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Excess hospital length of stay and extra cost attributable to primary prolonged postoperative ileus in open alimentary tract surgery: a multicenter cohort analysis in China

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Abstract

Background Prolonged postoperative ileus (PPOI) reportedly leads to compromised postoperative recovery and increased healthcare costs. However, the evidence for this claim was obtained from studies that included patients with both primary and secondary PPOI. How primary PPOI affects the hospital length of stay (LOS) and healthcare costs is not well documented. A multicenter cohort analysis was performed to investigate the potentially detrimental effect of primary PPOI on hospital LOS and healthcare costs.

Methods In total, 2083 patients who underwent open abdominal surgery from 22 tertiary hospitals in China were prospectively registered in a PPOI cohort. Of these, 1863 patients without secondary PPOI were analyzed. Poisson regression for hospital LOS and log-transformed linear regression for healthcare costs were performed to identify whether primary PPOI was an independent risk factor.

Results The incidence of primary PPOI was 13.2% (246/1863). The median LOS was significantly longer in the PPOI than non-PPOI group (12 vs. 11 days, $p < 0.001$). The median healthcare cost was significantly higher in the PPOI than non-PPOI group (70,672 vs. 67,597 CNY, $p = 0.016$). Multivariate Poisson regression and log-transformed linear regression showed that 12% of prolonged LOS and 4.6% of healthcare costs were due to primary PPOI.

Conclusions Primary PPOI is a potential source of prolonged hospital LOS and extra healthcare costs for patients undergoing open abdominal surgery. Cost-effective approaches are needed to manage and prevent primary PPOI.

Keywords Alimentary tract surgery, Hospital length of stay, Healthcare cost, Primary postoperative prolonged ileus

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Introduction

Patients who have undergone alimentary tract surgery often develop transient cessation of coordinated bowel motility, which is termed postoperative ileus (POI) (Vather et al. 2014). Generally, the POI lasts for 3 to 4 days until the occurrence of the first flatus or bowel movement. However, some patients endure prolonged POI (PPOI) without resolution for more than 4 days (Vather et al. 2013). PPOI is divided into primary and secondary PPOI according to whether precipitating complications are present (Quiroga-Centeno et al. 2020). Complications such as abdominal infection and anastomotic leakage are the most frequent etiologies of secondary PPOI. PPOI results in delayed enteral nutrition and prolonged parenteral nutrition, finally leading to compromised postoperative recovery. However, this non-life-threatening complication has not received adequate attention in the surgical community (Leede et al. 2018).

PPOI has been documented to cause increased healthcare costs (Asgeirsson et al. 2010; Mao et al. 2019; Iyer et al. 2009; Earnshaw et al. 2015; Seo et al. 2021; Tevis et al. 2015). Twenty years ago, the estimated economic burden attributed to POI in the USA healthcare system was US $1.5 billion annually (Delaney 2006). However, the studies from which these data were derived had several limitations. First, they involved retrospective collection of patients' data. The definition of PPOI or POI was retrieved through a coding system and was often inconsistent and confusing. Second, the studies did not distinguish primary PPOI from secondary PPOI. The postoperative complications that result in secondary PPOI increase the hospital length of stay (LOS) and cost. The economic burden of primary PPOI remains unclear. Third, these studies were conducted in single centers, and the participants were restricted to patients undergoing either colonic surgery (Earnshaw et al. 2015; Seo et al. 2021; Tevis et al. 2015) or gastrectomy. The absence of heterogeneous population and precise definition of PPOI prevents us from drawing robust conclusions for medical management decision-makers.

In the present study, we explored the hospital LOS and healthcare costs attributed to primary PPOI in patients who underwent open alimentary tract surgery.

This study (1) provides a comprehensive analysis from a multicenter cohort in China, offering a broader perspective on the impact of primary PPOI on hospital length of stay (LOS) and healthcare costs in open alimentary tract surgery. (2) It distinguishes between primary and secondary PPOI, shedding light on the specific impact of primary PPOI, which was previously confounded with secondary PPOI in economic evaluations. (3) With a large sample size and rigorous methodology, the study offers reliable data to inform medical management decisions and future research directions in the field of postoperative care.

Methods

Data source and study design

This was a retrospective cohort analysis of a registry PPOI dataset. The PPOI dataset was obtained from a prospective, multicenter, observational cohort study on the incidence of and risk factors for PPOI in patients undergoing major open abdominal surgery. In total, 2083 patients from 22 hospitals in different areas of China were registered in the dataset. The patients were consecutively admitted to the hospitals from 26 October 2016 to 5 November 2018. All patients underwent open major gastrointestinal surgery including gastric cancer surgery, colorectal cancer surgery, and pancreaticoduodenectomy. They were followed up after surgery until discharge from the hospitals. A consultant surgeon supervised the data collection at each center, ensuring that the data were collected in accordance with the established protocol. The final dataset was audited by an independent data validator.

This PPOI cohort study was approved by the Ethics Committee of Beijing Friendship Hospital (approval code: 2016-P2-064-01). The study was registered on the Chinese Clinical Trial Registry website (registry ID: ChiCTR-IOC-16009955) (http://www.chictr.org.cn/showproj.aspx?proj=16810).

The patients were divided into the PPOI group and non-PPOI group according to whether they had developed primary PPOI. The hospital LOS and healthcare costs were compared between the two groups.

Population inclusion and exclusion criteria

Inclusion criteria

Our study includes patients who are aged between 18 and 85 years and have undergone selective major open abdominal surgery, specifically colorectal resection, gastrectomy, or duodenopancreatectomy. A total of 2083 patients were prospectively registered in this cohort according to the inclusion criteria.

Exclusion criteria

The exclusion criteria were a lack of information on hospital LOS or healthcare cost in the medical record ($n=100$), lack of a PPOI diagnosis ($n=11$), and postoperative complications such as anastomotic leakage or abdominal infections that might result in secondary PPOI ($n=109$). Finally, 1863 patients were included in the analysis. Figure 1 shows a detailed flow chart to patient inclusion and exclusion.

Exposure variable and primary outcome

PPOI was the independent variable under investigation. The diagnostic criteria for PPOI used in this study followed the definition proposed by Auckland University, which was derived from a systematic review and global survey (Vather et al. 2013). PPOI was diagnosed if two or more of the following five criteria were met on or after day 4 postoperatively without prior resolution of POI: (1) nausea/vomiting over a 12-h period (nausea was measured using a numerical rating scale, with 1 indicating the least nausea and 10 indicating severe nausea; score of > 4 was positive); (2) inability to tolerate an oral diet for > 24 h or ingestion of a diet volume of < 25% of the normal volume during the past two meals; (3) the absence of flatus or stool for > 24 h or, if a stoma was created, absence of gas or stool in the ostomy bag; (4) abdominal distension, defined as an increased waist circumference and hollow sound through percussion; and (5) radiologic confirmation of a dilated, fluid-filled stomach or bowel by computed tomography or X-ray examination.

Hospital LOS and healthcare costs were the primary outcome. Hospital LOS was defined as the length of time from the day of surgery to the day of discharge. Healthcare cost, counted in CNY, was the total amount of money spent during the hospital stay for each patient, including cost of surgery and postoperative care.

Variables previously reported to be risk factors for PPOI, as well as those that influence hospital LOS and healthcare costs, were included as confounders (Quiroga-Centeno et al. 2020). Patient variables included age, sex, body mass index (BMI), and the American Society of Anesthesiologists (ASA) physical status classification. Surgery-related variables encompassed the National Nosocomial Infections Surveillance (NNIS) risk index, specific surgery name, surgical duration (minutes), blood

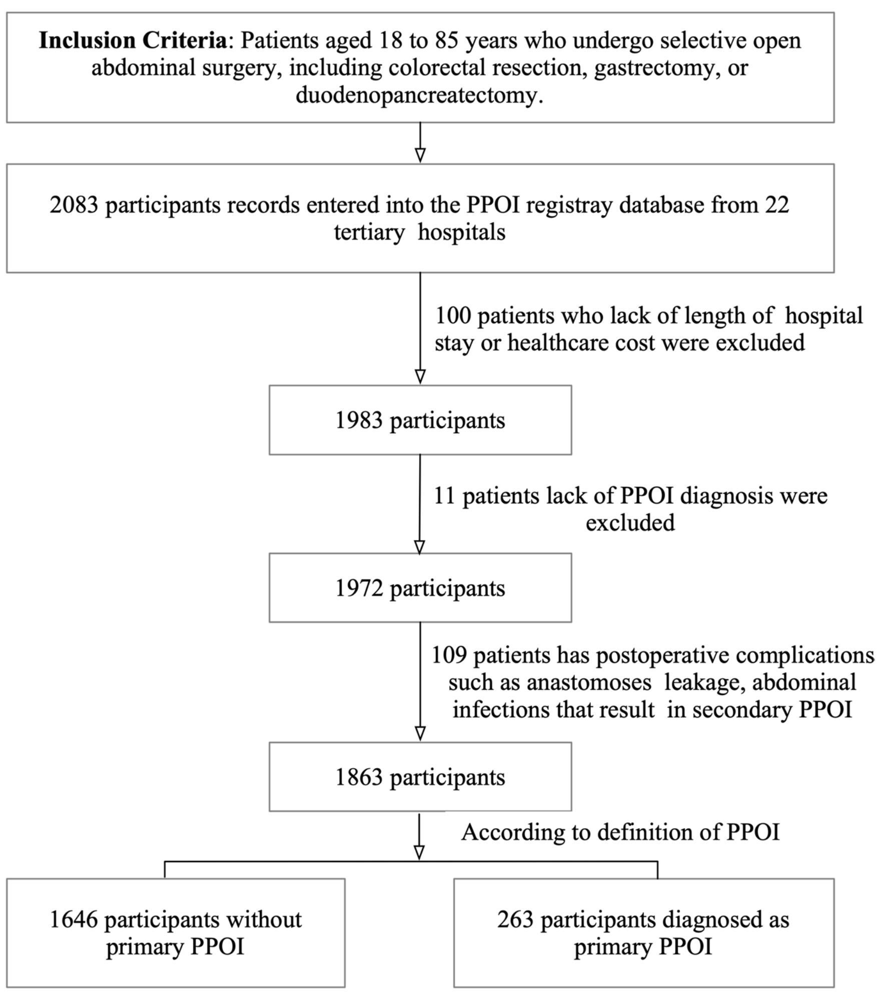

Fig. 1 Flow chart of study population selection. This flow diagram shows study population selection in PPOI cohort according to specific inclusion and exclusion criteria. Finally, 1863 primary patients with complete hospital length of stay and healthcare cost were included for analysis

loss during surgery, blood transfusion during and after surgery, and postoperative analgesic modalities.

Statistical analysis

There were > 10% missing values in some characteristics. The correlation analysis between complete and missing data showed balance, indicating that the data were missing completely at random. Multiple imputation was applied to impute the missing values for confounding characteristics.

The distribution of continuous data was assessed by the Shapiro–Wilk test. Normally distributed data are expressed as mean ± standard deviation and were compared using an independent-samples *t*-test. Non-normally distributed continuous data are expressed as median (interquartile range) and were compared using the Mann–Whitney *U*-test. Patient characteristics are presented as count (percentage) for categorical variables. The chi-square test or Fisher's exact test was used to compare categorical variables between the PPOI group and the non-PPOI group.

The hospital LOS and healthcare costs were left-skewed. A linear regression analysis was performed for log-transformed healthcare cost data, and Poisson regression analysis was used for hospital LOS (count data). Univariate and multivariate regressions were performed to examine whether PPOI had an independent effect on LOS and healthcare costs. Covariates such as surgery-related characteristics and patient status variables were entered into the regression model for adjustment. Effect estimates are presented as an incidence rate ratio (IRR) in Poisson regression and semi-elasticity (SE) in log-transformed linear regression. IRR/SE were calculated by regression coefficients using the following formula: IRR/SE = Exp^coefficient. Both IRR and SE mean the percent change in the outcome associated with unit change in the exposure.

The threshold of two-sided statistical significance was set at $p < 0.05$ a priori. All analyses were performed with SPSS 26.0 (IBM Corp., Armonk, NY, USA) and R 4.1.1 (http://www.R-project.org).

Results

Patients' demographic characteristics

Of the 1863 patients enrolled in this study, 246 developed primary PPOI during their hospital stay. The incidence of primary PPOI was 13.2% among patients who underwent open abdominal surgery. The times to first flatus (median 4 vs. 3 days, $p < 0.001$) and first bowel movement (median 5 vs. 4 days, $p < 0.001$) were significantly longer in the PPOI group than in the non-PPOI group (Table 1). A total of 71.5% of patients in the PPOI group received patient-controlled analgesia (PCA), which mainly consisted of opioid drugs, compared with 63.4% of patients in the non-PPOI group. The other surgery-related characteristics, such as the surgical organ, duration of surgery, and intraoperative blood transfusion, were comparable between the non-PPOI group and the PPOI group. The patient status-related characteristics, including age, sex, body mass index (BMI), and National Nosocomial Infections Surveillance (NNIS) score, were balanced between the two groups (Table 1). The median hospital LOS was 11.00 (9.00–14.00) days, and the median healthcare cost was 68,087 (58,304–81,703) CNY among all included patients.

The median hospital stay was significantly longer in the PPOI than non-PPOI group (12 vs. 11 days, $p < 0.001$). The median healthcare cost was significantly higher in the PPOI than non-PPOI group (70,672 vs. 67,597 CNY, $p = 0.016$).

Excess hospital LOS attributed to PPOI

Poisson regressions were used to identify the predictive factors for hospital LOS (Table 2). Age and BMI showed an IRR of 1.004 (95% *CI*, 1.003–1.005) and 1.009 (95% *CI*, 1.004–1.014) for prediction of the LOS, indicating that older age and higher BMI were risk factors for a longer LOS. Patients with an NNIS score of 2 and 3 tended to have a longer LOS than those with an NNIS score of 0 [*IRR*, 1.087 (95% *CI*, 1.002–1.178) and *IRR*, 1.134 (95% *CI*, 1.011–1.271)]. The other patient status-related characteristics, including sex, were not associated with LOS. The surgery-related characteristics prominently affected the LOS. Patients who underwent pancreaticoduodenal surgery had a significantly longer LOS than those who underwent gastric surgery [*IRR*, 1.184 (95% *CI*, 1.146–1.222)]. Blood transfusion after surgery was associated with a significantly increased LOS [*IRR*, 1.158 (95% *CI*, 1.106–1.214)]. Patients who received PCA consisting of an opioid drug had a longer LOS [*IRR*, 1.123 (95% *CI*, 1.089–1.158)]. The development of postoperative complications was another considerable factor that resulted in a longer LOS. More severe complications with higher Clavien–Dindo grades had higher IRRs for LOS. For complications, the *p* for trend was < 0.001.

Primary PPOI was a risk factor for prolonged LOS [*IRR*, 1.139 (95% *CI*, 1.099–1.182)] in the univariate Poisson regression. To control for all these confounders, multivariate Poisson regression analyses were performed to depict the contribution of PPOI on LOS. All significant factors in the univariate analysis were included in the multivariate analysis. Primary PPOI was an independent risk factor for prolonged LOS [*IRR*, 1.122 (95% *CI*, 1.081–1.165)]. It contributed to 12% of prolonged LOS in patients who underwent major abdominal surgery.

Table 1 Baseline characteristics of patients

	Overall	Data completion	Non-PPOI	PPOI	P
	N = 1863	*N*	*N = 1617*	*N = 246*	
Age, mean ± SD, year	61.4 ± 11.4	1834	61.3 ± 11.4	62.4 ± 11.8	0.164
Gender (%)		1863			0.452
Male	657 (35.3)		576 (35.6)	81 (32.9)	
Female	1206 (64.7)		1041 (64.4)	165 (67.1)	
BMI, mean ± SD, kg/m^2	23.2 ± 3.28	1654	23.2 ± 3.27	23.2 ± 3.33	0.718
NNIS (%)		1620			0.111
0	423 (26.1)		370 (26.3)	53 (24.7)	
1	776 (47.9)		659 (46.9)	117 (54.4)	
2	370 (22.8)		328 (23.3)	42 (19.5)	
3	51 (3.15)		48 (3.42)	3 (1.40)	
Surgery (%)		1848			0.148
Gastric	753 (40.7)		642 (40.0)	111 (45.7)	
Pancreas-duodenum	526 (28.5)		457 (28.5)	69 (28.4)	
Colorectal	569 (30.8)		506 (31.5)	63 (25.9)	
Incision length, mean ± SD, cm	17.0 ± 4.1	1677	16.9 + 4.2	17.7 + 3.5	0.002
Blood transfusion during surgery (%)		1747			0.067
No	1474 (84.4)		1289 (85.0)	185 (80.1)	
Yes	273 (15.6)		227 (15.0)	46 (19.9)	
Surgery duration, mean ± SD, min	220 ± 93.9	1839	220 ± 95.0	215 ± 86.6	0.361
PCA (%)		1862			0.015
No	662 (35.6)		592 (36.6)	70 (28.5)	
Yes	1200 (64.4)		1024 (63.4)	176 (71.5)	
Postoperative blood transfusion (%)		1833			0.920
No	1667 (90.9)		1446 (90.9)	221 (91.3)	
Yes	166 (9.06)		145 (9.11)	21 (8.68)	
Clavien-Dindo (%)		1863			0.072
No	1751 (93.99)		1525 (94.31)	226 (91.87)	
I	70 (3.76)		60 (3.71)	10 (4.07)	
II	28 (1.50)		23 (1.42)	5 (2.03)	
III	9 (0.48)		5 (0.31)	4 (1.62)	
IV	5 (0.27)		4 (0.25)	1 (0.41)	
Time to first flatus, (median [IQR]), days	3.00 [2.00, 4.00]	1650	3.00 [2.00, 4.00]	4.00 [3.00, 5.00]	< 0.001
Time to first bowel movement, (median [IQR]), days	4.00 [3.00, 6.00]	1641	4.00 [3.00, 6.00]	5.00 [3.00, 7.00]	< 0.001
Healthcare cost, (median [IQR]), CNY	68,087 [58,304, 81,703]	1731	67,597 [57,532, 81,511]	70,672 [60,814, 82,964]	0.016
Length of hospital stay, (median [IQR]), days	11.0 [9.00, 14.0]	1848	11.0 [9.00, 14.0]	12.0 [10.0, 16.0]	< 0.001

PPOI prolonged postoperative ileus, *ASA* American Society of Anesthesiology, *NNIS* National Nosocomial Infections Surveillance, *PCA* patient-controlled analgesia

Extra healthcare cost due to PPOI

Linear regression for log-transformed healthcare cost was performed to identify the factors that affected healthcare cost (Table 3). Patients' age and NNIS scores were predictors of healthcare cost in the multivariate regression [*SE*, 1.003 (95% CI, 1.001–1.004) and *SE*, 1.209 (95% *CI*, 1.119–1.306), respectively]. The surgery-related characteristics were also significant predictive factors for healthcare costs. Compared with gastric surgery, pancreaticoduodenal surgery was higher in cost [*SE*, 1.034 (95% *CI*, 1.001–1.069)], and colorectal surgery was lower in cost [*SE* 0.918 (95% *CI*, 0.89–0.947)]. Blood transfusion either during or after surgery was significantly associated with increased expense [*SE*, 1.110 (95% *CI*, 1.068–1.154) and *SE*, 1.121 (95% *CI*, 1.068–1.175), respectively]. Patients who received PCA consisting of an opioid drug also had higher healthcare costs [*SE*, 1.084 (95% *CI*, 1.046–1.124)]. As expected, postoperative complications were also prominent

Table 2 Poisson regression for hospital length of stay

			Univariate		Multivariate	
	Length of stays, days Median [p25, p75]		IRR (95% CI)	*p*	IRR (95% CI)	*p*
Age, per year	11 [9, 14]		1.004 (1.003–1.005)	< 0.001	1.004 (1.003–1.005)	< 0.001
Sex						
Female	11 [9, 15]					
Male	11 [9, 14]		0.995 (0.969–1.022)	0.711		
BMI, per kg/m^2	11 [9, 14]		1.006 (1.001–1.011)	0.015	1.009 (1.004–1.014)	< 0.001
NNIS						
0	11 [9, 14]					
1	11 [9, 14]		0.967 (0.924–1.013)	0.147	1.007 (0.962–1.054)	0.757
2	12 [9, 15]		1.062 (1.007–1.12)	0.029	1.087 (1.002–1.178)	0.045
3	13 [9, 18]		1.167 (1.006–1.353)	0.044	1.134 (1.011–1.271)	0.034
Surgery						
Gastric	11 [9, 13]					
Pancreas-duodenum	13 [10, 18]		1.25 (1.214–1.288)	< 0.001	1.184 (1.146–1.222)	< 0.001
Colorectal	10 [8, 13]		0.983 (0.953–1.013)	0.265	1.02 (0.988–1.053)	0.229
Incision length, per cm	11 [9, 14]		1.000 (0.996–1.005)	0.834		
Blood transfusion during surgery						
No	11 [9, 14]	Ref.				
Yes	12 [10, 17]	1.161 (1.109–1.215)		< 0.001	1.031 (0.974–1.091)	0.270
Surgery duration, per min	11 [9, 14]	1.001 (1.001–1.001)		< 0.001	1.001 (1.001–1.001)	< 0.001
PCA						
No	10 [8, 13]					
Yes	11 [9, 15]	1.151 (1.119–1.183)		< 0.001	1.123 (1.089–1.158)	< 0.001
Postoperative blood transfusion						
No	11 [9, 14]	Ref.				
Yes	12 [10, 18]	1.256 (1.204–1.31)		< 0.001	1.158 (1.106–1.214)	< 0.001
PPOI						
No	11 [9, 14]					
Yes	12 [10, 16]	1.139 (1.099–1.182)		< 0.001	1.122 (1.081–1.165)	< 0.001
Clavien-Dindo						
No	11 [9, 14]					
I	14 [11, 21]	1.444 (1.365–1.528)		< 0.001	1.375 (1.296–1.459)	< 0.001
II	17 [10, 22]	1.355 (1.239–1.482)		< 0.001	1.307 (1.191–1.433)	< 0.001
III	33 [19, 38]	2.262 (2.003–2.555)		< 0.001	1.879 (1.65–2.14)	< 0.001
IV	10 [8, 12]	0.867 (0.667–1.127)		0.286	0.799 (0.614–1.041)	0.096

PPOI prolonged postoperative ileus, *ASA* American Society of Anesthesiology, *NNIS* National Nosocomial Infections Surveillance, *PCA* patient-controlled analgesia, *IRR* incidence rate ratio

factors that increased healthcare costs, but they did not reach statistical significance.

After adjusting for all these significant characteristics in the univariate analysis, primary PPOI was an independent risk factor for increased healthcare cost [*SE*, 1.046 (95% *CI*, 1.007–1.088)]. However, 4.6% of healthcare costs were due to primary PPOI.

Discussion

Our study cohort comprising a large sample of patients with prospectively diagnosed PPOI showed that primary PPOI was an independent risk factor for prolonged LOS and extra healthcare cost. Patients with primary PPOI spent 12% (1.34 days) more days hospitalized and 4.6% (3115 CNY) more CNY than those without primary PPOI. The economic burden attributed to primary PPOI in the present study was not as prominent as that in previous reports about PPOI.

Table 3 Linear regression for log-transformed healthcare costs

	Healthcare cost, CNY	Univariate analysis		Multivariate analysis	
	Median [p25, p75]	**SE/95% CI**	***p***	**SE/95% CI**	***P***
Age, per year	68,100 [58,303, 81,861]	1.002 (1.001–1.003)	< 0.001	1.003 (1.001, 1.004)	< 0.001
Sex (%)					
Female	66,773 [57,186, 80,358]				
Male	69,410 [58,932, 83,120]	1.033 (1.003–1.063)	0.029	1.011 (0.984–1.038)	0.422
BMI, per kg/m^2	68,100 [58,303, 81,861]	1 (0.996–1.005)	0.861		
NNIS					
0	67,342 [56,940, 82,308]			Ref	
1	67,529 [57,660, 78,717]	1.008 (0.972–1.046)	0.670	1.011 (0.974–1.043)	0.635
2	69,453 [59,777, 83,101]	1.046 (1.004–1.09)	0.032	1.025 (0.976–1.067)	0.364
3	88,430 [74,142, 101,760]	1.234 (1.132–1.344)	< .01	1.209 (1.119–1.306)	< 0.001
Surgery (%)					
Gastric	69,799 [60,086, 82,511]				
Pancreas-duodenum	72,225 [63,055, 89,682]	1.068 (1.033–1.105)	0.001	1.034 (1.001–1.069)	0.044
Colorectal	62,427 [52,592, 74,146]	0.901 (0.872–0.932)	< 0.001	0.918 (0.89–0.947)	< 0.001
Incision length, per cm	68,100 [58,303, 81,861]	0.999 (0.995–1.003)	0.503		
Blood transfusion during surgery					
No	67,010 [57,217, 79,541]				
Yes	77,718 [66,826, 93,925]	1.19 (1.145–1.236)	< 0.001	1.11 (1.068–1.154)	< 0.001
Surgery duration, per min	68,100 [58,303, 81,861]	1.001 (1.001–1.001)	< 0.001	1.001 (1.001–1.001)	< 0.001
PCA					
No	64,905 [55,376, 76,409]				
Yes	70,627 [59,984, 83,992]	1.086 (1.048–1.125)	< 0.001	1.084 (1.046–1.124)	< 0.001
Postoperative blood transfusion					
No	67,641 [57,806, 80,378]				
Yes	80,256 [64,590, 94,064]	1.179 (1.121–1.239)	< 0.001	1.121 (1.068–1.175)	< 0.001
PPOI					
No	67,719 [57,669, 81,979]				
Yes	70,853 [60,875, 83,612]	1.055 (1.011–1.101)	0.013	1.046 (1.007–1.088)	0.022
Clavien-Dindo					
No	68,000 [58,386, 81,384]				
I	69,010 [55,821, 90,683]	1.021 (0.951–1.097)	0.561	0.977 (0.914–1.044)	0.495
II	90,788 [67,850, 110,958]	1.254 (1.121–1.403)	< 0.001	1.171 (1.056–1.298)	0.003
III	93,517 [85,884, 107,537]	1.138 (0.935–1.385)	0.197	1.012 (0.835–1.198)	0.899
IV	85,032 [68,596, 99,427]	1.229 (0.945–1.598)	0.124	1.178 (0.921–1.477)	0.202

PPOI prolonged postoperative ileus, *ASA* American Society of Anesthesiology, *NNIS* National Nosocomial Infections Surveillance, *PCA* patient-controlled analgesia, *SE* semi-elasticity, US \$1 = 6.77 CNY (2023.01.08)

A retrospective study showed that 20 years ago, coded PPOI was associated with a nearly 99% higher cost than non-coded PPOI in patients who underwent abdominal surgery (Goldstein et al. 2007). The authors retrospectively retrieved data on patients with PPOI according to the International Classification of Diseases coding system. The main inclusion criterion was a diagnosis of paralytic ileus or digestive complications, not elsewhere classified (Goldstein et al. 2007). Another single-institution study on the economic outcome of PPOI in patients who underwent elective colorectal surgery showed that PPOI increased healthcare expenditures by 71% (Mao et al. 2019). Although PPOI was prospectively diagnosed in that study, the authors did not distinguish primary PPOI from secondary PPOI. Some cases of PPOI secondary to anastomotic leakage or abdominal infection might have been counted. The inclusion criteria in our study differ from these two reports. A prospective diagnosis of PPOI was required to eliminate retrospective bias, and patients with PPOI secondary to other complications were excluded to control confounding of postoperative complications. We focused on the economic burden of primary PPOI; secondary PPOI was resolved through management of precipitating conditions. Our results indicate that primary PPOI can increase the LOS and expenditures, but not to a substantial extent.

The development of postoperative complications was the factor that most strongly predicted higher healthcare costs and longer LOS in this study. More severe complications according to the Clavien–Dindo grading system were associated with a longer LOS. This predictive value persisted after adjusting for other confounding factors. The healthcare cost was also proportional to the severity of complications, but without statistical significance. This might have been due to the small number of patients who developed postoperative complications (Table 1). Taking scientific measures to reduce the incidence of postoperative complications would considerably mitigate the economic burden. PPOI secondary to anastomotic leakage or abdominal infection could be addressed through management of the original complication. However, different measures are needed to prevent primary PPOI.

In our study, patients who received PCA had higher healthcare costs and a more prolonged LOS. PCA was a significant risk factor for an increased economic burden. This is mainly due to the inhibitory effect on bowel propulsion by the opioid analgesic drug. Activation of μ-opioid receptors in the gastrointestinal tract inhibits gut motility (Kurz and Sessler 2012). Our data also show a positive correlation between PCA and the incidence of PPOI. PCA was received by 71.5% of patients in the PPOI group but by only 63.4% of those in the non-PPOI group. Inhibition of peripheral μ-opioid receptors by alvimopan can significantly enhance gastrointestinal recovery and result in a shorter LOS and reduction of healthcare cost (Bell et al. 2009). The use of alternative analgesics to reduce opioid consumption or an antagonist that blocks opioid receptors in the gut may help to reduce the rate of primary PPOI.

Primary PPOI is a complication related to greater consumption of healthcare resources, and more action must be taken to reduce its prevalence. Enhanced recovery after surgery (ERAS) is a new paradigm of perioperative care that has been proven to accelerate postoperative recovery. Patients who are managed using the ERAS protocol have a significantly shortened time to first flatus and bowel movement than patients managed using traditional protocols (Grass et al. 2017; Boitano et al. 2018). Laparoscopic surgery with minimal tissue trauma is hypothesized to lead to faster bowel function recovery. Studies comparing laparoscopic and open procedures have shown a shorter LOS and faster return to activity after laparoscopic surgery (Moghadamyeghaneh et al. 2016; Takada et al. 2003). Our previous study showed that the minimal incision length used in laparoscopic procedures independently contributed to faster recovery of bowel motility (Song et al. 2021). Unfortunately, our cohort patients are lacking the ERAS information for evaluation.

This study has two main limitations that should be considered. First, this retrospective study had > 10% missing values for some characteristics. However, multiple imputation was applied to eliminate selection bias due to missing values. Second, the estimated economic burdens in our study were based on the Chinese medical payment system, which differs from the systems used in other countries. Thus, our results should be interpreted with caution in countries that do not use the Chinese medical payment system. Third, key variables such as comorbidity, surgeon experience, and any preoperative medication use that might affect postoperation bowel function were not included.

Despite these limitations, the credibility of our findings is bolstered by the large, multicenter cohort and the precise definition of primary PPOI utilized in this study. Our comprehensive analysis, grounded in prospectively collected data and rigorous statistical methods, provides valuable insights into the economic implications of primary PPOI. The results have implications for healthcare policy and clinical practice, potentially influencing the development of strategies to reduce the incidence of primary PPOI and associated costs.

In conclusion, primary PPOI is a potential source of prolonged hospital LOS and extra healthcare costs for patients undergoing open abdominal surgery. Further research regarding risk factors for primary PPOI and cost-effective intervention is needed to mitigate the economic burden for these patients.

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Authors' contributions
SJN write the manuscript. GWX, JG, YYM, CL, and WY collect the patients data. YYC and ZZT supervise the progress of the project. All authors reviewed the manuscript.

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Data availability
Contact the first author for primary data if necessary.

Declarations

Ethics approval and consent to participate
This PPOI cohort study was approved by the Ethics Committee of Beijing Friendship Hospital (approval code: 2016-P2-064-01). The study was registered on the Chinese Clinical Trial Registry website (registry ID: ChiCTR-IOC-16009955) (http://www.chictr.org.cn/showproj.aspx?proj=16810).

Consent for publication
It has been confirmed all authors agreed to submit the article.

Competing interests
The authors declare no competing interests.

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