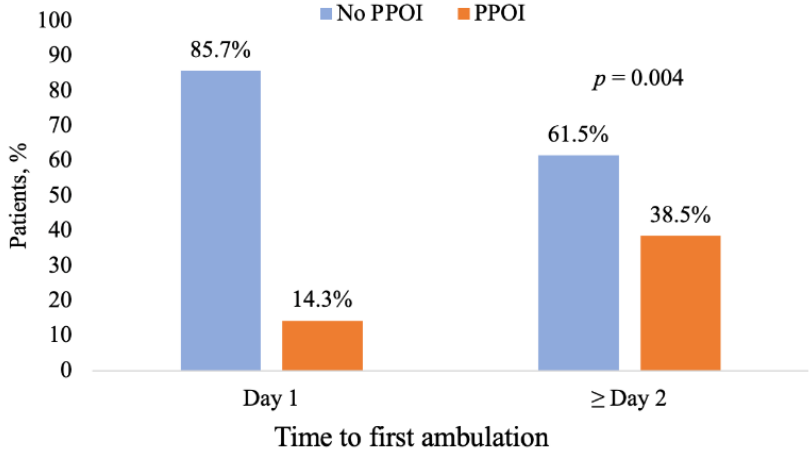

Fig 2. Association between time to first ambulation and prolonged postoperative ileus.

95% CI = 1.218–44.411, p = 0.046) and ambulation on or after postoperative day 2 (OR = 3.26, 95% CI = 1.254–8.501, p = 0.015) (Table 5).

DISCUSSION

This study demonstrated that 22% of patients undergoing major gastrointestinal surgery developed PPOI based on the criteria recommended by Vather et al.,[32] which have been validated and widely used to determine PPOI in several international studies. This study also found that preoperative anxiety and delayed postoperative ambulation were two significant predictors of PPOI. Interestingly, both preoperative anxiety and depression were investigated as psychological distress using HADS in this study, but only anxiety was a significant predictor of PPOI. Several recent studies have addressed the problem of clinical anxiety in elective surgery.[30,34–36] Preoperative anxiety in surgical patients develops for several reasons such as fear of complications, postoperative pain, disability, and death.[34,36] The association between psychological distress and changes in gastrointestinal function has been established in many studies.[37,38] It is known to alter autonomic innervation, specifically stimulated sympathetic innervation, which relaxes the smooth muscle, thus decreasing bowel motility. Another reason might be the release of catecholamine, which is triggered by psychological distress and causes altered mucosal blood flow.[26,27]

Our findings of anxiety (not depression) as a PPOI predictor were consistent with the study by Paine et al.,[39] who examined the relationship between anxiety and depression as well as 24-hour catecholamines in patients with untreated high blood pressure and highlighted that only anxiety is associated with sympathetic innervation

TABLE 5. Univariate and multivariate analysis of the risk factors for prolonged postoperative ileus (PPOI) following major gastrointestinal surgery.

Factors	Crude OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Age				
Early adulthood[ref]				
Middle adulthood	1.38 (0.33–5.80)	0.664	0.83 (0.15–4.52)	0.832
Old age	0.83 (0.20–3.44)	0.798	0.64 (0.13–3.26)	0.595
BMI (kg/m²)				
< 18.5[ref]				
18.5-22.9	1.32 (0.32–5.45)	0.705	1.19 (0.23–6.11)	0.838
23-27.5	0.56 (0.11–2.75)	0.472	0.57 (0.09–3.55)	0.543
> 27.5	0.74 (0.14–3.99)	0.727	0.73 (0.10–5.39)	0.754
HADS				
Anxiety subscale				
0-7[ref]				
8-10	1.65 (0.56–4.85)	0.359	1.62 (0.48–5.43)	0.439
11-21	5.86 (1.42–24.27)	0.025*	6.26 (1.22–44.41)	0.046*
Depression subscale				
0-7[ref]				
8-10	1.25 (0.43–3.57)	0.683	0.82 (0.24–2.84)	0.759
11-21	1.07 (0.21–5.57)	0.938	0.44 (0.048–3.99)	0.465
FTND score				
0-4[ref]				
5	0.43 (0.15–3.84)	0.989	0.91 (0.02–4.56)	0.899
6-10	0.94 (0.24–3.66)	0.933	0.95 (0.21–4.25)	0.942
First ambulation				
POD 1[ref]				
≥ POD 2	3.75 (1.54–9.12)	0.004*	3.26 (1.25–8.50)	0.015*

*Statistically significant (p-value < 0.05)

Abbreviations: CI; Confidence interval, OR; Odds ratio, BMI; Body mass index, HADS; Hospital Anxiety and Depression Scale, FTND; Fagerstrom Test for Nicotine Dependence, POD; Postoperative day

activation. Therefore, anxiety and depression might affect the gastrointestinal tract through a different mechanism. Another study of 162 surgical patients also confirmed a correlation between preoperative anxiety and delayed gastrointestinal recovery.[40]

The present study also demonstrated that delayed ambulation was significantly associated with PPOI, which concurred with a population-based study in New Zealand in which delayed ambulation was found to influence PPOI following elective colorectal surgery.[12] Meanwhile, early ambulation has been shown to enhance patients' overall recovery, including facilitating bowel motility.[41] Morisawa et al.[28] also found that the bowel sound of critically ill patients is significantly increased after passive exercise. They explained that ambulation can induce gastrointestinal motility by stretching the gastrointestinal tract and stimulating its parasympathetic innervation activity. Moreover, Kumar et al.[42] found that

bowel cleansing is more adequate in patients without ambulation difficulty. Interestingly, as no definition of early ambulation was specified, the results of the study suggested that early ambulation (i.e., postoperative day 1) is recommended, especially to reduce the development of PPOI following major gastrointestinal surgery.

Age was not identified as a significant predictor of PPOI in this study. This concurred with prior studies of colorectal surgery.[5,8,9,12,14,22] BMI was also unable to predict PPOI in this study, again consistent with previous studies.[4,7-9,12,14] Lastly, smoking status was not significantly associated with PPOI in this study, in line with the findings of previous research.[5,9,12]

Although this was a prospective study, some limitations need to be addressed. First, all types of major gastrointestinal surgery were included given that the extent of surgery may vary depending on the nature of the disease (benign versus malignancy) and organ involvement. Second, due to the relatively small number of smokers, the power of smoking could not be determined in this study. Lastly, although PPOI was defined by the international definition proposed by Vather et al.,[32] PPOI may manifest beyond the period of study or after discharge. An extended period of study could provide additional information for calculating the risk factors for the delayed presentation of PPOI.

CONCLUSION

PPOI occurred in 22% of patients following major gastrointestinal surgery. Preoperative anxiety and delayed postoperative ambulation were significant predictors of PPOI. Therefore, it is reasonable that preoperative anxiety should be assessed and treated (if present) under a multidisciplinary team approach. Early ambulation on the first day after the operation is also encouraged alongside effective nursing care and pain control.

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Abbreviations

POI; Postoperative Ileus
PPOI; Prolonged Postoperative Ileus
BMI; Body Mass Index
HADS; Hospital Anxiety and Depression Scale
FTND; The Fagerstrom Test for Nicotine Dependence

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