Association between flurbiprofen axetil use and operative complications occurring following colorectal surgery

WEISI DING[1], KAI SHEN[2], WENHUI REN[3], XUE TIAN[1] and YI FENG[1]

[1]Department of Anesthesiology, Peking University People's Hospital, Beijing 100044, P.R. China;
[2]Department of Gastroenterology Surgery, Peking University People's Hospital, Beijing 100044, P.R. China;
[3]Department of Clinical Epidemiology and Biostatistics, Peking University People's Hospital, Beijing 100044, P.R. China

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Abstract. The aim of the present study was to investigate the association between the perioperative use of flurbiprofen axetil and the incidence of intestinal complications in patients undergoing radical colorectal surgery. For this purpose, the present retrospective study collected the medical records of patients who underwent their first radical colorectal surgery at Peking University People's Hospital (Beijing, China) between January 2018 and March 2022. Data included patient demographics, surgical details, intraoperative drug administration and postoperative intestinal complications. Univariate and multivariate analyses were performed to identify the risk factors for intestinal complications. A total of 1,364 patients were analyzed, of whom 89 (6.5%) developed postoperative intestinal complications, including ileus (45 patients, 3.3%), anastomotic leakage (40 patients, 2.9%) and celiac fistula (9 patients, 0.7%). In total, 5 patients experienced two types of intestinal complications. Age [odds ratio (OR), 1.022; 95% confidence interval (CI), 1.002-1.042; P=0.028], perioperative use of flurbiprofen axetil (OR, 2.072; 95% CI, 1.223-3.508; P=0.007), duration of surgery >3 h (OR, 2.032; 95% CI, 1.181-3.496; P=0.010) and intraoperative consumption of opioids (OR, 1.012; 95% CI, 1.003-1.022; P=0.009) were independent risk factors for postoperative intestinal complications. Overall, the present study demonstrates that age, the perioperative use of flurbiprofen axetil, the duration of surgery >3 h and high intraoperative consumption of opioids may increase the risk of developing postoperative intestinal complications in patients undergoing radical colorectal surgery.

Correspondence to: Professor Yi Feng or Dr Xue Tian, Department of Anesthesiology, Peking University People's Hospital, 11 Xizhimen South Street, Xicheng, Beijing 100044, P.R. China
E-mail: doctor_yifeng@sina.com
E-mail: justine_troy@163.com

Abbreviations: AL, anastomotic leakage; NSAID, non-steroid anti-inflammatory drug; COX, cyclooxygenase; ASA, American Society of Anesthesiologists; ICU, Intensive Care Unit; Hb, hemoglobin; OR, odds ratio; CI, confidence interval

Key words: flurbiprofen axetil, intestinal complications, colorectal cancer, retrospective study, NSAID

Introduction

Colorectal cancer is a leading cause of mortality worldwide, the third most common cancer and the second leading cause of cancer-associated mortality, with increasing rates of morbidity and mortality in recent years (1,2). In 2025 cancer statistics, colorectal cancer accounted for almost one-half (48%) of all cancer cases in men. For women, colorectal cancer accounts for 51% of all new diagnoses (3). Postoperative intestinal complications are critical determinants of patient prognosis. Among these complications, anastomotic leakage (AL) is considered the most severe due to its association with increased morbidity and mortality rates, adverse effects on both functional and oncological outcomes, and substantial strain on healthcare resources (4).

Systemic opioid analgesics have long been used to manage severe trauma-related pain; however, their use is associated with significant risks, including respiratory depression, opioid use disorder and potentially fatal overdose (5,6). The higher the dose and the longer the duration of opioid use, the greater the risk of developing both physical and psychological dependence. In recent years, multimodal analgesia has been increasingly advocated for various types of surgery, including gastrointestinal procedures (7). To minimize opioid consumption and its associated adverse effects, multimodal analgesia incorporates alternative analgesic strategies, such as non-steroidal anti-inflammatory drugs (NSAIDs), regional nerve blocks and other adjuncts.

NSAIDs are recommended for the management of perioperative pain in a variety of surgical procedures, including colorectal surgery, to reduce the perioperative use of opioid use and accelerate postoperative recovery (8,9). However, the use of high doses of NSAIDs has been linked to an elevated risk of developing intestinal complications, rendering their use in colorectal cancer surgery a subject of ongoing debate (10,11). Notably, a large study reported that diclofenac treatment could increase the incidence of AL following colorectal surgery (12).

Flurbiprofen axetil, a non-selective cyclooxygenase (COX) inhibitor, is commonly used in clinical practice as an antipyretic and analgesic (13). When combined with oxycodone

in patient-controlled intravenous analgesia, flurbiprofen axetil effectively reduces pain intensity, particularly visceral pain, and may help counteract the immunosuppressive state during the radical resection of colorectal cancer (14). However, despite its widespread use, the association between flurbiprofen axetil and intestinal complications remains poorly understood. The present study thus aimed to investigate the association between the perioperative use of flurbiprofen axetil and the incidence of intestinal complications following colorectal surgery through a retrospective analysis.

Materials and methods

Ethical considerations. This single-center retrospective study was conducted at Peking University People's Hospital (Beijing, China) on data retrieved from patients who underwent their first radical colorectal surgery between January 1, 2018, and March 31, 2022. The study was performed in accordance with the principles of the Declaration of Helsinki and ethical approval was obtained from the Medical Ethics Committee of Peking University People's Hospital (approval no. 2022PHB131-001).

Inclusion and exclusion criteria. Patients aged ≥18 years who underwent elective radical colorectal resection were included in the present study. Inclusion criteria required an American Society of Anesthesiologists (ASA) grade (15) of I to III and the performance of radical colorectal surgery. Exclusion criteria included patients who underwent a second surgery or more during the same hospital admission, those admitted to the Intensive Care Unit (ICU) prior to surgery, those with missing or incomplete prognostic records and those who received intraspinal analgesia due to concerns about interference with the administration of flurbiprofen axetil. In addition, patients with severe liver, kidney and coagulation dysfunction, for which the use of flurbiprofen axetil is prohibited, were excluded from the study.

Patient characteristics. Comprehensive patient data were collected, including age, sex, body mass index, ASA classification and medical history (for example, hypertension, diabetes, coronary heart disease, and pulmonary, hepatic, renal, immune and coagulation disorders). Additionally, medication history, such as use of antiplatelet or anticoagulant therapy, preoperative chemotherapy, anti-hypertensive drugs and steroid hormones, was documented. Laboratory evaluations included the assessments of preoperative albumin levels, hemoglobin (Hb) levels and sodium levels, which were recorded from the last preoperative laboratory report prior to surgery. The cut-off point of the Hb level was defined as Hb <80 g/l, which was the criterion for blood transfusion in the operating room.

In addition to the patient characteristics, detailed data on surgical and anesthetic procedures were collected. These data included the duration of surgery, the use of laparoscopy, regional block techniques, intraoperative fluid infusion volume, blood loss, blood transfusion, the use of vasopressor agents, the administration of flurbiprofen axetil, the intraoperative consumption of opioids, the maximum diameter of the tumor, the presence of lymph node metastasis, detection of an intravascular tumor thrombus and postoperative transfer to the ward or ICU.

Anesthetic procedure. All patients received general anesthesia, induced with intravenous propofol (1.5 to 2.5 mg/kg), sufentanil (0.3 μg/kg) and rocuronium (0.6 mg/kg). Anesthesia was maintained with the inhalation of sevoflurane or desflurane, supplemented with the continuous infusion of propofol (100-300 μg/kg/min) and remifentanil (0.05-0.2 μg/kg/min) to maintain a bispectral index between 40 and 60. Flurbiprofen axetil was the only NSAID used during the perioperative period, with its use determined by the attending anesthesiologist and surgeon. Postoperatively, the patients were extubated in the Post-Anesthesia Care Unit or Operating Room or transferred to the ICU with endotracheal intubation, if necessary. Extubation criteria included the recovery of consciousness, respiratory and circulatory stability, muscle strength, and patients would then be returned to the ward. Postoperative analgesia was managed (patient-controlled analgesia) with opioids (sufentanil patient-controlled analgesia) (3 μg each, with locking time 15 min).

Vasopressor agents such as phenylephrine (with a dose of 50 μg) were used empirically during surgery by the anesthesiologist, based on the initial and intraoperative blood pressure of the patient. Between the flurbiprofen axetil group (FBP) group and non-flurbiprofen axetil group (N-FBP), there was no significant difference in the proportion of colon/rectal surgeries (P=0.601) or anastomosis method (data not shown). Surgeons determined whether to use the end-to-end or end-to-side anastomosis method based on surgical site, with both groups operated on by the same surgical team, eliminating potential operator bias.

Outcomes. The primary outcome was the incidence of postoperative intestinal complications within 30 days of surgery. These complications included AL, ileus and celiac fistula. AL was defined according to a modified Reisinger criterion, which includes the extraluminal presence of contrast fluid, leakage with evidence of bowel content extravasation, intraabdominal collection, or gas on contrast-enhanced CT scan or radiographic enema, upon re-laparotomy or during endoscopy, requiring reintervention or treatment (16).

Ileus was defined as bowel occlusion or paralysis preventing the forward passage of intestinal contents, leading to accumulation proximal to the blockage site. The diagnosis was determined by gastrointestinal surgeons in combination with imaging examinations and clinical symptoms, which included bloating, cramps and the retention of stool and flatus (17). Chylous ascites was defined as the non-infectious extravasation of milky or creamy peritoneal fluid in the drain tubes at a volume of ≥200 ml/day and a triglyceride level ≥110 mg/dl (18,19). All complications were diagnosed by gastrointestinal surgeons through the comprehensive evaluation of clinical symptoms, CT scans and other imaging techniques.

Statistical analyses. Statistical analyses were performed using SPSS 26.0 software (IBM Corp.). Continuous variables are presented as the median (interquartile range) and compared using non-parametric tests, specifically the Mann-Whitney U test. Categorical variables are expressed as percentages and analyzed using the χ^2 test or Fisher's exact test. In the present study, the subjects were divided into the FBP group and N-FBP group. Univariable analysis was performed for the initial

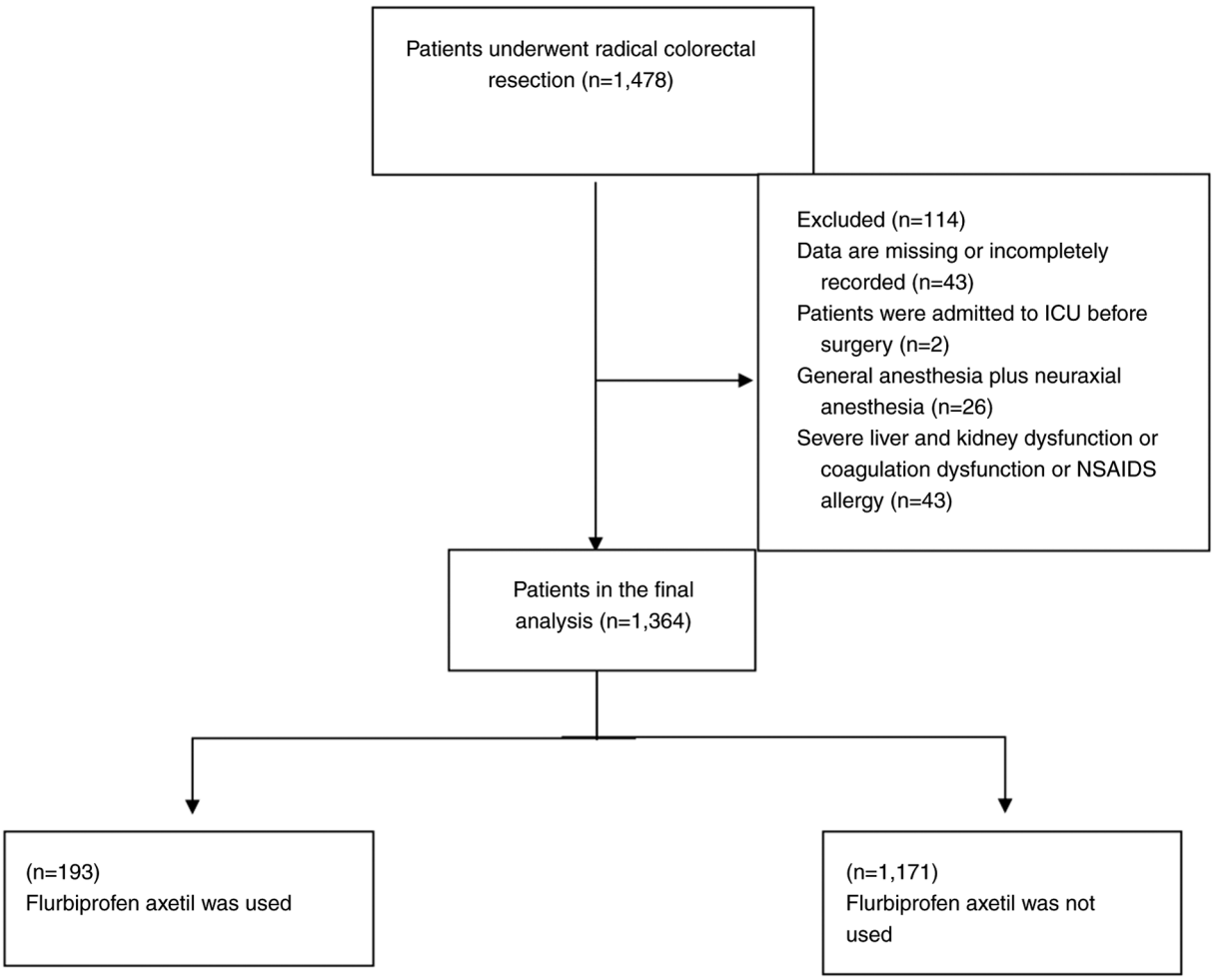

Figure 1. Process of data filtering used in the present study. ICU, Intensive Care Unit; NSAID, non-steroid anti-inflammatory drug.

screening of risk factors. Factors with P<0.1 in the univariable analysis and factors associated with outcomes in clinical experience were included in the multivariable analysis. The results are reported as odds ratios (ORs) with 95% confidence intervals (CIs). P<0.05 was considered to indicate a statistically significant difference.

Results

Patient demographic and baseline characteristics. A total of 1,478 patients were included in the study. According to the screening criteria, 114 patients were excluded, including 43 patients with incomplete records, 2 patients who were admitted to the ICU before the operation, 26 patients who received general anesthesia combined with epidural anesthesia, and 43 patients with severe liver, kidney function or coagulation dysfunction. Finally, a total of 1,364 patients were enrolled, comprising 804 men and 560 women (Fig. 1). The patients were divided into two groups as follows: The FBP group, consisting of 193 patients (14.1%) who received flurbiprofen axetil perioperatively, and the N-FBP group, which included 1,171 patients (85.9%) who did not receive the drug. Among the 193 patients in the FBP group, 112 (58.0%) received flurbiprofen axetil intraoperatively, 68 (35.2%) received it postoperatively, and 13 (6.7%) were administered the drug during both the intraoperative and postoperative periods. The administered dose of flurbiprofen axetil was typically 50-100 mg during surgery and/or 50 mg twice daily postoperatively. A comparison of the baseline characteristics of the patients revealed no statistically significant differences between the FBP and N-FBP groups, apart from the difference in surgical method (P=0.007) (Table I).

Intestinal complications. Postoperative intestinal complications were observed in 89 patients, accounting for 6.5% of the study population. These complications included ileus (45 patients; 3.3%), AL (40 patients; 2.9%) and celiac fistula (9 patients; 0.7%) (Table II).

Ileus. Ileus was identified in 45 patients (3.3% of the study population), including 10 patients (5.2%) in the FBP group and 35 patients (3.0%) in the N-FBP group.

AL. AL was observed in 40 patients (2.9% of the study cohort), with 11 patients in the FBP group (5.7%) and 29 patients (2.5%) in the N-FBP group.

Celiac fistula. A total of 9 patients (0.7%) developed celiac fistula, and none of them had received flurbiprofen axetil during or following surgery.

Table I. Comparison of patient demographics and intraoperative findings between groups.

Patient data	FBP (n=193)	N-FBP (n=1,171)	P-value
Patient characteristics			
Age, years[a]	66 (57-76)	66 (58-74)	0.972
Male, n (%)	112 (58.0)	692 (59.1)	0.781
BMI, n (%)			0.188
>28 kg/m^2	27 (14.0)	126 (10.8)	
≤28 kg/m^2	166 (86.0)	1,045 (89.2)	
ASA classification, n (%)			0.618
Grade III	47 (24.4)	305 (26.0)	
Less than grade III	146 (75.6)	866 (74.0)	
Previous history, n (%)			
Hypertension	77 (39.9)	476 (40.6)	0.844
Diabetes	45 (23.3)	230 (19.6)	0.238
Coronary heart disease	24 (12.4)	131 (11.2)	0.613
Chronic lung disease	4 (2.1)	18 (1.5)	0.811
Two or more comorbidities	36 (18.7)	210 (17.9)	0.810
Albumin[a]	38.8 (36.2-41.6)	39.2 (36.7-41.5)	0.704
Hb<80 g/l	4 (2.1)	32 (2.7)	0.596
Na^{+}[a]	141.2 (139.4-143)	141.4 (139.7-143)	0.447
Preoperative medication, n (%)			
Antiplatelet or anticoagulant therapy	24 (12.4)	149 (12.7)	0.911
Chemotherapy	27 (14.0)	175 (14.9)	0.729
ACEIs/ARBs	20 (10.4)	171 (14.6)	0.116
Statins	22 (11.4)	134 (11.4)	0.986
Other antihypertensive drugs	49 (25.4)	377 (32.2)	0.059
Diuretics	5 (2.6)	35 (3.0)	0.761
Steroid hormones	18 (9.3)	90 (7.7)	0.434
Surgery and anesthesia			
Duration, n (%)			0.506
>3 h	122 (63.2)	769 (65.7)	
≤3 h	71 (36.8)	402 (34.3)	
Surgical method, n (%)			0.007
Laparoscopy	143 (74.1)	964 (82.3)	
Open abdomen	50 (25.9)	207 (17.7)	
Intraoperative use of vasopressors, n (%)	137 (71.0)	786 (67.1)	0.288
Intraoperative blood transfusion, n (%)	20 (10.4)	87 (7.4)	0.160
Intraoperative fluid infusion volume[a]	2.6 (2.1-3.4)	2.6 (2.1-3.1)	0.600
Intraoperative blood loss, n (%)			0.090
<100 ml	102 (52.8)	695 (59.4)	
≥100 ml	91 (47.2)	476 (40.7)	
Use regional block, n (%)	30 (15.5)	173 (14.8)	0.781
Postoperative return, n (%)			0.380
The ward	140 (72.5)	885 (75.6)	
ICU	53 (27.5)	287 (24.5)	
Lymph node metastasis, n (%)	52 (26.9)	355 (30.3)	0.343
Tumor emboli in blood vessels, n (%)	35 (18.1)	200 (17.1)	0.719
Maximum diameter of tumor, n (%)			0.181
<5 cm	117 (60.6)	768 (65.6)	
≥5 cm	76 (39.4)	403 (34.4)	
Intraoperative opioid consumption[a]	35 (30-40)	35 (30-45)	0.143

[a]Median (25th percentile-75th percentile). FBP, flurbiprofen axetil; BMI, body mass index; ASA, American Society of Anesthesiologists; ICU, Intensive Care Unit; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin-receptor blocker; Na^{+}, sodium; Hb, hemoglobin.

Table II. Postoperative intestinal-related complications.

Postoperative complications	Total, n (%)	FBP, n (%)	N-FBP, n (%)
Ileus	45 (3.3)	10 (5.2)	35 (3.0)
AL	40 (2.9)	11 (5.7)	29 (2.5)
Celiac fistula	9 (0.7)	0 (0.0)	9 (0.8)

FBP, flurbiprofen axetil; AL, anastomotic leak.

Univariate analysis identified several relevant factors, including age (P=0.030), male sex (P=0.033), preoperative use of steroid hormones (P=0.016), perioperative use of flurbiprofen axetil (P=0.008), duration of surgery >3 h (P=0.003), intraoperative use of vasopressors (P=0.040), and intraoperative opioid consumption (P=0.038). Based on the results, a multivariate analysis was then performed. Logistic regression was mainly used in multivariate analysis; it identified age (OR, 1.022; 95% CI, 1.002-1.042; P=0.028), perioperative use of flurbiprofen axetil (OR, 2.072; 95% CI, 1.223-3.508; P=0.007), duration of the surgery >3 h (OR, 2.032; 95% CI, 1.181-3.496; P=0.010) and intraoperative consumption of opioids (OR, 1.012; 95% CI, 1.003-1.022; P=0.009) as significant risk factors for the development of postoperative intestinal complications (Table III).

Discussion

In the present study, all four statistically significant factors exhibited an OR >1, indicating that an advanced age, perioperative flurbiprofen axetil use, a prolonged duration of surgery and increased opioid consumption were identified as potential risk factors for postoperative intestinal complications. The present study investigated the incidence of intestinal complications, including AL, ileus and chylous fistula, which affect the prognosis of patients undergoing colorectal surgery. These findings revealed that age (P=0.028), the perioperative use of flurbiprofen axetil (P=0.007), duration of the surgery >3 h (P=0.010) and intraoperative opioid consumption (P=0.009) are significant risk factors for the development of these complications. Among these, the perioperative use of flurbiprofen axetil is an influencing factor that has not been previously mentioned, at least to the best of our knowledge.

NSAIDs are among the most widely used medications globally, both via prescription and over-the-counter, for treating fever, acute or chronic pain, and inflammatory conditions such as rheumatic diseases. It is estimated that >30 million individuals use NSAIDs daily (20). These drugs inhibit COXs, key enzymes involved in the synthesis of prostaglandins from arachidonic acid. Traditional NSAIDs inhibit both COX-1 and COX-2 isoforms, while selective NSAIDs primarily inhibit COX-2, and low-dose aspirin specifically inhibits COX-1 (21).

In colorectal surgery, NSAIDs are often utilized for their opioid-sparing effects. Numerous epidemiological studies have demonstrated that the long-term use of NSAIDs is associated with a significant reduction in cancer incidence and can delay the progression of malignant disease. Additionally, NSAID use has been linked to a reduced risk of cancer-related mortality and distant metastasis (22,23). As a non-selective COX inhibitor, flurbiprofen axetil is commonly used in postoperative analgesia. However, studies on the impact of NSAIDs on bowel function recovery have indicated that these drugs may not be entirely safe for patients undergoing radical colorectal surgery (24-26). Specifically, the early postoperative use of NSAIDs has been significantly associated with AL in patients undergoing colorectal cancer surgery at high-volume tertiary care centers (27). Similar findings have been reported in a meta-analysis (28). Another study examined the prophylactic use of flurbiprofen to prevent mesenteric traction syndrome during abdominal surgery. It reported an increased risk of postoperative leakage or bleeding in patients who did not develop mesenteric traction syndrome but received flurbiprofen axetil prophylactically (29).

The results of the present study align with these findings, indicating that the perioperative use of flurbiprofen axetil is associated with an increased risk of intestinal complications following radical colorectal surgery. Flurbiprofen axetil may impair the intestinal healing process by suppressing COX-2 expression, thereby increasing the risk of intestinal complications. Another proposed mechanism is that NSAID treatment may reduce collagen production and impair angiogenesis, further contributing to these complications (30). However, with regard to its safety in patients, particularly in those undergoing gastrointestinal surgery, studies have demonstrated differential results. A retrospective cohort study investigated the short-term postoperative use of flurbiprofen in patients undergoing elective gastrointestinal surgery for cancer resection. The study found no significant increase in AL rates among patients who received flurbiprofen compared with that in patients who did not (1.62% vs. 1.46%; P=0.70) (31). However, only postoperative use was included in the study, and flurbiprofen axetil is often used intraoperatively, when patients have not yet left the operating room. Moreover, AL is not the only related complication that raises concern.

Furthermore, the present study suggests that older patients, a prolonged surgical duration and the increased use of opioids during the surgery may lead to an increased risk of developing intestinal complications following colorectal surgery. These observations are consistent with the findings of previous studies (32,33). An advanced age has long been recognized as an independent risk factor for postoperative complications across various surgical procedures. Elderly patients typically present with more preoperative comorbidities, decreased physiological resilience to anesthesia and surgical stress, and slower postoperative recovery compared with younger

Table III. Univariate and multivariate analysis of intestinal complications.

Patient data	Intestinal complications (n=89)	No complications (n=1,275)	Univariate P-value	Multivariate analysis			
				OR	95% CI Lower	95% CI Upper	P-value
Patient characteristics							
Age, years[a]	69 (64-76)	66 (57-74)	0.030	1.022	1.002	1.042	0.028
Males, n (%)	62 (69.7)	742 (58.2)	0.033	1.513	0.941	2.435	0.088
BMI, n (%)			0.733				
>28 kg/m^2	9 (10.1)	144 (11.3)					
≤28 kg/m^2	80 (89.9)	1,131 (88.7)					
ASA, n (%)			0.796				
Grade III	24 (27.0)	328 (25.7)					
Less than grade III	65 (73.0)	947 (74.3)					
Previous history, n (%)							
Hypertension	35 (39.3)	518 (40.6)	0.809				
Diabetes	18 (20.2)	257 (20.2)	0.988				
Coronary heart disease	8 (9.0)	147 (11.5)	0.465				
Chronic lung disease	2 (2.2)	20 (1.6)	0.955				
Two or more comorbidities	15 (16.9)	231 (18.1)	0.764				
Albumin[a]	39.1 (36.4-41.8)	39.2 (36.7-41.5)	0.776				
Hb <80 g/l	0 (0.0)	36 (2.8)	0.206				
Na^{+}[a]	141.4 (139.2-142.8)	141.4 (139.7-143)	0.689				
Preoperative medication, n (%)							
Antiplatelet or anticoagulant therapy	11 (12.4)	162 (12.7)	0.924				
Chemotherapy	18 (20.2)	184 (14.4)	0.137				
ACEIs/ARBs	14 (15.7)	177 (13.9)	0.627				
Statins	13 (14.6)	143 (11.2)	0.331				
Other anti-hypertensive drugs	29 (32.6)	397 (31.1)	0.776				
Diuretics	4 (4.5)	36 (2.8)	0.563				
Steroid hormones	13 (14.6)	95 (7.5)	0.016	1.888	1.000	3.565	0.050
Surgery and anesthesia, n (%)							
Perioperative use of flurbiprofen axetil	21 (23.6)	172 (13.5)	0.008	2.072	1.223	3.508	0.007
Duration			0.003	2.032	1.181	3.496	0.010
>3 h	71 (79.8)						
≤3 h	18 (20.2)	455 (35.7)					
Surgical method			0.829				
Laparoscopy	73 (82.0)	1,034 (81.1)					
Open abdomen	16 (18.0)	241 (18.9)					
Intraoperative use of vasopressors	69 (77.5)	854 (67.0)	0.040	1.534	0.907	2.594	0.111
Intraoperative blood transfusion	5 (5.6)	102 (8.0)	0.419				
Intraoperative fluid infusion volume[a]	2.6 (2.3-3.1)	2.6 (2.1-3.1)	0.905				
Intraoperative blood loss			0.657				
<100 ml	54 (60.7)	743 (58.3)					
≥100 ml	35 (39.3)	532 (41.7)					
Use regional block during operation	8 (9.0)	195 (15.3)	0.106				
Postoperative return			0.764				
The ward	68 (76.4)	956 (75.0)					
ICU	21 (23.6)	319 (25.0)					

Table III. Continued..

Patient data	Intestinal complications (n=89)	No complications (n=1,275)	Univariate P-value	Multivariate analysis			
				OR	95% CI Lower	95% CI Upper	P-value
Surgery and anesthesia, n (%)							
Lymph node metastasis	21 (23.6)	386 (30.3)	0.183				
Tumor emboli in blood vessels	17 (19.1)	218 (17.1)	0.629				
Maximum diameter of tumor			0.328				
<5 cm	62 (69.7)	823 (64.5)					
≥5 cm	27 (30.3)	452 (35.5)					
Intraoperative opioid consumption	40 (30-50)	35 (30-45)	0.038	1.012	1.003	1.022	0.009

[a]Median (25th percentile-75th percentile). BMI, body mass index; ASA, American Society of Anesthesiologists; ICU, intensive care unit; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin-receptor blocker.

individuals. As a result, they are more susceptible to postoperative complications, often related to underlying health conditions or infections (34). In the present study, the findings suggest that advanced age may contribute to the risk of postoperative intestinal complications. This may possibly be due to impaired baseline bowel function and delayed gastrointestinal recovery in older patients.

In addition to age, a prolonged surgical duration (>3 h) and excessive perioperative opioid use were also identified as significant contributors to postoperative intestinal complications. Unlike NSAIDs, whose administration generally follows a standardized protocol, opioid consumption tends to increase with the length and complexity of surgery. Notably, collinearity diagnostics indicated no significant multicollinearity between operative time and opioid use, suggesting these variables likely exert independent effects or interact with distinct confounding factors. Therefore, the multivariate analysis performed herein incorporated a comprehensive set of covariates to improve the robustness and interpretability of the model.

Surgical duration plays a crucial role in determining postoperative outcomes. Even with intraoperative fluid management, extended operative times often indicate greater surgical complexity and are associated with increased fluid loss, more extensive tissue trauma and slower postoperative recovery (35). At the same time, opioid use contributes to gastrointestinal side-effects, such as nausea and vomiting, and inhibits bowel motility, thereby delaying the return of normal gastrointestinal function (36).

It is important to acknowledge the potential limitations of the present single-center study. Although real-world data were used to explore the association between flurbiprofen axetil and intestinal complications, the design of the study may introduce certain biases. Flurbiprofen axetil was the only NSAID included in the present study, and it was administered intraoperatively or postoperatively in single or intermittent doses ranging from 50 to 100 mg. The lack of a standardized dosage regimen for all patients complicates the interpretation of whether dosage directly affects the incidence or severity of postoperative complications. Therefore, further research is required to provide more robust evidence on the association between NSAIDs and intestinal complications.

In conclusion, the present study demonstrates that the perioperative use of flurbiprofen axetil may increase the risk of developing postoperative intestinal complications in patients undergoing radical colorectal resection. Further studies are warranted in order to establish standardized protocols for the use of NSAIDs in this patient population to minimize these risks.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

YF and XT were responsible for the overall content as the guarantors. YF proposed the research conception and designed the study. WD drafted the manuscript and collected the data. XT performed the data analysis and revised the manuscript. KS contributed to the diagnosis of the complications described in the study. WR provided advice on the study design and statistical analysis. All authors have read and approved the final manuscript. WD and XT confirm the authenticity of all the raw data.

Ethics approval and consent to participate

The present study was approved by the Medical Ethics Committee of Peking University People's Hospital (Beijing, China; approval no. 2022PHB131-001). All methods were performed according to the relevant guidelines and regulations.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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