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ORIGINAL ARTICLE

Preoperative risk factors for prolonged postoperative ileus after colorectal resection

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Abstract
Purpose Prolonged postoperative ileus (PPOI) after colorectal resection significantly impacts patients' recovery and hospital stay. Because treatment options for PPOI are limited, it is necessary to focus on prevention strategies. The aim of this study is to investigate risk factors associated with PPOI in patients undergoing colorectal surgery.
Methods Data from all consecutive patients who underwent colorectal resection in our department were retrospectively analyzed from a prospective database over a 9-month period. PPOI was defined as the necessity to insert a nasogastric tube in a patient who experienced nausea and two episodes of vomiting with absence of bowel function. Multivariable analysis was performed considering a prespecified list of 16 potential preoperative risk factors.
Results A total of 523 patients (mean age 59 years; 52.2% males) were included, and 83 patients (15.9%) developed PPOI. Statistically significant independent predictors of PPOI were male sex (OR 2.07; $P = 0.0034$), open resection (OR 4.47; $P < 0.0001$), conversion to laparotomy (OR 4.83; $P = 0.0015$), splenic flexure mobilization (OR 1.72; $P = 0.063$), and rectal resection (OR 2.72; $P = 0.0047$). Discriminative ability of this prediction model was 0.72.
Conclusions Therapeutic strategies aimed to prevent PPOI after colorectal resection should focus on patients with increased risk. Patients and medical staff can be informed of the higher PPOI risk, so that early treatment can be started.

Keywords Postoperative ileus · Risk factors · Colorectal surgery

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Introduction

Postoperative ileus (POI) is defined as a temporary decrease in gastrointestinal motility following surgery. It is characterized by nausea and vomiting, inability to eat or drink, abdominal distension and pain, and delayed passage of flatus and stool [1–3]. As POI develops in almost every patient after abdominal surgery, it may be considered as a normal physiologic response after surgery. Usually, it resolves within 3 days, but may persist or reoccur, in which case it is called prolonged postoperative ileus (PPOI) [1, 4]. The point at which POI becomes PPOI has not been clearly established. Definitions of PPOI either take a certain time interval (in days) between surgery and ileus into account, or a therapeutic act (insertion of a nasogastric tube) [5]. PPOI impacts patient recovery and prolongs hospital stay, and it is a significant predictor of hospital resource utilization [6]. Its incidence following colorectal resection is reported to be between 3 and 32% [7]. Because treatment options for PPOI are limited, it is necessary to focus on prevention strategies. Therefore, identification of risk factors for PPOI can contribute to preventing PPOI in the future. Moreover, knowledge of possible risk factors is useful to counsel patients and raise awareness in all caregivers. The aim of the present study was to evaluate preoperative factors that could predict a higher rate of PPOI in a large cohort of consecutive patients who had undergone colorectal resection.

Materials and methods

A prospectively maintained institutional review board-approved database of all elective colorectal operations was assessed retrospectively. This is a morbidity-mortality database concerning all procedures performed by three surgeons (ADH, AW, AdBvO). Consecutive intra-abdominal procedures performed during a 9-month period were identified. Only colonic or rectal resections were included. No patients were systematically excluded for any reason. Operations were performed by three staff general surgeons, specialized in colorectal diseases and uniquely performing colorectal surgery. Nasogastric tubes were not routinely used postoperatively. Perioperative care was not standardized, but several aspects of fast-track protocols were incorporated in patient care including no mechanical bowel preparation for colonic resections, standard deep vein thrombosis prophylaxis with low-molecular-weight heparin, early postoperative feeding and mobilization, stepwise analgesia progression, and restrictive intravenous fluid therapy as advocated by Wind et al. [8]. All patients were offered a clear oral fluid diet on postoperative day 1 and were progressively advanced to a solid diet as tolerated.

During weekly medical staff meetings, all patients after colorectal resection were discussed regarding PPOI occurrence. PPOI was defined as the necessity of nasogastric tube insertion in a patient who experienced nausea and two episodes of vomiting, and had absence of adequate bowel function (failure to pass flatus or stool) with abdominal distension and lack of bowel sounds. In a recent systematic review and meta-analysis, those criteria were most commonly used to define PPOI [5]. A single surgeon (AW) assessed all patients with PPOI to ensure that the same PPOI definition was respected. This was done during data collection for the database, so PPOI was coded according to the judgment of one surgeon. Diagnosis was made on a clinical basis, and no routine abdominal plain film or CT scan was performed. Patients with PPOI were compared with those who did not develop PPOI.

Variables recorded included patient demographics (gender, age, body mass index (BMI), American Society of Anaesthesiologists (ASA) classification) and other factors such as primary diagnosis (cancer, inflammatory bowel disease, endometriosis, other benign disease), a history of previous abdominal surgery, previous resection of colorectal cancer, and comorbid conditions such as cardiac disorders, respiratory comorbidity, chronic renal failure, cerebrovascular comorbidity, peripheral vascular disease, diabetes, hypertension, and hyperlipidemia.

Details of surgery included type of surgery (open, laparoscopic, converted), type of operation (segmental colectomy, including total colectomy with or without ileostomy (3.2 and 2.4%, respectively) and Hartmann's procedures (4.5%), rectal resection (including total mesorectal excision (TME)), including abdominoperineal resections (13.3%)), length of preoperative hospital stay, urgent or elective operation, mobilization of the splenic flexure, formation of a stoma, and type of postoperative analgesia: patient-controlled epidural analgesia (PCEA) or patient-controlled intravenous analgesia (PCIA), or no patient-controlled analgesia. An urgent operation was defined as surgery required within 6 h. The hospital's pain management service provided PCEA or PCIA catheters as discussed with the patient before the operation. For elective colorectal resection (open and laparoscopically), it is standard of care to provide a PCEA. A thoracic PCEA catheter was inserted between T8 and T12. Postoperative analgesia was provided by continuous epidural infusion of 0.125% levobupivacaine and 1 mg/ml sufentanil, and supplemented by a patient-controlled bolus capability of 2 ml with a 20-min lockout period. Standard PCIA pumps contained 2 mg/ml morphine and were set at a patient-controlled bolus capability of 1.5 mg with a 7-min lockout period.

Statistical analysis

Fisher's exact and Mann-Whitney U tests were used to compare categorical and continuous variables between two groups, respectively. Univariate and multivariable binary logistic regression models were used to predict presence of PPOI. The multivariable model was based on a predefined set of 16 preoperatively available variables. A multivariable prediction model was obtained by applying a backward selection procedure with 0.157 as critical level for the p value. This critical value corresponded to the use of the Akaike information criterion (AIC) for model selection. With AIC, we required the increase in model X^2 to be larger than twice the degrees of freedom. To quantify the discriminative ability of the prediction model, the area under the ROC curve (AUC), also known as the concordance index (c-index), was reported. This index ranged from 0.5 (random prediction) to 1 (perfect discrimination). An optimism-corrected estimate of the performance (AUC) was obtained using a bootstrap resampling procedure. In the multivariable model, pairwise interactions between predictors were verified. All analyses were performed using SAS software, version 9.2 of the SAS System for Windows.

Results

A total number of 523 patients were included, with a mean age of 59 years, and 52.2% were male patients. Overall, 83 (15.9%) patients developed PPOI. When patients with PPOI were compared with the others, demographic characteristics suggested predominance of male patients with PPOI ($P < 0.001$), but comparable mean age (58.6 vs 60.8 years; $P = 0.37$) and similar mean BMI (25.2 vs 25.9 kg/m^2; $P = 0.204$) between groups (Table 1). None of the comorbidities that were investigated showed any significant correlation with PPOI. Moreover, no significant differences were noted between these groups with respect to previous abdominal surgery, urgent operation, and previous resection of colorectal cancer. Overall, 240 patients had a laparoscopic resection and 257 patients underwent open surgery. Of the 137 patients who had had previous abdominal surgery, 85 patients had already had a midline laparotomy, which was an indication for open colorectal resection in our department. This means that 257–85 = 172 patients (33%) had a primary open colorectal resection. More patients in the PPOI group had had an open procedure (74.7 vs 44.3%; $P < 0.001$). Mobilization of the splenic flexure and formation of a stoma was also more frequent in patients with PPOI (44.6 vs 26.4%; $P = 0.001$, 39.8 vs 25%: $P = 0.007$, respectively). Patient-controlled epidural analgesia was more frequent in the PPOI group (89.2 vs 68%; $P = 0.041$). There were more patients with cancer or IBD in the PPOI group (50.6 vs 46.6%; 24.1 vs 16.8%, respectively: $P = 0.039$). Rectal resection was significantly higher in the PPOI group: 48.2 vs 23.4%, $P < 0.001$. There were no reoperations for mechanical small bowel obstruction, and none of the patients experienced a second episode of PPOI after resumption of the transit. The duration of nasogastric tube insertion was a mean ± SD of 4.3 ± 3.3 days (median of 3 days, range 1–19 days). One 76-year-old patient experienced PPOI for over 2 weeks (19 days) after open left hemicolectomy for tumor. He was given total parenteral nutrition, and CT scan ruled out mechanical causes of ileus. The postoperative hospital stay was a mean ± SD of 10.2 ± 11.4 days (range 1–146 days) for patients without PPOI vs 16.3 ± 12.6 days (range 6–104 days) for patients with PPOI ($P < 0.001$).

Univariable logistic regression analysis identified male sex (OR 2.596, 95% CI 1.56–4.32; $P = 0.0002$), open resection (OR 5.133, 95% CI 2.79–9.45; $P < 0.0001$), conversion to laparotomy (OR 5.947, 95% CI 2.14–16.51; $P = 0.0006$), rectal resection (OR 3.044, 95% CI 1.88–4.94; $P < 0.0001$), PCEA (OR 2.430, 95% CI 1.16–5.08; $P = 0.018$), splenic flexure mobilization (OR 2.247, 95% CI 1.39–3.64; $P = 0.001$), and formation of a stoma (OR 1.980, 95% CI 1.21–3.23; $P = 0.006$) as the only seven predictive factors for developing PPOI (Table 2).

After multivariate analysis using a backward selection strategy and only considering a prespecified list of variables, the following variables were significantly associated with PPOI: male sex (OR 2.205, 95% CI 1.24–3.92; $P = 0.007$), open resection (OR 4.328, 95% CI 2.11–8.87; $P < 0.0001$), conversion to laparotomy (OR 6.233, 95% CI 2.07–18.74; $P = 0.0011$), splenic flexure mobilization (OR 1.716, 95% CI 0.97–3.03; $P = 0.063$), and rectal resection (OR 2.718, 95% CI 1.36–5.44; $P = 0.0047$). From the logistic regression model, PPOI can be predicted using the formula 100 * exp(M) / (1 + exp(M)) where M equals −3.53 + 0.806 (if male) + 1.693 (if converted) + 1.399 (if open) + 0.714 (if rectal resection) + 0.467 (if splenic flexure mobilization). For example, a male patient undergoing an open rectal resection with splenic flexure mobilization had a 100 * exp(−0.144) / (1 + exp.(−0.144)) = 46.4% probability of prolonged POI. Discriminative ability of this prediction model, after correction for overoptimism, showed an AUC of 0.718 (95% CI 0.67–0.77).

Discussion

In the present study, a 15.9% rate of PPOI was observed. This incidence is similar to that reported by Chapuis et al. (14%), Millan et al. (15.9%), and Iyer et al. (15.3%) [6, 9, 10]. Moreover, it did not greatly differ from 10% reported in a recent meta-analysis on PPOI after colorectal surgery [5]. Multivariable analysis of 16 potential predictors of PPOI identified the following independent risk factors: male sex, open resection, conversion to laparotomy, splenic flexure mobilization, and rectal resection. In literature, independent risk factors of PPOI have been investigated. Previous studies found male sex, increasing age, respiratory comorbidity, peripheral vascular disease, previous abdominal surgery, preoperative use of narcotics, total postoperative opiate dose, duration of surgery, stoma formation, hemoglobin drop, and blood transfusion to be associated with PPOI after colorectal surgery (Table 3) [7, 9–13]. Compared to the literature, the present analysis revealed male sex and open or converted technique as common risk factors. In contrast to Chapuis et al. [9] and Millan et al. [10], respiratory comorbidity, peripheral vascular disease, an urgent operation, or stoma formation was not observed to be associated with PPOI in our series. Open colorectal resection was a risk factor for PPOI, and this is in keeping with findings in randomized controlled trials [14–17]. For example, laparoscopic colectomy performed as part of a fast-track protocol had a faster recovery of gastrointestinal function compared to open resection [17]. The aim of this retrospective study was to predict PPOI by preoperatively available potential risk factors. Therefore, duration of surgery, blood loss, perioperative blood transfusion, and postoperative intravenous fluid management and laboratory findings were not assessed in this analysis. The reason for their exclusion was that these factors are not available at the start of the operation. In contrast, regarding conversion to laparotomy, we strictly adhere to an “early conversion” policy, so decision regarding feasibility of a laparoscopic resection is made at the start. Therefore, also this information is available at the beginning of the procedure. The main goal was to select patients at risk of PPOI in order to focus on

Table 1 Patient characteristics and operative details

Variable	Overall (*n* = 523)	No PPOI (*n* = 440)	PPOI (*n* = 83)	*P*
Age (mean ± SD)	59 ± 17.3	58.6 ± 17.4	60.8 ± 16.3	0.37
Sex				
Female	250 (47.8%)	226 (51.4%)	24 (28.9%)	<0.001
Male	273 (52.2%)	214 (48.6%)	59 (71.1%)	
ASA class				0.011
I	53 (10.1%)	51 (11.5%)	2 (2.4%)	
II	329 (62.9%)	266 (60.5%)	63 (75.9%)	
III	136 (26%)	119 (27.1%)	17 (20.5%)	
IV	5 (1%)	4 (0.9%)	1 (1.2%)	
BMI (mean ± SD)	25.3 ± 4.8	25.2 ± 4.9	25.9 ± 4.7	0.204
Diagnosis				0.064
Cancer	247 (47.2%)	205 (46.6%)	42 (50.6%)	
IBD	94 (18%)	74 (16.8%)	20 (24.1%)	
Benign disease	139 (26.6%)	120 (27.3%)	19 (22.9%)	
Endometriosis	43 (8.2%)	41 (9.3%)	2 (2.4%)	
Previous abdominal surgery				0.057
No	386 (73.8%)	332 (75.5%)	54 (65.1%)	
Yes	137 (26.2%)	108 (24.5%)	29 (34.9%)	
Urgent operation				0.501
No	505 (96.6%)	425 (96.6%)	80 (96.4%)	
Yes	18 (3.4%)	15 (3.4%)	3 (3.6%)	
Previous CRC resected				0.138
No	461 (88.2%)	392 (89.1%)	69 (83.1%)	
Yes	62 (11.8%)	48 (10.9%)	14 (16.9%)	
Cardiac comorbidity				0.631
No	437 (83.6%)	369 (83.9%)	68 (82%)	
Yes	86 (16.4%)	71 (16.1%)	15 (18%)	
Respiratory comorbidity				0.472
No	457 (87.4%)	382 (86.8%)	75 (90.4%)	
Yes	66 (12.6%)	58 (13.2%)	8 (9.6%)	
Chronic renal failure				0.475
No	488 (93.3%)	412 (93.6%)	76 (91.6%)	
Yes	35 (6.7%)	28 (6.4%)	7 (8.4%)	
Cerebrovascular comorbidity				1.000
No	500 (95.6%)	420 (95.5%)	80 (96.4%)	
Yes	23 (4.4%)	20 (4.5%)	3 (3.6%)	
Peripheral vascular disease				0.279
No	481 (92%)	407 (92.5%)	74 (89.2%)	
Yes	42 (8%)	33 (7.5%)	9 (10.8%)	
Diabetes				0.211
No	475 (90.8%)	403 (91.6%)	72 (86.8%)	
Yes	48 (9.2%)	37 (8.4%)	11 (13.2%)	
Hypertension				0.294
No	368 (70.4%)	314 (71.4%)	54 (65.1%)	
Yes	155 (29.6%)	126 (28.6%)	29 (34.9%)	
Variable	Overall (*n* = 523)	No PPOI (*n* = 440)	PPOI (*n* = 83)	*P*
Hyperlipidemia				0.250
No	409 (78.2%)	348 (79.1%)	61 (73.5%)	
Yes	114 (21.8%)	92 (20.9%)	22 (26.5%)	
Any comorbidity				0.704
No	176 (33.6%)	150 (34.1%)	26 (31.3%)	
Yes	347 (66.4%)	290 (65.9%)	57 (68.7%)	

Table 1 (continued)

Variable	Overall (n = 523)	No PPOI (n = 440)	PPOI (n = 83)	P
Patient-controlled analgesia				0.041
No	106 (20.3%)	97 (22.1%)	9 (10.8%)	
PCIA	80 (15.3%)	68 (15.4%)	12 (14.5%)	
PCEA	337 (64.4%)	275 (62.5%)	62 (74.7%)	
Preoperative length of stay				0.871
>1 day	84 (16.1%)	70 (15.9%)	14 (16.9%)	
≤1 day	439 (83.9%)	370 (84.1%)	69 (83.1%)	
Splenic flexure mobilization				0.001
No	370 (70.8%)	324 (73.6%)	46 (55.4%)	
Yes	153 (29.2%)	116 (26.4%)	37 (44.6%)	
Stoma				0.007
No	380 (72.7%)	330 (75%)	50 (60.2%)	
Yes	143 (27.3%)	110 (25%)	33 (39.8%)	
Technique/mode of resection				<0.001
Laparoscopic	240 (45.9%)	226 (51.4%)	14 (16.9%)	
Open	257 (49.1%)	195 (44.3%)	62 (74.7%)	
Converted	26 (5%)	19 (4.3%)	7 (8.4%)	
Operation type				<0.001
Segmental colectomy	380 (72.7%)	337(76.6%)	43 (51.8%)	
Rectal resection	143 (27.3%)	103 (23.4%)	40 (48.2%)	
Number of anastomoses (mean ± SD)	0.9 ± 0.5	0.9 ± 0.53	1.0 ± 0.47	0.547

prevention strategies. The pathophysiology of POI is still not clear, and it is likely to be multifactorial consisting of both endogenous and exogenous characteristics. There is evidence that bowel manipulation is associated with increased risk of developing PPOI, because of mechanical gastrointestinal trauma causing localized inflammatory response [18]. The degree of hypomotility directly correlates with the degree of manipulation and gastrointestinal inflammation [19]. Not surprisingly, laparoscopic colectomy had a lower incidence of PPOI when compared to open surgery in the present study: the observed PPOI incidence was 5.8 vs 24.1% for a laparoscopic vs open approach, respectively. Current research is focusing on the development of anti-inflammatory treatments in order to prevent PPOI. Although still under investigation, a promising strategy to reduce PPOI and to dampen the inflammatory response after intra-abdominal surgery is vagus nerve stimulation (VNS). In 2000, evidence was provided that the vagus nerve plays an important role in modulating the immune system [20, 21]. Notably, VNS attenuated systemic inflammation in a murine endotoxin model and even improved survival. In 2005, a similar beneficial effect of VNS was shown in a murine model of postoperative ileus. VNS reduced intestinal inflammation induced by surgery and enhanced recovery of intestinal transit [22]. In a recent study, we could show that laparoscopic VNS is feasible and safe with minimal extra operating time in a porcine model [23]. Hence, VNS could be a novel strategy in the prevention and treatment of PPOI. Alternatively, “sham feeding” by means of gum chewing could be used to activate the vagus nerve [24]. A meta-analysis has shown that gum chewing indeed shortens both time to flatus and time to defecation [25]. It can shorten both PPOI duration and length of hospital stay by approximately 1 day [26]. Moreover, it has also been shown that gum chewing significantly reduced inflammatory response and complication rate after colorectal surgery [27]. More recently, nicotine gum chewing has been proposed to shorten POI via vagus nerve activation [28]. Nicotine is a selective cholinergic agonist and an essential mediator of the cholinergic anti-inflammatory pathway [29]. The results presented in this study can be important, because no modifiable risk factors for PPOI could be found and therefore clinicians should focus on other measures to prevent PPOI in a population with a higher risk. The preoperative use of narcotics (opiate analgesia) and total postoperative opiate dose have been identified to predict ileus in two studies [7, 11], but in the present study it could not be assessed as it was not recorded in the database. This can be considered as a limitation of the study. However, it is surprising that patient-controlled analgesia had an effect on the occurrence of PPOI. Opiate analgesia has been shown to play a role in the pathophysiology of PPOI by decreasing gastrointestinal motility, especially colonic motility [30–32]. Several studies have shown epidural analgesia to be superior compared to PCIA with regard to ileus, and the present literature suggests that opiates delivered epidurally do not have the same effect on gastrointestinal motility when compared to systemic opiates [33–38]. Therefore, epidural analgesia is still recommended in the perioperative setting of laparoscopic colorectal surgery.

Table 2 Univariate and multivariable analysis of preoperative risk factors for PPOI

	Univariate analysis		Multivariable analysis		BIF (%)
	OR (95% CI)	*P*	OR (95% CI)	*P*	
Age	1.01 (0.99–1.02)	0.293	–		25
Sex (male)	2.60 (1.56–4.32)	0.0002	2.21 (1.24–3.92)	0.007	93
Body mass index (kg/m^2)	1.03 (0.98–1.08)	0.225	–		16
Length of preoperative hospital stay (days)	0.86 (0.73–1.01)	0.063	–		22
Respiratory comorbidity	0.70 (0.32–1.53)	0.375	–		42
Peripheral vascular disease	1.50 (0.69–3.26)	0.307	–		29
Any comorbidity	1.13 (0.69–1.88)	0.625	–		24
Previous abdominal surgery	1.65 (1.0–2.72)	0.05	–		16
Diagnosis		0.05	–		59
-Cancer	#				
-IBD	1.32 (0.73–2.39)	0.361			
-Benign disease	0.77 (0.43–1.39)	0.389			
-Endometriosis	0.24 (0.06–1.02)	0.054			
Patient-controlled analgesia		0.036	–		50
-No	#				
-PCEA	2.43 (1.16–5.08)	0.018			
-PCIA	1.9 (0.76–4.76)	0.17			
Urgent operation	1.09 (0.31–3.86)	0.893	–		54
Organ resected					90
-Colon	#				
-Rectum	3.04 (1.88–4.94)	<0.0001	2.72 (1.36–5.44)	0.004	
Mode of resection		<0.0001		0.0001	100
-Laparoscopy	#				
-Open	5.13 (2.79–9.45)	<0.0001	4.33 (2.11–8.87)	<0.0001	
-Conversion	5.95 (2.14–16.51)	0.0006	6.23 (2.07–18.74)	0.0011	
Splenic flexure mobilization	2.25 (1.39–3.64)	0.001	1.72 (0.97–3.03)	0.063	58
Number of anastomoses	1.11 (0.72–1.71)	0.638	–		17
Stoma created	1.98 (1.21–3.23)	0.006	–		44

BIF bootstrap importance frequency, − not retained in the final multivariable model after application of backward selection strategy with $P = 0.157$ as critical level, # reference category

Table 3 Reported risk factors for PPOI in literature

Author, year	No. of patients	Inclusion	PPOI incidence	Risk factors on multivariate analysis
Chapuis, 2013	2400	Colorectal cancer resection	14%	Male, respiratory comorbidity, peripheral vascular disease, duration of surgery ≥3 h, urgent operation, blood transfusion, stoma
Millan, 2012	773	Colorectal cancer resection	15.9%	Male, COPD, ileostomy
Kronberg, 2011	413	Laparoscopic colectomy	10.2%	Age, previous abdominal surgery, preoperative narcotics use
Vather, 2015	327	Elective colorectal surgery	26.9%	Male, decreasing albumin, open or converted technique, increasing wound size, operative difficulty and bowel handling, blood transfusion, intravenous crystalloid administration, delayed first mobilization
Vather, 2013	255	Elective colorectal surgery	19.6%	Increasing age, drop in hemoglobin
Artinyan, 2008	88	Open colonic or rectal resection	20.5%	Blood loss, total postoperative opiate dose
Present study	523	Colorectal resection	15.9%	Male, open resection, conversion to laparotomy, rectal resection, splenic flexure mobilization

As such, results presented in this study challenge statements and findings of previous studies. The results shown in this study regarding patient-controlled analgesia have not been investigated previously and might be an argument against the use of PCEA or PCIA as advocated in many fast-track protocols [8, 39]. Moreover, a recent study showed increased cost, increased length of stay, and no reduction of POI associated with epidural analgesia during laparoscopic colectomy [40].

Strengths of this study are the large number of consecutive non-selected patients included over a 9-month period, prospective data collection during weekly meetings without missing data, examination of many preoperatively available potential risk factors, and the scarce literature on risk factors of PPOI after colorectal resection. With the absence of a precise and validated definition of PPOI, and large variation of definition-related incidence, more robust studies on risk factors of PPOI are necessary. Moreover, Vather et al. have already proposed a methodology used here in their study [12].

Limitations of this study are the heterogeneity of the study population and results coming from a single colorectal unit. Confounding factors regarding technique of resection (e.g., open vs laparoscopic) and patient selection is another limitation of this study. Moreover, discriminating PPOI from postoperative nausea and vomiting might still be a problem, as always with studies regarding visceral surgery. Although all patients were stimulated for early postoperative feeding, postoperative care was not standardized by means of an enhanced recovery after surgery protocol. The impact of postoperative feeding, fluid management, and mobilization of the patient may play an important confounding role in the occurrence of PPOI and should be standardized. These issues are also reflected in the relatively long length of hospital stay in both groups. Despite these limitations, the risk factors associated with PPOI are significant and should be further investigated. Moreover, identification of risk factors is useful when therapeutic strategies aimed at prevention of PPOI are developed. Selection of high-risk patients who could benefit from potential treatment options in clinical trials is of paramount importance and warrants further research.

Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest.

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